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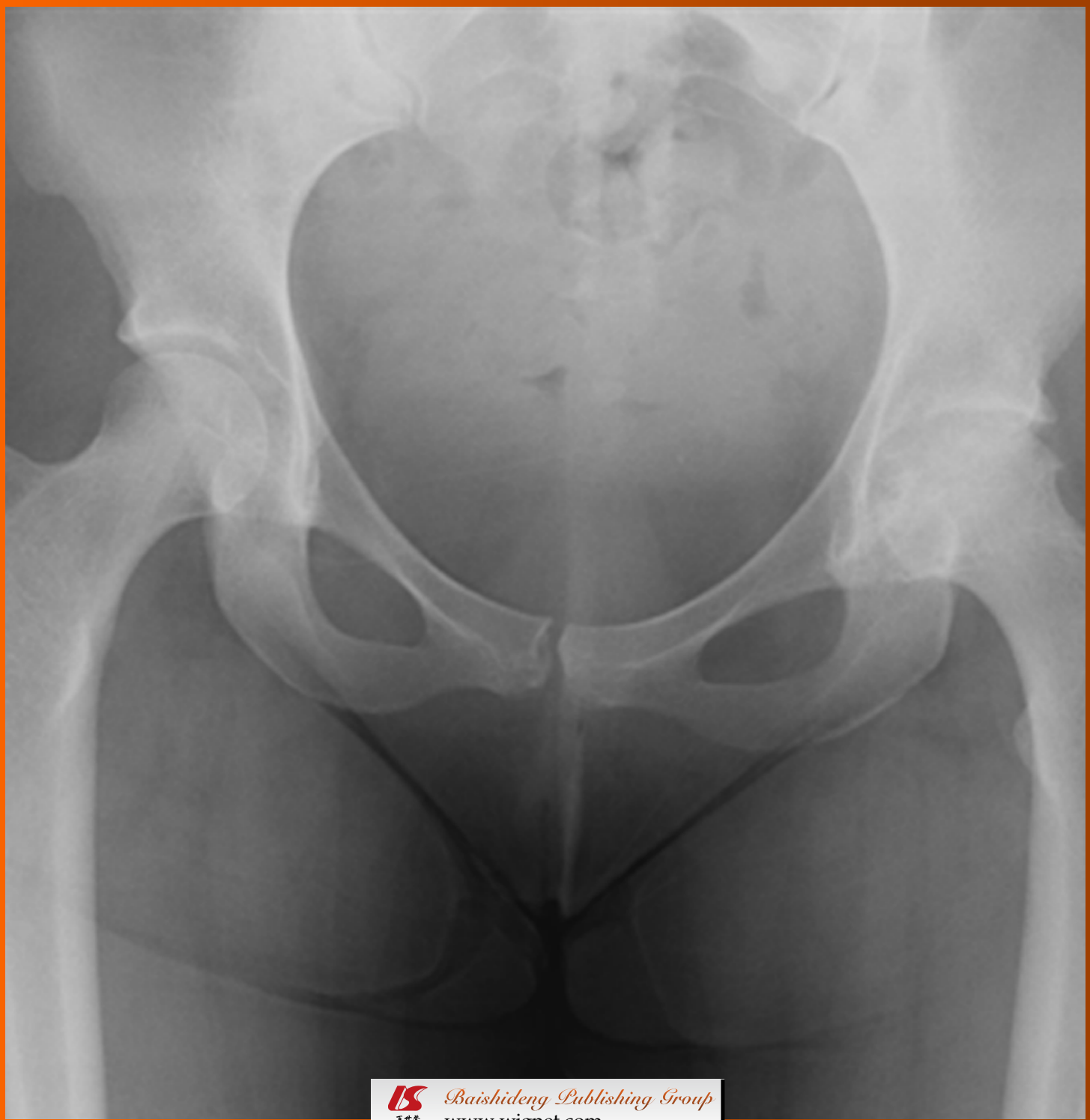

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TOPIC HIGHLIGHT

Quanjun Cui, MD, *Series Editor*

Total hip arthroplasty in developmental dysplasia of the hip: Review of anatomy, techniques and outcomes

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Abstract

Total hip arthroplasty (THA) in developmental dysplasia of the hip (DDH) presents many challenges to the reconstructive surgeon. The complex femoral and acetabular anatomy makes standard reconstruction technically challenging. Acetabular coverage can be improved by medialization of the component or augmentation of the deficient areas with bone graft. Femoral shortening osteotomies are considered in cases of severe dysplasia and frankly dislocated hips. Each patient's unique anatomy dictates what options of reconstruction are available. The functional outcomes of THA in DDH are generally excellent, though higher rates of mechanical failure have been reported in this group. This article reviews the anatomy, classification, technical considerations, and outcomes of THA in patients with DDH.

Key words: Developmental dysplasia of the hip; Total hip arthroplasty; Hip; Arthritis; Hip replacement

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INTRODUCTION

Developmental dysplasia of the hip (DDH) is a leading cause of hip arthritis in young adults. Although several non-arthroplasty options exist prior to the development of end stage osteoarthritis in these patients including proximal femoral and periacetabular osteotomies[1], total hip arthroplasty (THA) remains the standard of care when end stage osteoarthritis leads to significant pain and loss of function[2]. Abnormal contact stresses in the dysplastic hip predisposes patients with DDH to develop arthritic changes earlