ISSN 2218-5836 (online)

World Journal of *Orthopedics*

World J Orthop 2019 October 18; 10(10): 348-377

Published by Baishideng Publishing Group Inc

World Journal of Orthopedics

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Monthly Volume 10 Number 10 October 18, 2019

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World Journal of Orthopedics

Volume 10 Number 10 October 18, 2019

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INDEXING/ABSTRACTING

The *WJO* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Scopus, China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (CSTJ), and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Responsible Electronic Editor: *Mei-Yi Liu*

Proofing Production Department Director: *Xiang Li*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
ISSN 2218-5836 (online)

LAUNCH DATE
November 18, 2010

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Bao-Gan Peng

EDITORIAL BOARD MEMBERS
http://www.wjgnet.com/2218-5836/editorialboard.htm

EDITORIAL OFFICE
Ruo-Yu Ma, Director

PUBLICATION DATE
October 18, 2019

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
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ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Orthopedics

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World J Orthop 2019 October 18; 10(10): 348-355

DOI: 10.5312/wjo.v10.i10.348

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Retrospective Cohort Study

Two-stage revision arthroplasty for coagulase-negative staphylococcal periprosthetic joint infection of the hip and knee

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Author contributions: Veltman ES, Moojen DJF, van Ogtrop ML, and Poolman RW designed the study; Veltman ES performed extraction, synthesis, and interpretation of data; Veltman ES, Moojen DJF, van Ogtrop ML, and Poolman RW drafted and/or revised the manuscript.

Informed consent statement: This study was exempt from acquiring written informed consent by the OLVG medical ethics committee, with study number 15.080.

Conflict-of-interest statement: All authors have no conflicts of interest related to the manuscript.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised accordingly.

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Abstract

BACKGROUND

Periprosthetic joint infections (PJIs) are frequently caused by coagulase-negative Staphylococci (CoNS), which is known to be a hard-to-treat microorganism. Antibiotic resistance among causative pathogens of PJI is increasing. Two-stage revision is the favoured treatment for chronic CoNS infection of a hip or knee prosthesis. We hypothesised that the infection eradication rate of our treatment protocol for two-stage revision surgery for CoNS PJI of the hip and knee would be comparable to eradication rates described in the literature.

AIM

To evaluate the infection eradication rate of two-stage revision arthroplasty for PJI caused by CoNS.

METHODS

All patients treated with two-stage revision of a hip or knee prosthesis were retrospectively included. Patients with CoNS infection were included in the study, including polymicrobial cases. Primary outcome was infection eradication at final follow-up.

RESULTS

Forty-four patients were included in the study. Twenty-nine patients were treated for PJI of the hip and fifteen for PJI of the knee. At final follow-up after a mean of 37 mo, recurrent or persistent infection was present in eleven patients.

CONCLUSION

PJI with CoNS can be a difficult to treat infection due to increasing antibiotic

Manuscript source: Invited manuscript

Received: May 20, 2019
Peer-review started: May 20, 2019
First decision: July 31, 2019
Revised: August 14, 2019
Accepted: September 4, 2019
Article in press: September 4, 2019
Published online: October 18, 2019

P-Reviewer: DeSousa K, Peng BG, Widmer KH
S-Editor: Yan JP
L-Editor: Filipodia
E-Editor: Liu MY

resistance. Infection eradication rate of 70%-80% may be achieved.

Key words: Periprosthetic joint infection; Two-stage revision; Knee arthroplasty; Hip arthroplasty; Coagulase-negative Staphylococcus

Core tip: Periprosthetic joint infections of the hip and knee caused by coagulase-negative Staphylococci can be difficult to treat. We retrospectively reviewed all patients treated with two-stage revision arthroplasty for such an infection in our hospital between 2003 and 2016. We treated 44 patients with coagulase-negative Staphylococci infection of the hip or knee with a two-stage revision using an antibiotic-loaded spacer. At final follow-up, infection was eradicated in 33 of these patients.

Citation: Veltman ES, Moojen DJF, van Ogtrop ML, Poolman RW. Two-stage revision arthroplasty for coagulase-negative staphylococcal periprosthetic joint infection of the hip and knee. *World J Orthop* 2019; 10(10): 348-355
URL: https://www.wjgnet.com/2218-5836/full/v10/i10/348.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i10.348

INTRODUCTION

Coagulase-negative staphylococci (CoNS) are a hard-to-treat group of microorganisms in relation to implanted foreign materials, due to a high rate of methicillin resistance and biofilm formation[1]. In recent years, the incidence of infections with CoNS has increased[2,3]. Periprosthetic joint infection (PJI) is a devastating complication after hip and knee arthroplasty that occurs in 1%-2% of patients[4]. When infection persists despite debridement procedures or when infection is diagnosed more than 3 mo postoperatively, it is considered a chronic infection[5]. In case of chronic PJI, removal of the prosthesis is usually indicated[6]. Two-stage revision arthroplasty with the use of an antibiotic-loaded spacer is the gold standard treatment in case of persistent or chronic infection[7,8].

The type of spacer used during two-stage revision does not influence the infection eradication rate[9,10]. In contrast, characteristics of the causative microorganism do influence the chance of infection eradication after two-stage revision[11]. Resistance to commonly prescribed antibiotics is an increasing problem as well[11]. Bacteria such as CoNS can form a biofilm on the prosthesis that prevents elimination by host defences and antimicrobial therapy[1,12]. In orthopaedic revision arthroplasty, the rate of resistance to antibiotics by CoNS is increasing[13]. The effects of infection exclusively by CoNS on the outcome after two-stage revision arthroplasty have not yet been described. The objective of this study was to evaluate infection eradication rate after two-stage revision arthroplasty of the hip and knee in patients with CoNS PJI.

MATERIALS AND METHODS

Patients

We used the STROBE cohort checklist when writing our report[14]. This study was approved by the local medical ethics committee. After approval, we retrospectively reviewed the records of all patients who had two-stage revision arthroplasty of the hip or knee in our hospital between 2003 and 2016. We included all patients with CoNS PJI of the hip or knee in the study. Exclusion criteria were monomicrobial infection with bacteria other than CoNS and patients receiving one-stage revision. Patients with polymicrobial infection, in whom CoNS was one of the infecting organisms, were included in the study. In all patients, diagnosis of infection was affirmed according to the Musculoskeletal Infection Society criteria. Joint aspirations were routinely performed preoperatively and were positive in all patients.

First-stage surgery

During first-stage surgery, we removed the infected prosthesis including all bone cement (when present). Multiple tissue samples were taken for culture, after which

we administered cefuroxime antibiotic prophylaxis. We did not perform sonication of the removed prosthesis. After meticulous debridement, we implanted an antibiotic-loaded interval spacer with gentamicin and vancomycin. In patients with an infected total hip arthroplasty, we used either a functional articulating spacer or a prefabricated cement spacer (Figure 1A and B)[10]. Functional articulating spacers consist of (parts of) regularly used hip arthroplasty components combined with antibiotic-impregnated cement. Prefabricated cement spacers are commercially available in different head sizes and two different lengths. In patients with infected total knee arthroplasty we used either static spacers or dynamic spacers (Figure 1C and D)[15]. Static spacers are blocks of antibiotic-loaded cement that are moulded by hand intra-operatively. Patients were not allowed to bear weight on the static spacer and performing range of motion exercises was not possible. The dynamic spacers were either prefabricated cement blocks, or cement moulded by hand in the shape of a knee prosthesis.

We treated patients with antibiotics according to the recommendations as published by Zimmerli *et al*[4]. Patients received intravenous antibiotics for at least 2 wk based on the antibiogram of the cultured bacteria. Whenever possible, after 2 wk, we switched antibiotics to an oral substitute for an additional 4-wk minimum. The exact antibiotic treatment was determined in close consultation with a microbiologist and an infectious disease specialist. At 2 wk before the second-stage procedure, we discontinued antibiotics to achieve a 2-wk antibiotic free interval.

Second-stage surgery

During second-stage surgery, we extracted the antibiotic-loaded spacer. Again, we took multiple tissue samples for culture, after which we administered antibiotic prophylaxis. We adjusted the postoperative antibiotic prophylaxis for the antibiogram of the bacteria cultured after the first-stage procedure. We performed another thorough debridement, after which we implanted a revision prosthesis. Postoperatively, patients received intravenous cefuroxime until culture results were available after 2 wk. When culture results were negative, we ceased antibiotics and patients were discharged. In case cultures were still positive, we continued antibiotics for a total of 12 wk.

We retrieved general patient characteristics, preoperative and postoperative laboratory results, complications during treatment, and final outcomes from patients' records. Primary outcome was infection eradication after second-stage procedure, which was defined as the absence of clinical, radiological, or laboratory signs of infection at the latest follow-up, with a minimum of 1 year after second-stage surgery. Secondary outcomes were complications registered during the spacer period and at final follow-up.

Statistical analyses

Failure of treatment was defined as persistent or repeated infection after second-stage procedure, making it necessary to perform another revision, resection arthroplasty, arthrodesis, or amputation of the limb or use of suppressive antibiotics at final follow-up[16]. We used descriptive statistics, mean, and range to represent the demographics of the patients. Excel and SPSS software were used to perform calculations and statistical analyses. We analysed patients with two-stage revision of hip or knee as one group, and divided them into groups according to the joint treated and the interval spacer used.

RESULTS

Patient characteristics and general outcomes

Between 2003 and 2016 we treated 44 patients with CoNS PJI of a total hip or total knee prosthesis with two-stage revision arthroplasty using an antibiotic-loaded interval spacer. General patient characteristics can be found in Table 1. Polymicrobial infection was present in six patients. CoNS were sensitive to flucloxacillin or clindamycin in 19 patients. Due to antibiotic resistance to flucloxacillin and clindamycin, we treated 23 patients with vancomycin. We treated 2 patients with linezolid for 4 wk.

Laboratory results showed a mean C-reactive protein (CRP) level of 58 mg/L (range, 2-195) before first-stage surgery. During the spacer interval, the CRP gradually decreased to a mean 17 mg/L (range, 2-186) before second-stage surgery. At final follow-up, the CRP normalised at a mean 8 mg/L (range, 1-28). The leukocyte count remained within normal limits before first- and second-stage surgery and at final follow-up.

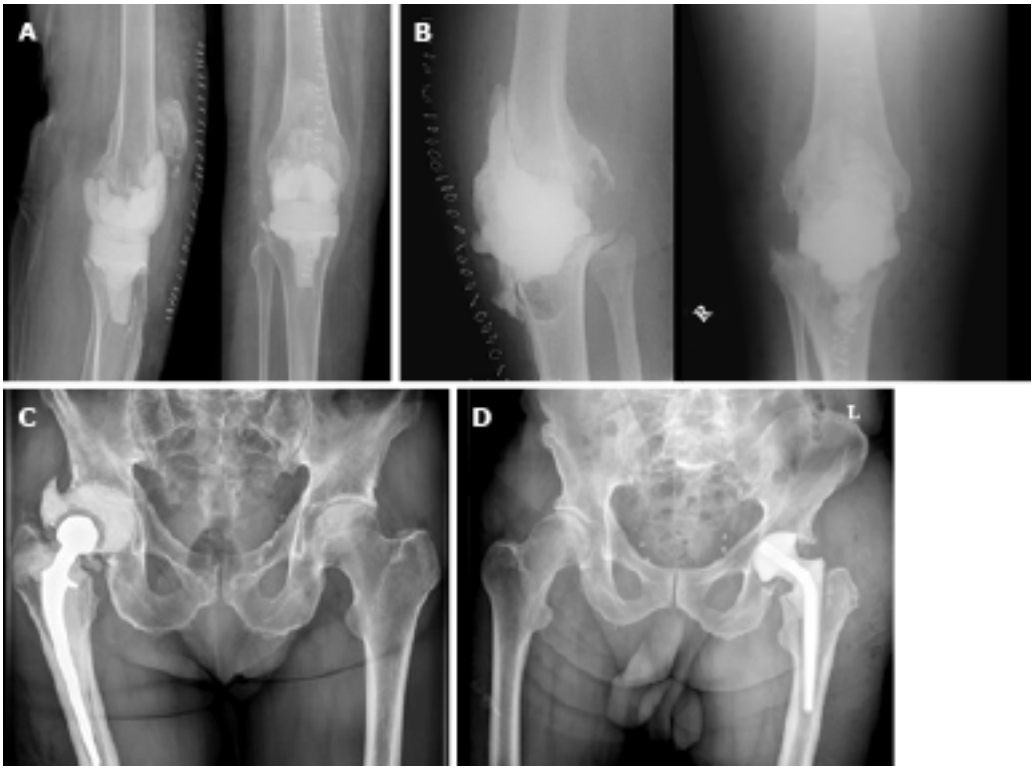

Figure 1 Types of antibiotic-loaded spacers of the hip and knee. A: Dynamic knee spacer; B: Static knee spacer; C: Functional articulating hip spacer; D: Prefabricated hip spacer.

At the time of final follow-up, three patients had died due to reasons unrelated to treatment. The mean follow-up period was 37 mo (range, 12-119 mo; median 31 mo). Recurrent infection was present in 11 patients (7 hips and 4 knees), of whom 4 had persistent infection with CoNS; the others had re-infection with other bacteria. In addition to the patients with persistent infection, we considered 2 more patients failure of treatment.

Two-stage revision total hip arthroplasty

We treated 29 patients with two-stage revision arthroplasty of an infected total hip prosthesis, for which we used 8 functional articulating spacers and 21 prefabricated spacers (Table 1). Polymicrobial infection was present in four patients. Additional causative microorganisms were *Propionibacterum acnes* in one patient, *Pseudomonas aeruginosa* in one patient, *P. aeruginosa* and *Enterococcus faecalis* in one patient, and haemolytic *Streptococci* group C in one patient. The other 25 patients had monomicrobial infection with CoNS.

The spacer interval was complicated by dislocation of the spacer in 4 of 21 patients with a prefabricated spacer, and in 1 of 8 patients with a functional articulating spacer. We performed spacer revision because of dislocation in two patients with a prefabricated spacer. Closed reduction was performed in the other two patients with a prefabricated spacer and the patient with a functional articulating spacer. Because of persistent wound effusion, we performed spacer revision within 2 wk after first-stage surgery in four patients with a prefabricated spacer. No spacer exchanges were performed after more than 2 wk.

Second-stage surgery was performed at a median of 8 wk (range, 2-15 wk) after the first-stage procedure. During revision surgery, an uncemented modular femoral revision stem was used in 17 patients and a dual mobility cup was used in 8 patients. All other components used were primary cemented or uncemented stems and cups (head diameter, 32 mm). Postoperatively, 12 patients received antibiotic treatment during the first 2 wk until culture results were negative. Four patients received antibiotic treatment for 6 wk, five patients received antibiotics for 12 wk, and one patient received antibiotics for 26 wk. Patients who had resection arthroplasty of the hip received antibiotics during 6 wk in four cases and during 12 wk in the other patient. Two patients received lifelong suppressive antibiotic therapy: The first due to persistent CoNS infection and the latter due to re-infection with another bacteria.

At final follow-up, we treated 22 patients successfully and considered 7 patients as failures after a mean follow-up of 42 mo (range, 12-119; median, 31 mo). Of the seven

Table 1 General patient characteristics

	Hip	Knee	Total
Number of patients	29	15	44
Mean age	66	64	66
Gender, female	15	11	26
Mean BMI	27	30	28
BMI > 30, patients	8	9	17
Indication for primary prosthesis			
Osteoarthritis	19	15	34
Posttraumatic	10	0	10
Comorbidity			
Immune suppression	3	2	5
Previous PJI	2	5	7
Diabetes mellitus	5	3	8
Obesity, BMI > 30	8	9	17
Active smoking	7	4	11
ASA 1/2/3	1/18/10	1/11/3	2/29/13

BMI: Body mass index; PJI: Periprosthetic joint infection; ASA: American Society of Anaesthesiologist score.

patients considered failure of treatment, six were treated with a prefabricated spacer. Due to persistent infection, we eventually accepted a Girdlestone situation in five patients. Two patients received lifelong suppressive antibiotics.

Two-stage revision total knee arthroplasty

We treated 15 patients with two-stage revision arthroplasty of an infected knee prosthesis, using 4 static and 11 dynamic spacers (Table 1). Polymicrobial infection was present in two patients. The additional causative microorganisms were *E. cloacae* in one patient and *E. faecalis* in one patient. The other 13 patients had a monomicrobial infection with CoNS. Spacer interval was complicated by spacer exchange because of persistent wound effusion in two patients with a static spacer. In one patient with a dynamic spacer, a quadriceps tendon rupture occurred peroperatively.

Second-stage surgery was performed at a median of 8 wk (range, 4-27 wk) after the first-stage procedure. During second-stage surgery, a hinged type prosthesis was implanted in 11 patients, a constrained prosthesis in 2 patients, and a primary prosthesis in 2 patients. All knee prostheses were cemented. Postoperatively, eight patients received antibiotic treatment during the first 2 wk until culture results were negative. Two patients received antibiotic treatment for 6 wk, two received antibiotics for 12 wk, and one received antibiotics for 26 wk. Two patients received lifelong suppressive antibiotic therapy, both due to persistent CoNS infection.

At final follow-up, we treated nine patients successfully and considered six patients as failures after a mean follow-up of 28 mo (range, 12-59; median 31 mo). Due to persistent infection of the knee, two patients treated with a static spacer underwent further surgical procedures. We performed a second two-stage revision procedure, which eradicated the infection in one patient and an arthrodesis of the knee in the other patient. Two patients treated with a dynamic spacer received lifelong suppressive antibiotics. We performed an above the knee amputation because of persistent pain in one patient, who was treated with a static spacer and arthrodesis of the knee because of insufficiency of the extension mechanism in one patient who was treated with a dynamic spacer. The latter two patients had no demonstrable infection during second-stage revision, but were considered to have failed treatment.

DISCUSSION

This study retrospectively evaluated the infection eradication rate after two-stage revision arthroplasty with the use of an antibiotic-loaded interval spacer of PJI of the hip and knee caused by CoNS. At final follow-up, infection was eradicated in 33 of 44 cases; however we considered 2 more cases as failure of treatment. Poor rates of infection eradication have been reported in cases with polymicrobial infection of the hip or knee[17]. In our series of six patients with polymicrobial infection, one patient

failed treatment. Existence of polymicrobial infection did not seem to influence chance of infection eradication negatively; however, the number of polymicrobial infections was too small to draw definite conclusions.

The infection eradication rate was comparable for two-stage revision of the hip (22 of 29) and the knee (11 of 15). The incidence of obesity (body mass index over 30) was higher in the knee group compared to the hip group (8 of 29 *vs* 9 of 15 patients). Obesity is a known risk factor for PJI[18-20]. In this series of patients, obesity was not related to a higher risk of persistent infection after two-stage revision arthroplasty of the hip or knee. Recurrence of infection after two-stage revision arthroplasty was also not related to gender, age, smoking status, ASA-classification, or time interval between the first- and second-stage procedure. Functional articulating spacers of the hip and dynamic spacers of the knee seem to lead to lower risk of failure; however the sample size of our study was too small to draw definite conclusions.

One-third of patients (10 of 29 patients) in the group of two-stage revisions of the hip received a primary hip prosthesis due to a proximal femoral fracture. In the other patients, the primary procedure was performed due to osteoarthritis of the hip. In the Netherlands, annually 4% of total hip arthroplasties are implanted because of a femoral neck fracture[21]. This suggests that the risk of infection is higher in patients receiving total hip arthroplasty after a femoral neck fracture. Physicians need to be aware of the increased risk of infection when providing information about hip arthroplasty to patients with hip fractures. Efforts should be made to optimally prepare the patient preoperatively. Treatment of comorbidities causing trauma, the timing and duration of surgery, perioperative antibiotic prophylaxis, and soft tissue management may all influence the chance of periprosthetic infection after total hip prosthesis for a proximal femur fracture. Infection eradication rate after two-stage revision hip arthroplasty was similar in trauma and elective patients (7 of 10 patients *vs* 14 of 19 patients, respectively, without infection at follow-up).

A limitation of this study is reflected by the retrospective design. The number of patients included in this study was relatively low, which was caused by the scarcity of PJI requiring two-stage revision and the fact that in this study we only focused on CoNS infections. Treatment of patients treated before 2007 was more heterogeneous compared to patients treated after 2007 due to the implementation of stricter perioperative protocols concerning treatment of infected prostheses.

Current literature lacks high-quality studies determining optimal treatment strategy in case of specific causative microorganisms such as CoNS in PJI of the hip and knee. As prospective studies of PJIs are hard to perform due to the scarcity of prosthetic infections, a retrospective multicentre study combining groups of patients to achieve a greater number of patients with CoNS PJI can provide more evidence on how to treat this specific infection. Orthopaedic surgeons should consider treating their patients with a functional articulating spacer of the hip or a dynamic spacer of the knee, as these may improve infection eradication rate. Whether or not functional outcome after two-stage revision with a functional articulating spacer of the hip or a dynamic spacer of the knee is improved compared to their more static counterparts has yet to be studied.

Due to biofilm formation CoNS can be a difficult to treat organism in PJI. The results of this study show that infection eradication rate comparable to that of other causative pathogens may be achieved following two-stage revision arthroplasty of the hip and knee[22-24].

ARTICLE HIGHLIGHTS

Research background

Coagulase-negative Staphylococci (CoNS) are difficult-to-treat microorganisms in periprosthetic joint infections (PJIs) of the hip and knee. The resistance of these bacteria to antibiotics is increasing.

Research motivation

To date, no infection eradication rates of treatment for this type of specific infection have been reported.

Research objectives

To evaluate the infection eradication rate of two-stage revision arthroplasty for CoNS PJI of the hip and knee.

Research methods

Retrospective cohort study of all patients treated with two-stage revision for CoNS PJI of a hip or knee prosthesis.

Research results
In 33 of 44 patients, the infections were eradicated at a mean of 37 mo after two-stage revision surgery of the hip and knee.

Research conclusions
Two-stage revision surgery of the hip and knee for PJI infections with CoNS leads to infection eradication rate comparable to other causative pathogens.

Research perspectives
Two-stage revision yields an acceptable infection eradication rate for treatment of CoNS infection of the hip and knee. Future studies should consider combining cohorts of patients from multiple centres to achieve larger cohorts of patients.

ACKNOWLEDGEMENTS

The authors acknowledge Eduard L.A.R. Mutsaerts and S. John Ham for their efforts in treating the patients included in this study.

REFERENCES

1 **Becker K**, Heilmann C, Peters G. Coagulase-negative staphylococci. *Clin Microbiol Rev* 2014; **27**: 870-926 [PMID: 25278577 DOI: 10.1128/CMR.00109-13]
2 **Murgier J**, Laffosse JM, Cailliez J, Cavaignac E, Murgier P, Bayle-Iniguez X, Chiron P, Bonnevialle P. Is the prognosis the same for periprosthetic joint infections due to Staphylococcus aureus versus coagulase-negative staphylococci? A retrospective study of 101 patients with 2-year minimum follow-up. *Arch Orthop Trauma Surg* 2016; **136**: 1357-1361 [PMID: 27481366 DOI: 10.1007/s00402-016-2533-6]
3 **Mühlhofer HML**, Deiss L, Mayer-Kuckuk P, Pohlig F, Harrasser N, Lenze U, Gollwitzer H, Suren C, Prodinger P, VON Eisenhart-Rothe R, Schauwecker J. Increased Resistance of Skin Flora to Antimicrobial Prophylaxis in Patients Undergoing Hip Revision Arthroplasty. *In Vivo* 2017; **31**: 673-676 [PMID: 28652437 DOI: 10.21873/invivo.11111]
4 **Zimmerli W**, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med* 2004; **351**: 1645-1654 [PMID: 15483283 DOI: 10.1056/NEJMra040181]
5 **Parvizi J**, Gehrke T. International consensus on periprosthetic joint infection: Let cumulative wisdom be a guide. *J Bone Joint Surg Am* 2014; **96**: 441 [PMID: 24647498 DOI: 10.2106/JBJS.N.00023]
6 **Lichstein P**, Gehrke T, Lombardi A, Romano C, Stockley I, Babis G, Bialecki J, Bucsi L, Cai X, Cao L, de Beaubien B, Erhardt J, Goodman S, Jiranek W, Keogh P, Lewallen D, Manner P, Marczynski W, Mason JB, Mulhall K, Paprosky W, Patel P, Piccaluga F, Polkowski G, Pulido L, Stockley I, Suarez J, Thorey F, Tikhilov R, Velazquez JD, Winkler H. One-stage versus two-stage exchange. *J Orthop Res* 2014; **32** Suppl 1: S141-S146 [PMID: 24464888 DOI: 10.1002/jor.22558]
7 **Gehrke T**, Alijanipour P, Parvizi J. The management of an infected total knee arthroplasty. *Bone Joint J* 2015; **97-B**: 20-29 [PMID: 26430083 DOI: 10.1302/0301-620X.97B10.36475]
8 **Citak M**, Argenson JN, Masri B, Kendoff D, Springer B, Alt V, Baldini A, Cui Q, Deirmengian GK, Del Sel H, Harrer MF, Israelite CL, Jahoda D, Jutte PC, Levicoff E, Meani E, Motta F, Pena OR, Ranawat AS, Safir O, Squire MW, Taunton MJ, Vogely CH, Wellman SS. Spacers. *J Arthroplasty* 2014; **29**: 93-99 [PMID: 24342279 DOI: 10.1016/j.arth.2013.09.042]
9 **Romanò CL**, Gala L, Logoluso N, Romanò D, Drago L. Two-stage revision of septic knee prosthesis with articulating knee spacers yields better infection eradication rate than one-stage or two-stage revision with static spacers. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 2445-2453 [PMID: 22270671 DOI: 10.1007/s00167-012-1885-x]
10 **Veltman ES**, Moojen DJ, Glehr M, Poolman RW. Similar rate of infection eradication for functional articulating, prefabricated and custom-made spacers in 2-stage revision of the infected total hip: A literature review. *Hip Int* 2016; **26**: 319-326 [PMID: 27373276 DOI: 10.5301/hipint.5000400]
11 **Carijo JH**, Courtney PM, Goswami K, Groff H, Kendoff D, Matos J, Sandiford NA, Scheper H, Schmaltz CAS, Shubnyakov I, Tan TL, Wouthuyzen-Bakker M. Hip and Knee Section, Pathogen Factors: Proceedings of International Consensus on Orthopedic Infections. *J Arthroplasty* 2019; **34**: S381-S386 [PMID: 30343968 DOI: 10.1016/j.arth.2018.09.022]
12 **Mirza YH**, Tansey R, Sukeik M, Shaath M, Haddad FS. Biofilm and the Role of Antibiotics in the Treatment of Periprosthetic Hip and Knee Joint Infections. *Open Orthop J* 2016; **10**: 636-645 [PMID: 28484579 DOI: 10.2174/1874325001610010636]
13 **Malhas AM**, Lawton R, Reidy M, Nathwani D, Clift BA. Causative organisms in revision total hip & knee arthroplasty for infection: Increasing multi-antibiotic resistance in coagulase-negative Staphylococcus and the implications for antibiotic prophylaxis. *Surgeon* 2015; **13**: 250-255 [PMID: 24821264 DOI: 10.1016/j.surge.2014.04.002]
14 **von Elm E**, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *BMJ* 2007; **335**: 806-808 [PMID: 17947786 DOI: 10.1136/bmj.39335.541782.AD]
15 **Pivec R**, Naziri Q, Issa K, Banerjee S, Mont MA. Systematic review comparing static and articulating spacers used for revision of infected total knee arthroplasty. *J Arthroplasty* 2014; **29**: 553-7.e1 [PMID: 24011676 DOI: 10.1016/j.arth.2013.07.041]
16 **Diaz-Ledezma C**, Higuera CA, Parvizi J. Success after treatment of periprosthetic joint infection: A Delphi-based international multidisciplinary consensus. *Clin Orthop Relat Res* 2013; **471**: 2374-2382 [PMID: 23440616 DOI: 10.1007/s11999-013-2866-1]
17 **Tan TL**, Kheir MM, Tan DD, Parvizi J. Polymicrobial Periprosthetic Joint Infections: Outcome of Treatment and Identification of Risk Factors. *J Bone Joint Surg Am* 2016; **98**: 2082-2088 [PMID:

28002371 DOI: 10.2106/JBJS.15.01450]
18 **Werner BC**, Higgins MD, Pehlivan HC, Carothers JT, Browne JA. Super Obesity Is an Independent Risk Factor for Complications After Primary Total Hip Arthroplasty. *J Arthroplasty* 2017; **32**: 402-406 [PMID: 27612609 DOI: 10.1016/j.arth.2016.08.001]
19 **Wagner ER**, Kamath AF, Fruth KM, Harmsen WS, Berry DJ. Effect of Body Mass Index on Complications and Reoperations After Total Hip Arthroplasty. *J Bone Joint Surg Am* 2016; **98**: 169-179 [PMID: 26842406 DOI: 10.2106/JBJS.O.00430]
20 **Kunutsor SK**, Whitehouse MR, Blom AW, Board T, Kay P, Wroblewski BM, Zeller V, Chen SY, Hsieh PH, Masri BA, Herman A, Jenny JY, Schwarzkopf R, Whittaker JP, Burston B, Huang R, Restrepo C, Parvizi J, Rudelli S, Honda E, Uip DE, Bori G, Muñoz-Mahamud E, Darley E, Ribera A, Cañas E, Cabo J, Cordero-Ampuero J, Redó MLS, Strange S, Lenguerrand E, Gooberman-Hill R, Webb J, MacGowan A, Dieppe P, Wilson M, Beswick AD; Global Infection Orthopaedic Management Collaboration. One- and two-stage surgical revision of peri-prosthetic joint infection of the hip: A pooled individual participant data analysis of 44 cohort studies. *Eur J Epidemiol* 2018; **33**: 933-946 [PMID: 29623671 DOI: 10.1007/s10654-018-0377-9]
21 Nederlandse Orthopaedische Vereniging and Stichting LROI. LROI jaarrapportage 2014-Orthopedische Implantaten in Beeld, 2014. Available from: https://www.lroi.nl/base/downloads/lroi-jaarrapportage-2014.pdf
22 **Johnson AJ**, Zywiel MG, Jones LC, Delanois RE, Stroh DA, Mont MA. Reduced re-infection rates with postoperative oral antibiotics after two-stage revision hip arthroplasty. *BMC Musculoskelet Disord* 2013; **14**: 123 [PMID: 23560775 DOI: 10.1186/1471-2474-14-123]
23 **Lange J**, Troelsen A, Thomsen RW, Søballe K. Chronic infections in hip arthroplasties: Comparing risk of reinfection following one-stage and two-stage revision: A systematic review and meta-analysis. *Clin Epidemiol* 2012; **4**: 57-73 [PMID: 22500127 DOI: 10.2147/CLEP.S29025]
24 **Leung F**, Richards CJ, Garbuz DS, Masri BA, Duncan CP. Two-stage total hip arthroplasty: How often does it control methicillin-resistant infection? *Clin Orthop Relat Res* 2011; **469**: 1009-1015 [PMID: 21161741 DOI: 10.1007/s11999-010-1725-6]

World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2019 October 18; 10(10): 356-363

DOI: 10.5312/wjo.v10.i10.356

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Retrospective Study

Advanced septic arthritis of the shoulder treated by a two-stage arthroplasty

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Author contributions: Goetti P and Gallusser N designed the study and wrote the manuscript; Antoniadis A and Wernly D compiled the data and reviewed the literature; Vauclair F and Borens O critically reviewed the manuscript.

Institutional review board statement: The need for approval was waived by the institutional ethics committee of Lausanne University Hospital (CER-VD) for retrospective case series including 5 patients or less.

Informed consent statement: Patients were not required to give informed consent because the analysis used anonymous data that were obtained after each patient agreed to treatment by written informed consent.

Conflict-of-interest statement: The authors, their immediate family, and any research foundation with which they are affiliated did not receive any financial payments or other benefits from any commercial entity related to the subject of this article.

Data sharing statement: No additional data are available.

Open-Access: This article is an

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Abstract

BACKGROUND

The usual treatment of septic shoulder arthritis consists of arthroscopic or open lavage and debridement. However, in patients with advanced osteoarthritic changes and/or massive rotator cuff tendon tears, infection eradication can be challenging to achieve and the functional outcome is often not satisfying even after successful infection eradication. In such cases a two-stage approach with initial resection of the native infected articular surfaces, implantation of a cement spacer before final treatment with a total shoulder arthroplasty in a second stage is gaining popularity in recent years with the data in literature however being still limited.

AIM

To evaluate the results of a short interval two-stage arthroplasty approach for septic arthritis with concomitant advanced degenerative changes of the shoulder joint.

METHODS

We retrospectively included five consecutive patients over a five-year period and evaluated the therapeutic management and the clinical outcome assessed by disability of the arm, shoulder and hand (DASH) score and subjective shoulder value (SSV). All procedures were performed through a deltopectoral approach and consisted in a debridement and synovectomy, articular surface resection and insertion of a custom made antibiotic enriched cement spacer. Shoulder arthroplasty was performed in a second stage.

RESULTS

Mean age was 61 years (range, 47-70 years). Four patients had previous surgeries ahead of the septic arthritis. All patients had a surgical debridement ahead of the index procedure. Mean follow-up was 13 mo (range, 6-24 mo). Persistent

Manuscript source: Unsolicited manuscript

Received: April 3, 2019
Peer-review started: April 4, 2019
First decision: July 31, 2019
Revised: September 3, 2019
Accepted: September 15, 2019
Article in press: September 15, 2019
Published online: October 18, 2019

P-Reviewer: Zhai KF, Anand A, Peng BG
S-Editor: Tang JZ
L-Editor: A
E-Editor: Liu MY

microbiological infection was confirmed in all five cases at the time of the first stage of the procedure. The shoulder arthroplasties were performed 6 to 12 wk after insertion of the antibiotic-loaded spacer. There were two hemi and three reverse shoulder arthroplasties. Infection was successfully eradicated in all patients. The clinical outcome was satisfactory with a mean DASH score and SSV of 18.4 points and 70% respectively.

CONCLUSION
Short interval two-stage approach for septic shoulder arthritis is an effective treatment option. It should nonetheless be reserved for selected patients with advanced disease in which lavage and debridement have failed.

Key words: Septic arthritis; Shoulder; Arthroplasty; Spacer; Antibiotic; Enriched; Infection; Native joint

Core tip: Shoulder septic arthritis associated with advanced osteoarthritic changes and/or rotator cuff tendon tears is challenging to treat. The classic approach of lavage and debridement is burdened by a higher failure rate with insufficient eradication of the infection and unsatisfactory functional outcomes. A two-stage approach with initial resection of the articular surfaces, implantation of an antibiotic enriched cement spacer before final treatment with a total shoulder arthroplasty is an appealing therapeutic option. Our retrospective case-series of five patients reveals that this approach is effective to eradicate infection and provides a satisfactory clinical outcome.

Citation: Goetti P, Gallusser N, Antoniadis A, Wernly D, Vauclair F, Borens O. Advanced septic arthritis of the shoulder treated by a two-stage arthroplasty. *World J Orthop* 2019; 10(10): 356-363
URL: https://www.wjgnet.com/2218-5836/full/v10/i10/356.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i10.356

INTRODUCTION

The shoulder represents the third most common location for septic arthritis in adults[1]. Primary management consists of arthroscopic or open irrigation and debridement and is usually combined with local and systemic antibiotherapy to eradicate the infection. Even after successful elimination of bacteria, cartilage and bone destruction is the consequence of prolonged inflammatory arthritis mediated by pro-inflammatory cytokines[2-6]. Early, aggressive treatment is crucial in order to alleviate pain and restore optimal function[7].

When dealing however with a degenerative joint with advanced osteoarthritis, irreparable or massive rotator cuff tears or in presence of endocutaneous fistulas, this classic approach is burdened by a higher failure rate with insufficient eradication of the infection and unsatisfactory functional outcomes. A recent review on shoulder septic arthritis from 2018 reported a 28% revision rate (mean age of 63.9 years), and a 21% complication rate (mean age of 63.7 years) after primary debridement[1]. In the recent years, several authors reported promising results using a two-stage approach to arthroplasty in infected osteoarthritic knees[8,9]. The main advantage of this novel approach is that by treating the underlying bony pathology in terms of resecting the arthritic bone the chances of successful infection eradication are increased and at the same time it allows for adequate pain control and improvement of functional outcomes.

Unfortunately, the evidence in the literature regarding this treatment approach is limited and the outcome of patients with native advanced septic arthritis is merged in published cohorts of infected total shoulder arthroplasties[10-15]. The aim of this study was therefore to evaluate the results of a short interval two-stage arthroplasty approach for septic arthritis with concomitant advanced degenerative changes of the shoulder joint.

MATERIAL AND METHODS

Inclusion criteria and patient characteristics

We retrospectively reviewed our institutions database between January 2012 and December 2017. We included five consecutive patients treated by a two-stage arthroplasty for advanced shoulder septic arthritis. The mean age in our case-series was 61 years (range, 47-70 years). Four of the five patients had undergone previous surgeries on their shoulders (open reduction and plate osteosynthesis of the proximal humerus in 2 cases, arthroscopic rotator cuff repair in 2 cases), while one patient presented a primary septic arthritis (Table 1). Mean follow-up was 36.8 mo (range, 12-59 mo). Deep infection was documented in all five cases at the time of initial debridement. All patients had positive cultures from articular puncture and had their follow-up at our institution. There was no exclusion.

Surgical technique and perioperative care

A standard deltopectoral approach was used in all cases. An extensive debridement and synovectomy were performed taking care to remove any devitalized soft-tissue or bone. Similarly to revision arthroplasty due to infection, at least five tissue samples or more were collected for microbiology. With a low-pressure irrigation device, a minimum of nine-liter physiological solution was used to wash out the joint. Free-hand bone cuts were made taking care to remove any bone cysts or foreign bodies in the humeral head. The medullary canal was then opened and reamed to remove any sclerotic tissue. A custom-made cement spacer was molded intra-operatively and loaded with 4 g of Vancomycine and 1, 2 g of Tobramycine per bag of 40 g of Palacos® cement (containing 0.5 g of Gentamycine) (Figure 1). An intra-articular suction drain was placed through the subacromial space at time of closure. Patients were allowed to actively move the shoulder starting day one after surgery. A 2 wk parenteral antibiotherapy was administered according to preoperative and peroperative cultures and in conjunction with a musculoskeletal infectious disease consultant. The type of arthroplasty was adapted to each situation and was performed in a standard manner during a second stage procedure after a mean interval of 6 wk (range, 6-12 wk) (Figure 2).

Absence of persistent infection was based on normalized laboratory markers [C-reactive protein (CRP) and white blood cell counts] and absence of clinical signs of infections. An articular puncture was not performed before second stage, but the spacer and several deep tissue samples were collected for microbiology. Oral antibiotics were maintained for a 3 mo period beginning at the first-stage procedure.

Clinical evaluation and functional outcomes

Digital patient's files were screened for residual pain using the visual analogue scale, range of motion and post-operative complications (including hematoma, seroma, blood transfusion, deep venous thrombosis, and revision surgeries). Biologic outcome was based on dosage of the CRP and the X-rays at last follow-up were evaluated for signs of persistent infection (including osteolysis, bone apposition, and component loosening). Pain was assessed using the visual analogue scale. We further recorded shoulder range of motion (ROM), disability of the arm, shoulder, and hand (DASH) score and subjective shoulder value at last follow-up.

RESULTS

Perioperative complications

The mean intraoperative blood loss was 880 mL (range, 200-2000 mL) for first stage (debridement and spacer) and 717 mL (range, 218-1800) for the second stage (arthroplasty). The average operation duration, defined as the time past from incision to the end of suturing was 106 min (range, 67-132 min) for the first stage and 115 min (range, 60-174 min) for the second stage. One patient was required to stay in the intermediate care unit for 1 night postoperatively before being transferred to the surgical ward. None of the patients had to be transferred to the intensive care unit postoperatively.

Complication rate and revision

Several complications of glenohumeral septic arthritis could be noted before the first stage of our treatment. Patients number 3 and 4 had draining skin fistulas, patient number five had developed a septic thrombosis of the humeral vein. The shoulder prostheses were implanted 6 wk after the first stage in 4 cases and with an interval of 12 wk in one case. There were two hemi and three reverse shoulder arthroplasties. No

Table 1 Patients with advanced septic arthritis treated by a two-stage shoulder arthroplasty

Case	Gender	Age(yr)	Microbiology at thetime of debridement	Previous surgeries to the index procedure
1	Female	59	Streptococcus pyogenes	Open debridement
2	Male	69	Staphylococcus epidermidis	Arthroscopic rotator cuff repair (2 times), open debridement
3	Male	47	Cutibacterium acnes	Proximal humerus fracture plate osteosynthesis, open debridement (5 times)
4	Male	60	Cutibacterium acnes	Proximal humerus fracture plate osteosynthesis
5	Male	70	Streptococcus anginosus	Arthroscopic rotator cuff repair

intraoperative or postoperative complications were noted.

Functional outcomes

At final follow-up mean elevation in our series was 102 degrees (range, 70-130 degrees), external rotation was 25 degrees (range, 10-45 degrees). The mean subjective shoulder value was 70% (range, 40%-95%) and DASH score was 18.4 points (range, 7.5-40 points). Detailed results are presented in Table 2. Furthermore, none of them had clinical, biological or radiological signs of persistent infection at last follow-up and therefore considered cured from infection.

DISCUSSION

Septic arthritis of the glenohumeral joint is a relatively rare entity representing 3% to 15% of septic arthritis. It can nonetheless lead to major complications such as bone and cartilage destruction if treatment is delayed[7,16-18]. Early treatment is therefore mandatory to alleviate pain and restore optimal function. Open or arthroscopic irrigation and debridement associated with targeted intravenous antibiotic therapy is effective to eradicate the infection[1,18,19]. While arthroscopic procedure seems to lead to better forward flexion and less persistent postoperative pain than open surgery[1,7,20], the number of required procedures is higher and increases further with the severity of infection[21-23].

Functional results after arthroscopic irrigation and debridement are inferior for patients with delayed diagnosis or treatment, as for those with associated rotator cuff tears[22]. Several authors recently reported encouraging results using a two-stage approach to arthroplasty in osteoarthritic knees[8,9]. This treatment enables to address degenerative arthritis condition coexistent with septic arthritis and leads to successful infection control and better post-operative knee mobility. While this concept has been recently applied to the treatment of active primary glenohumeral arthritis, the current data in the literature are contradictory in terms of functional outcomes and patient satisfaction. Nonetheless, as summarized in Table 3 the available studies which deal with the topic of two-stage revision are focused on infected total shoulder arthroplasty. The results of patients with native advanced septic arthritis which are merged in theses cohorts, with no separate analysis provided for this specific subgroup. Further only in a small percentage of the patients in theses series a second-stage procedure with spacer removal and shoulder arthroplasty was performed[10-15]. The available data concerning functional and clinical outcomes is therefore limited to three cases reported by Magnan *et al*[15]. In their retrospective study, 3 patients were treated with a two-stage arthroplasty for primary septic arthritis with Constant shoulder score ranging 78-85 points and American shoulder and elbow society score ranging 20-22 points.

In our series, despite the short interval for re-implantation, none of the patient had clinical or radiological sign of persistent infection at last follow-up. In a systematic review, McFarland reported a mean interval of 6 mo (range, 2-18 mo) to re-implantation among the different series[24]. Several authors reported a substantial risk of persistent infection after two-stage prosthesis exchange in case of prosthetic shoulder infections with recurrence rates ranging from 0% to 40%[25-32]. Nonetheless, two retrospective series reported no recurrence of infection after shoulder prosthesis implantation following a resection arthroplasty[18,29].

In our patients we used a custom made stemmed antibiotic-impregnated polymethyl methacrylate spacer. This technique has the potential to minimize intraarticular scaring, diminish dead space and provide a high local antibiotic concentration[32]. A recent retrospective study reported no statistical difference between stemmed and stemless spacer in term of reinfection rate, operation time, complication rate, or functional outcome after reimplantation. However, in our

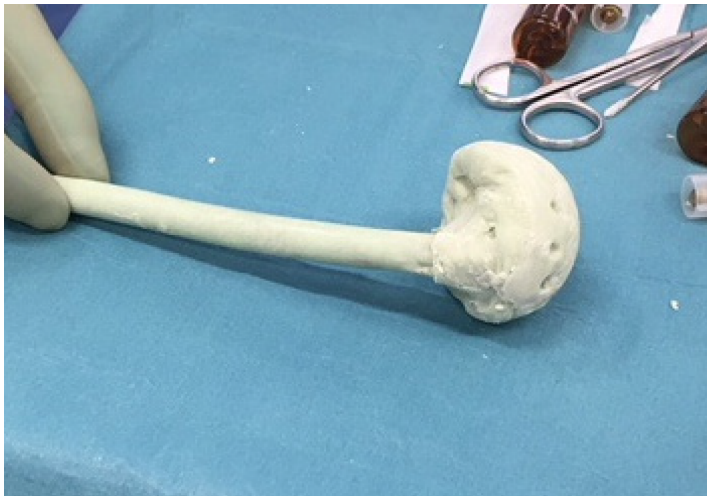

Figure 1 Custom made spacer of the shoulder joint.

institution we still favor the potential advantage of a well fitted custom-made stemmed spacer being aware of the fact that there is limited evidence for optimal treatment even in the setup of prosthetic shoulder infections[33,34]. Definitive treatment with antibiotic spacer has been shown to be a reliable option in low-demand patients. There is a potential risk of glenoid erosions that could put in jeopardy a future reimplantation[24,35]. This option should therfore be carefully discussed with the patient.

In our series, ROM and functional scores at final follow-up were satisfying taking into consideration that functional results are low in case of irrigation and debridement for septic arthritis of higher stages or with associated rotator cuff tear[21,36]. Jeon *et al*[22] reported, in a retrospective series, a University of California at Los Angeles score of 23.7 points in patients with rotator cuff tear, and 29.0 points in patients without rotator cuff tear. In a retrospective series, Sabesan *et al*[26] reported average forward flexion of 123 ± 33°, external rotation of 26 ± 8° and mean Penn score of 66.4 points in patients treated with a two-staged reverse shoulder arthroplasty. Other series showed postoperative forward elevation from 89° to 119° and external rotation from 19° to 43°[21-23,25]. Garofalo *et al*[18] retrospectively reviewed ten patients with late sequelae of septic arthritis of the glenohumeral joint with open joint debridement, humeral head resection, and implantation of an antibiotic spacer. Five of them underwent a delayed (4 to 6 mo) reverse shoulder arthroplasty. At last follow-up, they demonstrated a mean active elevation of 98° and abduction of 70° (range 90–55°). The mean constant score was 56 points. No intraoperative or postoperative complications were observed.

Although we had no complication to deplore in our small series, the complication rates of two-stage reimplantation of shoulder prosthesis is high and vary from 35% to 73% including persistent infection, dislocation, fracture, pulmonary embolism among others[26,27,30,31].

This study should be interpreted in light of its potential limitations, mostly inherent to the retrospective design. However, due to the standardized clinical and radiological follow-up protocol and the excellent documentation through the orthopedic surgeons of our institution, most of the patient data we needed were available for the current analysis. Furthermore, the small number of patients included in this study should be mentioned. However, the data in the literature are limited and consist mainly of small case-series or case-reports.

In conclusion, our results indicate that salvage surgery, as described in our study, is a valuable treatment option in septic arthritis of the shoulder. The rising number of shoulder procedures performed in aging population with inherent higher risk factors could potentially lead to a growing number of septic glenohumeral arthritis. Multicenter studies are necessary to achieve a higher case load and evidence regarding these rare indications. Short interval two-stage approach for septic glenohumeral arthritis is a valid alternative treatment option for patient with advanced degenerative condition and/or irreparable rotator cuff tears. In our opinion, it should be reserved for selected patients with higher stage of infection, who failed to heal with arthroscopic or open lavage and debridement.

Table 2 Information and data on patient outcome

Case	Spacer (wk)	HA/RTSA	Follow-up (mo)	VAS	Elevation	External rotation	CRP	DASH score	SSV
1	12	HA	59	0	90°	30°	1	9.2	95
2	6	RTSA	46	0	130°	20°	NA	10.8	90
3	6	HA	53	1	70°	15°	8	26.7	45
4	6	RTSA	14	1	100°	10°	5	40	40
5	6	RTSA	12	2	120°	45°	3	7.5	80

CRP: C-reactive protein; DASH: Disabilities of the arm, shoulder, and hand score; HA: Hemiarthroplasty; NA: None available; RTSA: Reverse total shoulder arthroplasty; SSV: Subjective shoulder value; VAS: Visual analog scale for pain.

Table 3 Review of the published data

Authors	Year of publication	Design	Native septic arthritis treated with cement spacer	Patients reimplanted	Mean interval	Mean follow-up
Themistocleous *et al*[11]	2007	Retrospective	7/11 2/11	2/11[1]	4 mo	22 mo (15-26 mo)
Hattrup *et al*[10]	2010	Retrospective	5/21	21/21	6.6 mo (Median: 3 mo)	49 mo (24-109 mo)
Stine *et al*[12]	2010	Retrospective	9/30	15/30[1]	3-4 mo	29 mo
Coffey *et al*[13]	2010	Retrospective	5/16	12/16[1]	3 mo (6-30 wk)	20.5 mo (12-30 mo)
Twiss *et al*[14]	2010	Retrospective	5/30	20/30[1]	9.3 wk (6-30 wk)	21.2 mo (12-40 mo)
Magnan *et al*[15]	2014	Retrospective	5/7	3/7	7 mo (6-8 mo)	40 mo

[1]The reimplantation is achieved after treatment of native or prosthetic joint infection without specified data.

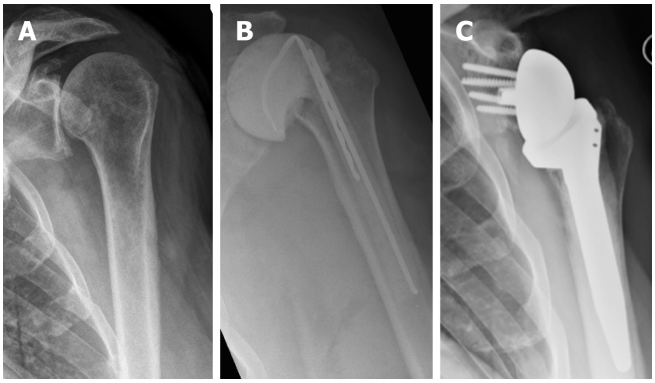

Figure 2 Illustration of case number 2: Anteroposterior radiographs of the left shoulder. A: Preoperative; B: After spacer insertion; C: After reverse shoulder arthroplasty.

ARTICLE HIGHLIGHTS

Research background

Septic arthritis of the glenohumeral joint is a relatively rare entity representing 3% to 15% of septic arthritis. It can nonetheless lead to major complications such as bone and cartilage destruction if treatment is delayed. Early treatment is therefore mandatory to alleviate pain and restore optimal function. Open or arthroscopic irrigation and debridement associated with targeted intravenous antibiotic therapy is effective to eradicate the infection. However, in patients with advanced osteoarthritic changes and/or massive rotator cuff tendon tears, infection eradication can be challenging to achieve and the functional outcome is often not satisfying even after successful infection eradication.

Research motivation

The motivation behind this study was to evaluate a two-stage approach with initial resection of

the native infected articular surfaces, implantation of a cement spacer before final treatment with a total shoulder arthroplasty in a second stage. While this treatment option is gaining popularity in recent years, the evidence in the literature remains limited.

Research objectives

The available studies which deal with the topic of two-stage revision are focused on infected total shoulder arthroplasty. The results of patients with native advanced septic arthritis which are merged in theses cohorts, with no separate analysis provided for this specific subgroup. The aim of our study was reported our results of a short interval two-stage arthroplasty approach for septic arthritis with concomitant advanced degenerative changes of the shoulder joint.

Research methods

We retrospectively included five consecutive patients over a five-year period and evaluated the therapeutic management and the clinical outcome assessed by disability of the arm, shoulder and hand (DASH) score and subjective shoulder value (SSV). All procedures were performed through a deltopectoral approach and consisted in a debridement and synovectomy, articular surface resection and insertion of a custom made antibiotic enriched cement spacer. Shoulder arthroplasty was performed in a second stage.

Research results

Mean age was 61 years (range, 47-70 years). Four patients had previous surgeries ahead of the septic arthritis. All patients had a surgical debridement ahead of the index procedure. Mean follow-up was 13 mo (range, 6-24 mo). Persistent microbiological infection was confirmed in all five cases at the time of the first stage of the procedure. The shoulder arthroplasties were performed 6 to 12 wk after insertion of the antibiotic-loaded spacer. There were two hemi and three reverse shoulder arthroplasties. Infection was successfully eradicated in all patients. The clinical outcome was satisfactory with a mean DASH score and SSV of 18.4 points and 70%, respectively.

Research conclusions

Our study indicates that short interval two-stage approach for septic glenohumeral arthritis is a valid alternative treatment option for patient with advanced degenerative condition and/or irreparable rotator cuff tears. The main advantage of this novel approach is that by treating the underlying bony pathology in terms of resecting the arthritic bone the chances of successful infection eradication are increased and at the same time it allows for adequate pain control and improvement of functional outcomes. In our opinion, it should be reserved for selected patients with higher stage of infection, who failed to heal with arthroscopic or open lavage and debridement

Research perspectives

The rising number of shoulder procedures performed in aging population with inherent higher risk factors could potentially lead to a growing number of septic glenohumeral arthritis. Multicenter studies are necessary to achieve a higher case load and evidence regarding these rare indications.

REFERENCES

1 **Memon M**, Kay J, Ginsberg L, de Sa D, Simunovic N, Samuelsson K, Athwal GS, Ayeni OR. Arthroscopic Management of Septic Arthritis of the Native Shoulder: A Systematic Review. *Arthroscopy* 2018; **34**: 625-646.e1 [PMID: 29096980 DOI: 10.1016/j.arthro.2017.07.038]

2 **Sultana S**, Dey R, Bishayi B. Dual neutralization of TNFR-2 and MMP-2 regulates the severity of S. aureus induced septic arthritis correlating alteration in the level of interferon gamma and interleukin-10 in terms of TNFR2 blocking. *Immunol Res* 2018; **66**: 97-119 [PMID: 29218573 DOI: 10.1007/s12026-017-8979-y]

3 **Farrow L**. A systematic review and meta-analysis regarding the use of corticosteroids in septic arthritis. *BMC Musculoskelet Disord* 2015; **16**: 241 [PMID: 26342736 DOI: 10.1186/s12891-015-0702-3]

4 **Zhai KF**, Duan H, Cui CY, Cao YY, Si JL, Yang HJ, Wang YC, Cao WG, Gao GZ, Wei ZJ. Liquiritin from Glycyrrhiza uralensis Attenuating Rheumatoid Arthritis *via* Reducing Inflammation, Suppressing Angiogenesis, and Inhibiting MAPK Signaling Pathway. *J Agric Food Chem* 2019; **67**: 2856-2864 [PMID: 30785275 DOI: 10.1021/acs.jafc.9b00185]

5 **Zhai KF**, Duan H, Chen Y, Khan GJ, Cao WG, Gao GZ, Shan LL, Wei ZJ. Apoptosis effects of imperatorin on synoviocytes in rheumatoid arthritis through mitochondrial/caspase-mediated pathways. *Food Funct* 2018; **9**: 2070-2079 [PMID: 29577119 DOI: 10.1039/c7fo01748k]

6 **Zhai KF**, Duan H, Khan GJ, Xu H, Han FK, Cao WG, Gao GZ, Shan LL, Wei ZJ. Salicin from Alangium chinense Ameliorates Rheumatoid Arthritis by Modulating the Nrf2-HO-1-ROS Pathways. *J Agric Food Chem* 2018; **66**: 6073-6082 [PMID: 29852739 DOI: 10.1021/acs.jafc.8b02241]

7 **Leslie BM**, Harris JM, Driscoll D. Septic arthritis of the shoulder in adults. *J Bone Joint Surg Am* 1989; **71**: 1516-1522 [PMID: 2592392 DOI: 10.2106/00004623-198971100-00010]

8 **Shaikh AA**, Ha CW, Park YG, Park YB. Two-stage approach to primary TKA in infected arthritic knees using intraoperatively molded articulating cement spacers. *Clin Orthop Relat Res* 2014; **472**: 2201-2207 [PMID: 24599649 DOI: 10.1007/s11999-014-3545-6]

9 **Nazarian DG**, de Jesus D, McGuigan F, Booth RE. A two-stage approach to primary knee arthroplasty in the infected arthritic knee. *J Arthroplasty* 2003; **18**: 16-21 [PMID: 14560405 DOI: 10.1016/S0883-5403(03)00343-7]

10 **Hattrup SJ**, Renfree KJ. Two-stage shoulder reconstruction for active glenohumeral sepsis. *Orthopedics*

2010; **33**: 20 [PMID: 20055348 DOI: 10.3928/01477447-20091124-05]
11 **Themistocleous G**, Zalavras C, Stine I, Zachos V, Itamura J. Prolonged implantation of an antibiotic cement spacer for management of shoulder sepsis in compromised patients. *J Shoulder Elbow Surg* 2007; **16**: 701-705 [PMID: 17931905 DOI: 10.1016/j.jse.2007.02.118]
12 **Stine IA**, Lee B, Zalavras CG, Hatch G, Itamura JM. Management of chronic shoulder infections utilizing a fixed articulating antibiotic-loaded spacer. *J Shoulder Elbow Surg* 2010; **19**: 739-748 [PMID: 20137977 DOI: 10.1016/j.jse.2009.10.002]
13 **Coffey MJ**, Ely EE, Crosby LA. Treatment of glenohumeral sepsis with a commercially produced antibiotic-impregnated cement spacer. *J Shoulder Elbow Surg* 2010; **19**: 868-873 [PMID: 20392651 DOI: 10.1016/j.jse.2010.01.012]
14 **Twiss TJ**, Crosby LA. Treatment of the Infected Total Shoulder Arthroplasty With Antibiotic-Impregnated Cement Spacers. *Seminars in Arthroplasty* 2010; **21**: 204-208 [DOI: 10.1053/j.sart.2010.06.013]
15 **Magnan B**, Bondi M, Vecchini E, Samaila E, Maluta T, Dall'Oca C. A preformed antibiotic-loaded spacer for treatment for septic arthritis of the shoulder. *Musculoskelet Surg* 2014; **98**: 15-20 [PMID: 23670275 DOI: 10.1007/s12306-013-0268-x]
16 **Le Dantec L**, Maury F, Flipo RM, Laskri S, Cortet B, Duquesnoy B, Delcambre B. Peripheral pyogenic arthritis. A study of one hundred seventy-nine cases. *Rev Rhum Engl Ed* 1996; **63**: 103-110 [PMID: 8689280]
17 **Lossos IS**, Yossepowitch O, Kandel L, Yardeni D, Arber N. Septic arthritis of the glenohumeral joint. A report of 11 cases and review of the literature. *Medicine (Baltimore)* 1998; **77**: 177-187 [PMID: 9653429 DOI: 10.1097/00005792-199805000-00003]
18 **Garofalo R**, Flanagin B, Cesari E, Vinci E, Conti M, Castagna A. Destructive septic arthritis of shoulder in adults. *Musculoskelet Surg* 2014; **98**: 35-39 [PMID: 24659194 DOI: 10.1007/s12306-014-0317-0]
19 **Duncan SF**, Sperling JW. Treatment of primary isolated shoulder sepsis in the adult patient. *Clin Orthop Relat Res* 2008; **466**: 1392-1396 [PMID: 18347887 DOI: 10.1007/s11999-008-0213-8]
20 **Pfeiffenberger J**, Meiss L. Septic conditions of the shoulder--an up-dating of treatment strategies. *Arch Orthop Trauma Surg* 1996; **115**: 325-331 [PMID: 8905106 DOI: 10.1007/BF00420325]
21 **Stutz G**, Kuster MS, Kleinstück F, Gächter A. Arthroscopic management of septic arthritis: stages of infection and results. *Knee Surg Sports Traumatol Arthrosc* 2000; **8**: 270-274 [PMID: 11061294 DOI: 10.1007/s001670000129]
22 **Jeon IH**, Choi CH, Seo JS, Seo KJ, Ko SH, Park JY. Arthroscopic management of septic arthritis of the shoulder joint. *J Bone Joint Surg Am* 2006; **88**: 1802-1806 [PMID: 16882905 DOI: 10.2106/JBJS.E.00917]
23 **Böhler C**, Pock A, Waldstein W, Staats K, Puchner SE, Holinka J, Windhager R. Surgical treatment of shoulder infections: a comparison between arthroscopy and arthrotomy. *J Shoulder Elbow Surg* 2017; **26**: 1915-1921 [PMID: 28601485 DOI: 10.1016/j.jse.2017.04.001]
24 **McFarland EG**, Rojas J, Smalley J, Borade AU, Joseph J. Complications of antibiotic cement spacers used for shoulder infections. *J Shoulder Elbow Surg* 2018; **27**: 1996-2005 [PMID: 29778591 DOI: 10.1016/j.jse.2018.03.031]
25 **Coste JS**, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. *J Bone Joint Surg Br* 2004; **86**: 65-69 [PMID: 14765868 DOI: 10.1302/0301-620X.86B1.14089]
26 **Sabesan VJ**, Ho JC, Kovacevic D, Iannotti JP. Two-stage reimplantation for treating prosthetic shoulder infections. *Clin Orthop Relat Res* 2011; **469**: 2538-2543 [PMID: 21359591 DOI: 10.1007/s11999-011-1774-5]
27 **Strickland JP**, Sperling JW, Cofield RH. The results of two-stage re-implantation for infected shoulder replacement. *J Bone Joint Surg Br* 2008; **90**: 460-465 [PMID: 18378920 DOI: 10.1302/0301-620X.90B4.20002]
28 **Sperling JW**, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. *Clin Orthop Relat Res* 2001; 206-216 [PMID: 11153989 DOI: 10.1097/00003086-200101000-00028]
29 **Cuff DJ**, Virani NA, Levy J, Frankle MA, Derasari A, Hines B, Pupello DR, Cancio M, Mighell M. The treatment of deep shoulder infection and glenohumeral instability with debridement, reverse shoulder arthroplasty and postoperative antibiotics. *J Bone Joint Surg Br* 2008; **90**: 336-342 [PMID: 18310757 DOI: 10.1302/0301-620X.90B3.19408]
30 **Buchalter DB**, Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Two-stage revision for infected shoulder arthroplasty. *J Shoulder Elbow Surg* 2017; **26**: 939-947 [PMID: 27887875 DOI: 10.1016/j.jse.2016.09.056]
31 **Jacquot A**, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicenter study of reoperation in 32 patients. *J Shoulder Elbow Surg* 2015; **24**: 1713-1722 [PMID: 25957111 DOI: 10.1016/j.jse.2015.03.007]
32 **Ramsey ML**, Fenlin JM. Use of an antibiotic-impregnated bone cement block in the revision of an infected shoulder arthroplasty. *J Shoulder Elbow Surg* 1996; **5**: 479-482 [PMID: 8981275 DOI: 10.1016/S1058-2746(96)80022-X]
33 **Padegimas EM**, Narzikul A, Lawrence C, Hendy BA, Abboud JA, Ramsey ML, Williams GR, Namdari S. Antibiotic Spacers in Shoulder Arthroplasty: Comparison of Stemmed and Stemless Implants. *Clin Orthop Surg* 2017; **9**: 489-496 [PMID: 29201302 DOI: 10.4055/cios.2017.9.4.489]
34 **Romanò CL**, Borens O, Monti L, Meani E, Stuyck J. What treatment for periprosthetic shoulder infection? Results from a multicentre retrospective series. *Int Orthop* 2012; **36**: 1011-1017 [PMID: 22331125 DOI: 10.1007/s00264-011-1467-4]
35 **Mahure SA**, Mollon B, Yu S, Kwon YW, Zuckerman JD. Definitive Treatment of Infected Shoulder Arthroplasty With a Cement Spacer. *Orthopedics* 2016; **39**: e924-e930 [PMID: 27359283 DOI: 10.3928/01477447-20160623-07]
36 **Kirchhoff C**, Braunstein V, Buhmann Kirchhoff S, Oedekoven T, Mutschler W, Biberthaler P. Stage-dependant management of septic arthritis of the shoulder in adults. *Int Orthop* 2009; **33**: 1015-1024 [PMID: 18600324 DOI: 10.1007/s00264-008-0598-8]

World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2019 October 18; 10(10): 364-370

DOI: 10.5312/wjo.v10.i10.364

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Prospective Study

Posterior ankle impingement–an underdiagnosed cause of ankle pain in pediatric patients

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Author contributions: Kushare I designed and performed the research; Kastan K and Allahabadi S contributed to data acquisition; Kushare I, Allahabadi S analyzed the data and wrote the article; Kushare I, Kastan K and Allahabadi S contributed to editing, reviewing and final approval of article.

Institutional review board statement: The study was reviewed and approved by Baylor College of Medicine Institutional Review Board.

Clinical trial registration statement: Since this is a descriptive study and not a clinical trial, it was not registered.

Informed consent statement: The legal guardians of all the study participants provided written, informed consent about personal and medical data collection prior to enrollment in the study.

Conflict-of-interest statement: There is no conflict of interest associated with the senior author or other coauthors who contributed their efforts in this manuscript. All the authors have no conflict of interest related to the manuscript.

CONSORT 2010 statement: The authors have read the CONSORT 2010 Statement, and the manuscript (even though it was

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Abstract

BACKGROUND

Posterior ankle impingement syndrome (PAIS) is a cause of ankle pain due to pinching of bony or soft tissue structures in the hindfoot. The diagnosis is primarily made based on detailed history and accurate clinical examination. The delay in its diagnosis has not yet been described in the pediatric and adolescent population.

AIM

To identify and characterize misdiagnosed cases of PAIS in pediatric and adolescent patients.

METHODS

This descriptive prospective study at a tertiary children's hospital included patients ≤ 18 years who underwent posterior ankle arthroscopy after presenting with chronic posterior ankle pain after being diagnosed with PAIS. Collected data included: Demographics, prior diagnoses and treatments, providers seen, time to diagnosis from presentation, and prior imaging obtained. Visual Analogue Scale (VAS) for pain and American Orthopedic Foot Ankle Society (AOFAS) ankle-hindfoot scores were noted at initial presentation and follow-up.

RESULTS

35 patients (46 ankles) with average age of 13 years had an average 19 mo (range 0-60 mo) delay in diagnosis from initial presentation. 25 (71%) patients had previously seen multiple medical providers and were given multiple other diagnoses. All 46 (100%) ankles had tenderness to palpation over the posterior ankle joint. Radiographs were reported normal in 31/42 (72%) exams. In 32 ankles who underwent MRI, the most common findings included os trigonum

not a randomized control trial) was prepared and revised according to the CONSORT 2010 Statement as applicable.

Manuscript source: Unsolicited manuscript

Received: June 3, 2019
Peer-review started: June 4, 2019
First decision: July 31, 2019
Revised: August 8, 2019
Accepted: September 15, 2019
Article in press: September 15, 2019
Published online: October 18, 2019

P-Reviewer: Doets HC, van Bergen CJA
S-Editor: Wang J
L-Editor: A
E-Editor: Liu MY

(47%)/Stieda process (47%). Conservative treatment had already been attempted in all patients. Ankle impingement pathology was confirmed during arthroscopy in 46 (100%) ankles. At an average follow-up of 13.1 mo, there was an improvement of VAS (pre-op 7.0 to post-op 1.2) and AOFAS scores (pre-op 65.1 to post-op 94).

CONCLUSION
This is the first study which shows that PAIS is a clinically misdiagnosed cause of posterior ankle pain in pediatric and adolescent population; an increased awareness about this diagnosis is needed amongst providers treating young patients.

Key words: Ankle impingement; Ankle pain; Os trigonum; Delayed diagnosis; Ankle arthroscopy; Pediatric

Core tip: Our prospective study included 35 patients under 18 years of age diagnosed with posterior ankle impingement syndrome (PAIS) who underwent arthroscopic treatment for failed conservative management. We found that there was an average of 19 mo delay in diagnosis from initial presentation to a medical provider. All patients had posterior ankle tenderness which was used to make the clinical diagnosis. The pain relief with arthroscopic debridement, as evidenced by improvement of Visual Analogue Scale and American Orthopedic Foot Ankle Society scores was used to confirm our clinical diagnosis of PAIS. Our study shows that there needs to be an increased awareness about PAIS is needed amongst providers treating young patients.

Citation: Kushare I, Kastan K, Allahabadi S. Posterior ankle impingement–an underdiagnosed cause of ankle pain in pediatric patients. *World J Orthop* 2019; 10(10): 364-370
URL: https://www.wjgnet.com/2218-5836/full/v10/i10/364.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i10.364

INTRODUCTION

Posterior ankle impingement syndrome (PAIS) is a common cause of posterior ankle pain that has been classically described in ballet dancers and soccer players[1-4]. It is caused by mechanical pinching of bony or soft tissue structures during terminal plantar-flexion in the posterior part of the ankle[1-5]. Even though it can present acutely, PAIS more commonly presents with chronic pain secondary to repetitive stresses in the posterior ankle with forced plantar-flexion activities. With several causes (soft tissue, bony, or both) and heterogenous pathological anatomic features, the diagnosis was coined as posterior ankle impingement "syndrome"[2,6]. This diagnosis is primarily made based on an accurate history and detailed clinical exam[2,3,7-9]. To our knowledge, there has not been any prior literature that highlights the delay in making this diagnosis in the pediatric and adolescent population. The aim of our study was to identify any delay in diagnosis and further characterize the misdiagnosed cases of posterior ankle impingement exclusively in the pediatric and adolescent population.

MATERIALS AND METHODS

Patient selection

This was a descriptive prospective study conducted at a tertiary children's hospital after approval from the Institutional Review Board. The study included patients 18 years and younger from 2016 to 2019 who presented with posterior ankle pain, were diagnosed with posterior ankle impingement, and underwent arthroscopic debridement due to failure of conservative treatment. Informed written consent was obtained from all patients prior to enrollment in the study.

Collected data

Collected data included the following: Age, gender, previous diagnoses and treatment received, prior specialists seen for ankle pain, time to diagnosis from initial presentation, and radiologic imaging obtained-including plain radiographs and magnetic resonance imaging (MRI). Diagnosis of PAIS was made based on history and clinical exam (posterior joint line tenderness, pain on forced plantar flexion) supplemented by radiographic imaging. Delay in diagnosis was defined as the time between initial presentation to a medical provider with ankle pain until the diagnosis of PAIS was made. Indication for arthroscopic debridement was failure of conservative treatment which included rest and immobilization, with or without physical therapy. Visual Analogue scale (VAS) for pain and American Orthopedic Foot Ankle Society (AOFAS) ankle-hindfoot scores at presentation pre-operatively and post-operative follow-up visits were compared using the paired *t* or Wilcoxon signed-rank tests with statistical significance set at $P < 0.05$. Descriptive statistical analyses were conducted and summarized as means with range values or frequencies with corresponding percentages.

RESULTS

Treatment outcome and statistical analysis

Prospective data was collected in 35 patients (16 males, 19 females). A total of 46 ankles were included with a mean patient age of 13 years (range 8.6-17.9). 33 (94%) patients had a delay in the diagnosis of PAIS from the initial presentation with symptoms to a medical provider, the average delay being 19 mo (range 0-60). 22/35 (62%) patients were athletes, the most common sports included American football (4 patients), soccer and gymnastics (3 patients each). 25 (71%) patients had previously seen multiple health care professionals and specialists and were given multiple other diagnoses as a cause of their ankle pain (Table 1). All 46 (100%) ankles had specific tenderness to palpation over the posterior ankle joint which was located between the peroneal tendons and Achilles tendon. 42 (91%) ankles had at least one preoperative radiograph obtained (Figure 1), and 15 (43%) patients had multiple radiographs prior to actual diagnosis. The radiographs were reported "normal" with no significant findings by local radiologist in 31 (74%) exams. 30 (86%) patients (32 ankles) had an MRI study done, the most common findings of which were os trigonum (47%) (Figure 2) or Stieda process (47%). 22 of the 32 ankles (69%) with an MRI performed had osseous edema indicative of the inflammation seen in PAIS.

Conservative treatment

All 35 (100%) patients had attempted and failed prolonged and exhaustive conservative management for several months. Conservative treatment included rest from sports and physical activities (including physical education at school), immobilization with boot, brace or cast, and/or physical therapy. One patient had a prior ankle corticosteroid injection. Pain typically subsided temporarily with conservative treatment but recurred with return to activity/sports. All 46 (100%) ankles had exquisite tenderness to palpation over posterior ankle joint, anterior to the Achilles tendon.

Surgical treatment

All 46 ankles had PAIS pathology, either soft tissue, bony, or a combination of both, confirmed during arthroscopic treatment, including os trigonum (Figure 3), Stieda process, hypertrophic ligaments and synovium–these three were the most common findings seen in majority (42/46) of the ankles. Uncommon findings were cysts of the flexor hallucis longus tendonitis (FHL) (2 cases), and a low-lying FHL muscle belly (2 cases). At an average follow-up of 13.1 mo, there was significant improvement of mean VAS pain scale (pre-op 7.0 to post-op 1.2, $P < 0.001$) and mean AOFAS ankle scores (pre-op 65.1 to post-op 94, $P < 0.001$). Three patients had inadequate documentation; the remaining 32 (91%) patients returned to their previous level of activity/sports at average 7.8 wk after treatment. None of the patients had recurrence of symptoms at their last follow-up which supports our diagnosis of PAIS.

DISCUSSION

Posterior ankle impingement syndrome has been well-described in the literature, particularly in dancers and soccer players[1,2,4]. PAIS is due to the mechanical pinching of structures in the posterior ankle, which may be secondary to bony or soft tissue causes, or a combination of both[1,2]. An average delay of over one and a half years (19

Table 1 Spectrum of providers seen and list of prior diagnoses before the diagnosis of posterior ankle impingement syndrome was assigned

Previous providers seen	Previous diagnoses given
Pediatricians	Sever's apophysitis
Orthopedic surgeons	Peroneal tendon subluxation
Primary care sports physicians	Peroneal tendinopathy
Physical medicine and rehabilitation physicians	Achilles tendonitis
Podiatrists	Chronic regional pain syndrome
Physical therapists	Ankle sprain
Chiropractors	Sural neuralgia
Pain clinic	"Deconditioned ankle"

mo) from the time of initial symptomatic presentation to making the diagnosis in a high percentage (94%) of patients indicates that PAIS is usually not on the radar of physicians treating ankle pain in the pediatric and adolescent population.

The diagnosis of PAIS is primarily based on an accurate history and clinical examination[1-3]. The classic etiologic activities that have been described are dance (especially ballet), soccer, downhill running, and additional forced plantar-flexion activities[1-4]. The pain is aggravated by the aforementioned activities and is typically relieved by rest. The ankle pain is described as consistent, sharp, dull and deep; it is usually difficult for patients to indicate the exact location of the pain in the hindfoot[10,11]. On examination there is posterior joint line tenderness, and more specifically it is typically between the Achilles and peroneal tendons[2,4], which is important to help differentiate it from other causes of posterior foot and ankle pain such as Sever's apophysitis and ankle sprain. The clinical exam finding of posterior joint line tenderness was seen in all of the ankles in our study; we suggest that this examination should be included in the evaluation of all patients presenting with ankle pain so that the diagnosis of posterior ankle impingement is not missed. A diagnostic local infiltration may also be performed to confirm the diagnosis, which can be guided by ultrasound[2].

History and clinical examination are most important in diagnosing PAIS and they can be supported by imaging findings. Standard lateral plain radiographs can identify bony pathology in the form of os trigonum (Figure 1) or Stieda process[12]. However, in young patients with open physes, os trigonum can very well be small or cartilaginous[4] and radiographs could often be reported as "normal". Entrapment, hypertrophy and inflammation of soft tissues, FHL are common pathologies seen in posterior ankle impingement, but the fact that these are not well-visualized on radiographs can lead to delay in treatment and more expensive imaging[13]. Many of our patients had multiple radiographic imaging procedures performed of the painful ankle; and normal reported radiographs which likely contributed to the delayed diagnosis of PAIS. MRI is considered a useful diagnostic modality for assessment of the pathology in ankle impingement[6,14]. However, MRI has been shown to be an insensitive modality for ankle imaging in the pediatric population[15]. The most common MRI findings in our study included the presence of an os trigonum or Stieda process, with associated osseous and soft tissue edema which is similar to what prior studies in the literature have reported[6,12,14,16].

The most common treatment for posterior ankle impingement is conservative management which includes rest and immobilization of the ankle (with brace/boot/cast) to aid in decreasing the inflammation. This can be supplemented with physical therapy. Corticosteroid injections in the ankle have been described in literature, and are more typically used in athletes to help them complete a season[5]. Prolonged conservative treatment for several months was already attempted in all our patients, which lead to temporary pain relief but persisted/recurred with return to activity/sports. Persistent pain with activity despite conservative management was likely the reason why a high percentage (71%) of our patients saw multiple medical providers for treatment. Return of ankle pain with activity is commonly seen in ankle impingement as the pinching of structures in the hindfoot typically occurs with plantar flexion of the ankle causing recurrence of inflammation and pain[3,9,17,18].

The indication of arthroscopy in our patient population was persistent symptoms despite prolonged conservative management as mentioned above. Arthroscopic treatment is now an established modality of treatment for patients who fail conservative management[19-21]. Arthroscopic visualization of the ankle and hindfoot during surgery is also a reliable way to confirm the correct diagnosis[22]. Various

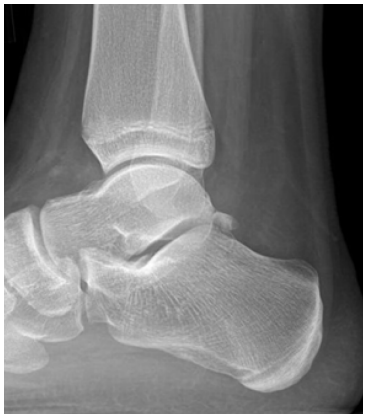

Figure 1 Fifteen-year old male with posterior ankle pain with os trigonum seen on lateral ankle radiograph.

pathologies which have already been well-described as sources of bony and/or soft tissue causes of posterior ankle impingement were encountered during arthroscopic treatment of our cohort, including os trigonum, Stieda process, hypertrophic ligaments and synovium, cysts of the FHL, and a low-lying FHL muscle belly[2,6,16,18,22-24]. The pain relief after treatment as indicated by improvement in VAS and AOFAS scores, along with return to prior level of sports and activity in our patient cohort supports the clinical diagnosis of posterior ankle impingement.

Weaknesses of our study include data collected at a single institution, small sample size, and no comparative non-operative cohort. The patients referred to a tertiary center like ours may not be representative of the whole population, and the referral could possibly increase the delay. The mean follow-up of 13.1 mo is relatively short; however, the focus of this study is on the delay in clinical diagnosis of PAIS, and not on the surgical outcomes. We have included the arthroscopic findings and treatment outcomes primarily to supplement our clinical diagnosis of PAIS. The strength of our study is the prospective nature of data collection and consecutive enrollment of pediatric patients, both of which help minimize biases that could result from a retrospective study. Collecting long-term multi-center data and including non-operatively treated patients for comparison are recommended for future studies. To conclude, posterior ankle impingement syndrome can be misdiagnosed in young patients presenting with posterior ankle pain, thus leading to a delay in diagnosis. This prospective study in the pediatric population is the first study which highlights the need for increased awareness about this condition and its clinical diagnosis amongst pediatric orthopedic surgeons, pediatricians, primary care sports doctors, and other physicians involved in treating young athletes to avoid delay in treatment.

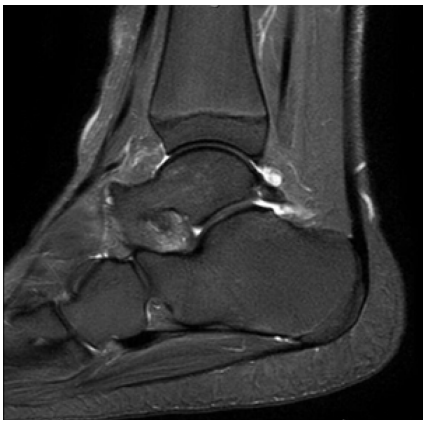

Figure 2 Magnetic resonance imaging-sagittal image demonstrating edema-like signal intensity adjacent to the os trigonum in the previously mentioned 15-year-old patient in Figure 1.

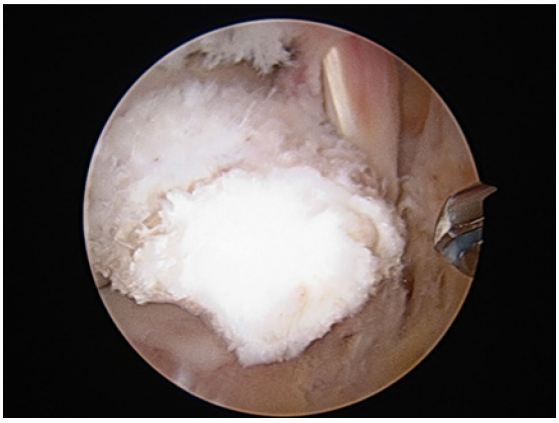

Figure 3 Arthroscopic appearance of the os trigonum of the same patient in Figures 1 and 2 before excision.

ARTICLE HIGHLIGHTS

Research background

Posterior ankle impingement is a known cause of ankle pain which has been well described in adults but not as much in the pediatric literature.

Research motivation

The diagnosis of posterior ankle impingement syndrome (PAIS) is made based on detailed history and clinical findings. We came across patients with missed diagnosis of PAIS in clinic and realized that without adequate awareness, this diagnosis can possibly be missed in pediatric and adolescent patients.

Research objectives

The purpose of our study was to identify and characterize the delay in making the diagnosis of PAIS in the young patient population.

Research methods

We started a prospective study to enroll patients under 18 years of age who were diagnosed with PAIS and underwent arthroscopic treatment after failed conservative management. Data collection was done to try and identify any delay in making this diagnosis by the previous treating medical providers. Pre and post treatment pain and American Orthopedic Foot Ankle Society (AOFAS) scores were also noted and compared.

Research results

35 patients (46 ankles) with average age of 13 years had an average 19 mo (range 0-60 mo) delay in diagnosis from initial presentation to a medical provider. 25 (71%) patients had previously seen multiple medical providers. All 46 (100%) ankles had tenderness to palpation over the posterior ankle joint. Radiographs were reported normal in 31/42 (72%) exams. In 32 ankles who underwent MRI, the most common findings included os trigonum (47%)/Stieda process (47%). At an average follow-up of 13.1 mo after treatment, there was significant improvement of VAS

(pre-op 7.0 to post-op 1.2) and AOFAS scores (pre-op 65.1 to post-op 93.4) ($P < 0.001$).

Research conclusions

The study concludes that PAIS is a misdiagnosed condition in the pediatric population.

It was shown that a variety of medical providers (pediatricians, orthopedic surgeons, sports physicians, *etc*.) missed this diagnosis. There needs to be increased awareness about this condition among medical providers treating young patients.

Research perspectives

The study makes us aware about the delayed diagnosis if PAIS which can be prevented by detailed history taking and examination. This research can be potentially improved in the future by collecting multi-center data to include larger cohort of patients.

REFERENCES

1 **Russell JA**, Kruse DW, Koutedakis Y, McEwan IM, Wyon MA. Pathoanatomy of posterior ankle impingement in ballet dancers. *Clin Anat* 2010; **23**: 613-621 [PMID: 20821398 DOI: 10.1002/ca.20991]
2 **Giannini S**, Buda R, Mosca M, Parma A, Di Caprio F. Posterior ankle impingement. *Foot Ankle Int* 2013; **34**: 459-465 [PMID: 23520307 DOI: 10.1177/1071100713477609]
3 **Roche AJ**, Calder JD, Lloyd Williams R. Posterior ankle impingement in dancers and athletes. *Foot Ankle Clin* 2013; **18**: 301-318 [PMID: 23707179 DOI: 10.1016/j.fcl.2013.02.008]
4 **Nault ML**, Kocher MS, Micheli LJ. Os trigonum syndrome. *J Am Acad Orthop Surg* 2014; **22**: 545-553 [PMID: 25157036 DOI: 10.5435/JAAOS-22-09-545]
5 **Kudaş G**, Dönmez MS, Işık Ç, Çelebi M, Çay N, Bozkurt M. Posterior ankle impingement syndrome in football players: Case series of 26 elite athletes. *Acta Orthopaedica et Traumatologica Turcica* 2016; **50**: 649-654 [DOI: 10.1016/j.aott.2016.03.008]
6 **Peace KA**, Hillier JC, Hulme A, Healy JC. MRI features of posterior ankle impingement syndrome in ballet dancers: a review of 25 cases. *Clin Radiol* 2004; **59**: 1025-1033 [PMID: 15488852 DOI: 10.1016/j.crad.2004.02.010]
7 **Maquirriain J**. Posterior ankle impingement syndrome. *J Am Acad Orthop Surg* 2005; **13**: 365-371 [PMID: 16224109 DOI: 10.5435/00124635-200510000-00001]
8 **Smyth NA**, Zwiers R, Wiegerinck JI, Hannon CP, Murawski CD, van Dijk CN, Kennedy JG. Posterior hindfoot arthroscopy: a review. *Am J Sports Med* 2014; **42**: 225-234 [PMID: 23868522 DOI: 10.1177/0363546513491213]
9 **Bojanić I**, Janjić T, Dimnjaković D, Križan S, Smoljanović T. [Posterior ankle impingement syndrome]. *Lijec Vjesn* 2015; **137**: 109-115 [PMID: 26065289]
10 **Yasui Y**, Hannon CP, Hurley E, Kennedy JG. Posterior ankle impingement syndrome: A systematic four-stage approach. *World J Orthop* 2016; **7**: 657-663 [PMID: 27795947 DOI: 10.5312/wjo.v7.i10.657]
11 **Coetzee JC**, Seybold JD, Moser BR, Stone RM. Management of Posterior Impingement in the Ankle in Athletes and Dancers. *Foot Ankle Int* 2015; **36**: 988-994 [PMID: 26163559 DOI: 10.1177/1071100715595504]
12 **Al-Riyami AM**, Tan HK, Peh WCG. Imaging of Ankle Impingement Syndromes. *Can Assoc Radiol J* 2017; **68**: 431-437 [PMID: 28865671 DOI: 10.1016/j.carj.2017.04.001]
13 **Wiegerinck JI**, Vroemen JC, van Dongen TH, Sierevelt IN, Maas M, van Dijk CN. The posterior impingement view: an alternative conventional projection to detect bony posterior ankle impingement. *Arthroscopy* 2014; **30**: 1311-1316 [PMID: 25023737 DOI: 10.1016/j.arthro.2014.05.006]
14 **Wong**, GNL, Tan TJ. MR imaging as a problem solving tool in posterior ankle pain: A review. *Eur J Radiol* 2016; **85**: 2238-2256 [PMID: 27842673 DOI: 10.1016/j.ejrad.2016.10.016]
15 **Vasukutty NV**, Akrawi H, Theruvil B, Uglow M. Ankle arthroscopy in children. *Ann R Coll Surg Engl* 2011; **93**: 232-235 [PMID: 21477438 DOI: 10.1308/003588411X564005]
16 **Sellon E**, Robinson P. MR Imaging of Impingement and Entrapment Syndromes of the Foot and Ankle. *Magn Reson Imaging Clin N Am* 2017; **25**: 145-158 [PMID: 27888845 DOI: 10.1016/j.mric.2016.08.004]
17 **Luk P**, Thordarson D, Charlton T. Evaluation and management of posterior ankle pain in dancers. *J Dance Med Sci* 2013; **17**: 79-83 [PMID: 23759482 DOI: 10.12678/1089-313X.17.2.79]
18 **Hayashi D**, Roemer FW, D'Hooghe P, Guermazi A. Posterior ankle impingement in athletes: Pathogenesis, imaging features and differential diagnoses. *Eur J Radiol* 2015; **84**: 2231-2241 [PMID: 26239710 DOI: 10.1016/j.ejrad.2015.07.017]
19 **Carreira DS**, Vora AM, Hearne KL, Kozy J. Outcome of Arthroscopic Treatment of Posterior Impingement of the Ankle. *Foot Ankle Int* 2016; **37**: 394-400 [PMID: 26646107 DOI: 10.1177/1071100715620857]
20 **Theodoulou MH**, Bohman L. Arthroscopic Approach to Posterior Ankle Impingement. *Clin Podiatr Med Surg* 2016; **33**: 531-543 [PMID: 27599438 DOI: 10.1016/j.cpm.2016.06.009]
21 **Miyamoto W**, Miki S, Kawano H, Takao M. Surgical outcome of posterior ankle impingement syndrome with concomitant ankle disorders treated simultaneously in patient engaged in athletic activity. *J Orthop Sci* 2017; **22**: 463-467 [PMID: 28087215 DOI: 10.1016/j.jos.2016.12.017]
22 **Miyamoto W**, Takao M, Matsushita T. Hindfoot endoscopy for posterior ankle impingement syndrome and flexor hallucis longus tendon disorders. *Foot Ankle Clin* 2015; **20**: 139-147 [PMID: 25726489 DOI: 10.1016/j.fcl.2014.10.005]
23 **Hopper MA**, Robinson P. Ankle impingement syndromes. *Radiol Clin North Am* 2008; **46**: 957-971, v [PMID: 19038606 DOI: 10.1016/j.rcl.2008.08.001]
24 **Rungprai C**, Tennant JN, Phisitkul P. Disorders of the Flexor Hallucis Longus and Os Trigonum. *Clin Sports Med* 2015; **34**: 741-759 [PMID: 26409593 DOI: 10.1016/j.csm.2015.06.005]

World Journal of Orthopedics

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World J Orthop 2019 October 18; 10(10): 371-377

DOI: 10.5312/wjo.v10.i10.371

ISSN 2218-5836 (online)

CASE REPORT

Low-velocity simultaneous bilateral femoral neck fracture following long-term antiepileptic therapy: A case report

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Informed consent statement: The patient provided informed consent for publication of this case and any related images.

Conflict-of-interest statement: All authors declare that they have no conflicts of interest related to this report.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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Abstract

BACKGROUND

Simultaneous bilateral femoral neck fractures are relatively rare injuries. They are usually associated with underlying metabolic bone disorders or systemic diseases. Long-term use of narcotics and bisphosphonates can also result in similar fracture patterns; however, association of this fracture type with long-term use of antiepileptic drugs is not very common. Only one such case has been reported in the literature. This article describes the second.

CASE REPORT

We report a case of simultaneous displaced bilateral femoral neck fractures in a 50-year-old epileptic patient, who had taken phenytoin for the past 3 years. The fractures were a result of low-velocity injury following a fall from the bed. The fractures were managed with a bilateral hemi-replacement arthroplasty. Oral bisphosphonates were given to improve the bone quality in the post-operative period. The patient had a good post-operative outcome, that was sustained throughout the entire follow-up period of 1 year.

CONCLUSION

Antiepileptic drugs should be supplemented with bisphosphonates and vitamin D to improve bone quality and prevent fractures in epileptic patients.

Key words: Case report; Bilateral femoral neck fracture; Antiepileptic drug therapy; Drug-induced osteopenia; Bisphosphonates; Vitamin D

Core tip: Drug-induced bilateral femoral neck fractures are extremely rare. The injury has been reported to be associated with long-term intake of bisphosphonates, narcotics, anti-retroviral therapy, and antiepileptic drugs. Only one case of simultaneous bilateral femoral neck fracture associated with long-term antiepileptic drug intake has been

Manuscript source: Unsolicited manuscript

Received: March 1, 2019
Peer-review started: March 4, 2019
First decision: June 12, 2019
Revised: July 21, 2019
Accepted: September 15, 2019
Article in press: September 15, 2019
Published online: October 18, 2019

P-Reviewer: Lim SC, Peng BG
S-Editor: Gong ZM
L-Editor: A
E-Editor: Liu MY

reported. Our case report of this type of injury further substantiates the association between long-term antiepileptic drug intake and reduced bone mineral density. Through our experience with this case, we recommend that supplementation of calcium, vitamin D and bisphosphonates along with antiepileptic drugs is essential to maintain bone quality and prevent fractures.

Citation: Sadiq M, Kulkarni V, Hussain SA, Ismail M, Nayak M. Low-velocity simultaneous bilateral femoral neck fracture following long-term antiepileptic therapy: A case report. *World J Orthop* 2019; 10(10): 371-377
URL: https://www.wjgnet.com/2218-5836/full/v10/i10/371.htm
DOI: https://dx.doi.org/10.5312/wjo.v10.i10.371

INTRODUCTION

Simultaneous bilateral femoral neck fracture is a relatively rare fracture pattern[1-4]. Most of these fractures are a result of low-velocity injury or atraumatic fracture over an underlying bone pathology[2]. Disorders of bone metabolism, like osteoporosis, osteomalacia, rickets, hyperparathyroidism and chronic renal failure, have all been reported with this fracture pattern[5-9]. Association with seizure disorders and electric shock injuries has also been reported[10-11]. Finally, this fracture pattern has been seen with long-term use of bisphosphonates, narcotic drug abuse, anti-retroviral therapy, and psychosomatic disorders, like anorexia nervosa[12-15].

Antiepileptic drugs (AEDs) are also a known cause of drug-induced osteoporosis. Enzyme-inducing AEDs cause a greater degree of osteoporosis than their non-inducing counterparts. This is explained by the increased metabolism of vitamin D and direct inhibitory effect on the proliferation of osteoblasts. To the best of our knowledge, there is only one previous case report of an atraumatic bilateral femoral neck insufficiency fracture in a patient with long-term intake of carbamazepine[11]. We present here a similar case of simultaneous displaced bilateral neck of femur fractures in a known epileptic on long-term phenytoin therapy following a trivial fall in the home.

CASE PRESENTATION

Chief complaints

A 50-year-old male patient presented to the Orthopaedics outpatient department of our hospital with complains of persistent pain in both hips that had begun 10 d prior, following a fall from the bed.

History of present illness

The patient had sustained injury to both hips following a fall from the bed in his home, after which he was unable to stand up and walk. Considering the trivial cause of injury, he did not consult any doctors for 8 d and received massage therapy from a local orthotist to address the persistent pain. When the pain did not subside, he presented to our hospital on the 10th d after injury.

Past history

The patient was a known epileptic on oral phenytoin treatment for the past 3 years. The last seizure episode was 1 year previous, and the present injury was not associated with any seizure episode. The patient had no other co-morbidities and was not on any other medications.

Physical examination

On examination, the patient was alert, oriented and cooperative. Vital parameters recorded were normal. The patient's weight was 59.2 kg (body mass index of 21.2 kg/m^2). There was tenderness in both groins. Both the lower limbs were in external rotation and passive movements were associated with severe pain.

Laboratory testing

Below normal levels were found for serum calcium (4.2 mg/dL; normal: 8-10 mg/dL), phosphorous (2 mg/dL; normal: 2.5-4.5 mg/dL), and vitamin D (9 ng/mL; normal:

20-50 ng/mL). Bone mineral density was assessed using dual-energy x-ray absorptiometry scan (OsteoPro Grand Mini; Aarna Systems, Rajasthan, India) which showed T score of -3. Results from the other blood investigations, including renal and liver function tests, were normal.

Imaging examination

A radiograph of pelvis for both hips showed completely displaced bilateral, transcervical femoral neck fractures (Figure 1). The greater trochanter was upridden on both sides. Significant osteopenia was noted (Singh's grade IV).

FINAL DIAGNOSIS

Based upon the patient's history and findings from clinical examination and imaging studies, displaced bilateral neck of femur fractures was diagnosed. Based upon the findings from lab investigations and imaging studies, the patient was diagnosed with severe osteoporosis, with possibility of being attributable to the prolonged intake of AEDs.

TREATMENT

Considering the delay in the diagnosis of the patient's fractures and underlying osteoporosis, a bilateral cemented modular hemiarthroplasty (Life Surgicals, Kerala, India) was performed. Intraoperatively, the bone was found to be weak, and in the process of trial reduction the patient suffered a fracture of the greater trochanter on the left side. The trochanter was fixed with stainless steel wire, and the patient was immobilized for 3 wk post-operatively.

OUTCOME AND FOLLOW UP

Partial weight bearing mobilization with walker was started after 3 wk and unassisted walking was allowed after 6 wk (Figure 2). Calcium and vitamin D supplementation was started from the 1st post-operative day. The patient was put on a weekly risedronate supplementation regimen for 6 mo post-operatively. The post-operative course was uneventful. The Harris hip score at the end of 1 year was 84 (good).

DISCUSSION

Simultaneous bilateral fracture of femoral neck is a relatively uncommon injury[1-4]. It has been seen in all age groups, from early childhood to the 9th decade of life[5,17]. It has also been reported to result from low-velocity as well as high-velocity injuries, an example of the latter being road traffic accidents[4,5]. The former can also present as a bilateral stress fracture in army recruits[18,19].

The low-velocity fractures have been associated with various underlying bony pathologies; a summary of these publications is presented in Table 1. Of all the systemic disorders related to these fractures in general, epilepsy is the most prevalent. For most of those cases, the fracture-inducing injury was related to seizure activity, mostly due to its manifestation of uncoordinated muscle contractions. AEDs are also an independent cause of drug-induced osteoporosis. Among the AEDs currently in use, the drugs which work as liver enzyme inducers have shown a higher negative effect on bone metabolism. The enzyme-inducing AEDs include carbamazepine, phenobarbitone, and phenytoin[23]. Research has uncovered several of the mechanisms by which AEDs affect bone metabolism; these include (1) decreasing growth velocity *via* significant reduction of procollagen; (2) modulating voltage-gated sodium channels and producing a negative effect on osteoblasts; (3) lowering of the levels of vitamin D, calcium and ionized calcium; and (4) decreasing bone mineral density around the femoral neck and lumbar spine.

There have been previous reports of this fracture pattern associated with epilepsy and AEDs[11,20-22]. But, most of these cases involved fractures that had occurred during a seizure episode. To the best of our knowledge, there is only one case of bilateral femoral neck stress fractures reported in the literature, and this involved a 26-year-old female who was on carbamazepine AED treatment for 12 years[11]. The patient presented with a 3-mo history of pain in the bilateral groins and was diagnosed with insufficiency fractures of the femoral necks. Considering that there was no history of

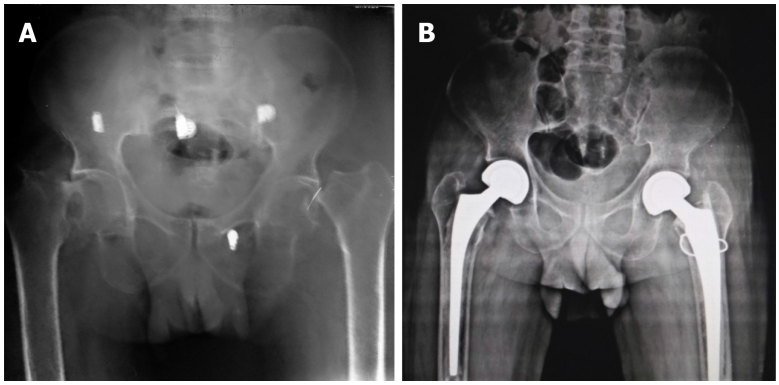

Figure 1 Radiograph. A: Preoperative radiograph showing bilateral displaced fracture neck of femur with significant osteopenia. B: Postoperative radiograph at three months. There was a fracture of the greater trochanter on the left side which was fixed with stainless steel wire. There is a good union of the greater trochanter.

trauma and the last seizure episode had occurred 6 mo prior, the authors correlated the femoral neck fractures to AED-induced osteoporosis.

In our case described herein, the male patient was on oral phenytoin therapy for the past 3 years and the last seizure episode had been 18 mo ago. The fracture resulted from a trivial fall from the bed at home. The x-rays showed completely displaced fractures. Such displacement in bilateral femoral neck fractures in a physiological young patient is usually associated with high-velocity injury. Considering the low velocity of injury and the patient's years-long history of enzyme-inducing AED treatment, we also correlated the fractures with primary AED-induced osteoporosis. As such, this is only the second case with such injury pattern resultant from AED-induced osteoporosis.

In most situations, these fractures can be picked up on plain radiographs. However, in the case of insufficiency fractures, MRI is considered the investigation of choice[11]. Complete blood investigations to identify the underlying pathology is an indispensable component in the management of these fractures. Usually there is an associated negative calcium balance with decreased serum calcium and phosphorous levels. There may also be associated vitamin D deficiency.

The treatment plan depends upon age at presentation, and likely duration after injury, bone quality, and chances of achieving union with the underlying bone pathology. In our case, since the fracture fragments were completely displaced and because the patient presented 10 d after the injury, we performed a hemi-replacement surgery. For minimally displaced fractures or stress fractures presenting within 24 h, fixation of the fracture can be attempted. Irrespective of the treatment, it is essential to improve the calcium balance in the post-operative period. Supplemental calcium and vitamin D should be provided to all patients. Injectable parathyroid hormone (parathyroid hormone-related protein, 'PTHrP') supplementation can also be given to build up the bone stock. Bisphosphonates should be used cautiously, as there is an additional association between their long-term use and these fractures[12].

EXPERIENCES AND LESSONS

Epilepsy is a very common disease among the general population, and AEDs are indispensable in the treatment of these patients. The reporting of this case sheds light on osteoporosis in epileptics, as it is a common adverse effect of the long-term use of AEDs. Regular monitoring of serum calcium levels, vitamin D levels, and bone mineral density is important in the follow-up of patients on AEDs. Prophylactic supplementation of vitamin D, oral calcium, and bisphosphonates should be considered in patients on long-term AEDs. Creating awareness of this problem among patients and the physicians treating them can help to prevent such major fractures and improve the quality of life of patients on AEDs.

CONCLUSION

Simultaneous bilateral femoral neck fractures are most commonly a result of low-velocity injury in an underlying weak bone. Enzyme-inducing AEDs produce significant osteoporosis and consequent susceptibility to fracture, even from trivial

Figure 2 Patient walking unsupported at three months after the surgery.

injury. The surgical management of these fractures represents only a part of the complete treatment protocol. The main goal of medical management should include correction of the drug-induced osteoporosis. Bisphosphonates and vitamin D supplementation should be used in the post-operative period for this purpose. Replacement surgery is a good treatment modality for displaced neck fractures with delayed presentation.

Table 1 Factors associated with simultaneous bilateral femoral neck fractures

Metabolic bone disease	Systemic disorder	Drug-induced
Osteoporosis[4]	Epilepsy and electric injuries[2,20-22]	Bisphosphonates[12]
Osteomalacia[7]	Anorexia nervosa[14]	Narcotics[13]
Rickets (vitamin D deficiency/hypophosphataemic)[1]	Metastatic tumours	Antiepileptic drugs[11]
Renal osteodystrophy[6]	Endocrinopathies (hyperparathyroidism)[5]	Anti-retroviral drugs[15]
Osteogenesis imperfecta	Cerebral palsy[24]	

REFERENCES

1 **Uzun E**, Günay AE, Kızkapan TB, Mutlu M. Atraumatic diplaced bilateral femoral neck fracture in a patient with hypophosphatemic rickets in postpartum period: A missed diagnosis. *Int J Surg Case Rep* 2016; **28**: 321-324 [PMID: 27771603 DOI: 10.1016/j.ijscr.2016.10.028]

2 **Marsh JP**, Leiter JR, Macdonald P. Bilateral femoral neck fractures resulting from a grand mal seizure in an elderly man with Down syndrome. *Orthop Rev (Pavia)* 2010; **2**: e10 [PMID: 21808693 DOI: 10.4081/or.2010.e10]

3 **Upadhyay A**, Maini L, Batra S, Mishra P, Jain P. Simultaneous bilateral fractures of femoral neck in children--mechanism of injury. *Injury* 2004; **35**: 1073-1075 [PMID: 15351681 DOI: 10.1016/S0020-1383(03)00190-6]

4 **Vijayvargiya M**, Shetty V, Makwana K, Agarwal N. Bilateral simultaneous neck femur fracture following domestic fall in an elderly patient: a rare case report. *Rev Bras Ortop* 2016; **52**: 363-365 [PMID: 28702399 DOI: 10.1016/j.rboe.2016.09.002]

5 **Negishi H**, Kobayashi M, Nishida R, Yamada H, Ariga S, Sasaki F, Fujimoto S. Primary hyperparathyroidism and simultaneous bilateral fracture of the femoral neck during pregnancy. *J Trauma* 2002; **52**: 367-369 [PMID: 11835004]

6 **V S**, Patel MT, S R, D N. Simultaneous Bilateral Femur Neck Fracture in A Young Adult with Chronic Renal Failure- A Case Report and Review of Literature. *J Orthop Case Rep* 2015; **5**: 24-26 [PMID: 27299091 DOI: 10.13107/jocr.2250-0685.337]

7 **Chamseddine AH**, Alasiry AA, Zein HK. Spontaneous simultaneous bilateral femoral neck fractures secondary to osteomalacia: a case report and review of the literature. *Eur J Orthop Surg Traumatol* 2012; **22** Suppl 1: 139-143 [PMID: 26662766 DOI: 10.1007/s00590-012-0979-y]

8 **Gao YS**, Zhu ZH, Zhang CQ. Simultaneous bilateral fractures of the femoral neck caused by high energy: A case report and literature review. *Chin J Traumatol* 2015; **18**: 304-306 [PMID: 26777717 DOI: 10.1016/j.cjtee.2015.11.003]

9 **Gilban HM**, Mirdad TM, Jenyo M. Simultaneous post traumatic bilateral cervico-trochanteric femoral neck fractures in a child: a case report. *West Afr J Med* 2005; **24**: 348-349 [PMID: 16483057]

10 **Sohal HS**, Goyal D. Simultaneous bilateral femoral neck fractures after electrical shock injury: a case report. *Chin J Traumatol* 2013; **16**: 126-128 [PMID: 23540905]

11 **Sariyilmaz K**, Gulenc B, Ozkunt O, Dikici F, Yazicioglu O. Bilateral femoral neck fractures secondary to chronic carbamazepine use treated by bilateral dynamic hip screw: A case report. *Int J Surg Case Rep* 2015; **6C**: 111-113 [PMID: 25528039 DOI: 10.1016/j.ijscr.2014.12.019]

12 **Capeci CM**, Tejwani NC. Bilateral low-energy simultaneous or sequential femoral fractures in patients on long-term alendronate therapy. *J Bone Joint Surg Am* 2009; **91**: 2556-2561 [PMID: 19884427 DOI: 10.2106/JBJS.H.01774]

13 **Hootkani A**, Moradi A, Vahedi E. Neglected simultaneous bilateral femoral neck fractures secondary to narcotic drug abuse treated by bilateral one-staged hemiarthroplasty: a case report. *J Orthop Surg Res* 2010; **5**: 41 [PMID: 20579374 DOI: 10.1186/1749-799X-5-41]

14 **Hernigou J**, Koulischer S, Maes R. Bilateral Simultaneous Femoral Neck Stress Fracture Despite Clinical Recovery from Anorexia Nervosa: A Case Report. *JBJS Case Connect* 2017; **7**: e12 [PMID: 29244693 DOI: 10.2106/JBJS.CC.16.00047]

15 **Chaganty SS**, James D. Bilateral sequential femoral neck stress fractures in young adult with HIV infection on antiretroviral therapy: A case report. *World J Orthop* 2019; **10**: 247-254 [PMID: 31259148 DOI: 10.5312/wjo.v10.i6.247]

16 **Singh VK**, Singh PK, Elliot AC. Simultaneous, Bilateral Pathological Displaced Intracapsular Hip Fractures Occurring Spontaneously Secondary to Osteomalacia of Hypomagnesemic Origin: A Case Report and Review of the Literature. *Eur J Trauma Emerg Surg* 2009; **35**: 81 [PMID: 26814539 DOI: 10.1007/s00068-008-7179-9]

17 **Popescu D**, Trandabaţ C, Puha B, Veliceasa B, Alexa O. MANAGEMENT OF BILATERAL FEMORAL NECK FRACTURE IN A NONAGENARIAN PATIENT--CASE REPORT. *Rev Med Chir Soc Med Nat Iasi* 2016; **120**: 376-379 [PMID: 27483720]

18 **Nemoto O**, Kawaguchi M, Katou T. Simultaneous bilateral femoral neck stress fractures in a 24-year old male recruit: a case report. *West Indian Med J* 2013; **62**: 552-553 [PMID: 24756744 DOI: 10.7727/wimj.2012.103]

19 **Naranje S**, Sezo N, Trikha V, Kancherla R, Rijal L, Jha R. Simultaneous bilateral femoral neck stress fractures in a young military cadet: a rare case report. *Eur J Orthop Surg Traumatol* 2012; **22** Suppl 1: 103-106 [PMID: 26662758 DOI: 10.1007/s00590-011-0864-0]

20 **Grimaldi M**, Vouaillat H, Tonetti J, Merloz P. Simultaneous bilateral femoral neck fractures secondary to epileptic seizures: treatment by bilateral total hip arthroplasty. *Orthop Traumatol Surg Res* 2009; **95**: 555-557 [PMID: 19801211 DOI: 10.1016/j.otsr.2009.04.018]

21 **Yüksel HY**, Hapa O, Can M, Kürklü M. Bilateral simultaneous femoral neck fractures secondary to a post-infarct generalized tonic-clonic seizure. A case report. *Hip Int* 2010; **20**: 287-291 [PMID: 20544651]

22 **Rahman MM**, Awada A. Bilateral simultaneous hip fractures secondary to an epileptic seizure. *Saudi Med J* 2003; **24**: 1261-1263 [PMID: 14647567]

23 **Miziak B**, Błaszczyk B, Chrościńska-Krawczyk M, Danilkiewicz G, Jagiełło-Wójtowicz E, Czuczwar SJ. The problem of osteoporosis in epileptic patients taking antiepileptic drugs. *Expert Opin Drug Saf* 2014; **13**: 935-946 [PMID: 24821596 DOI: 10.1517/14740338.2014.919255]

24 **Mariani P**, Buttaro M, Comba F, Zanotti E, Ali P, Piccaluga F. Bilateral simultaneous femoral neck fracture mimicking abdominal pain in a cerebral palsy patient. *Case Rep Orthop* 2014; **2014**: 925201 [PMID: 25506016 DOI: 10.1155/2014/925201]

25 **Templin F**, Schoppmeier K. [Combined total endoprosthesis implantation in bilateral femoral neck fracture with osteogenesis imperfecta tarda]. *Unfallchirurg* 1996; **99**: 454-456 [PMID: 8767143]

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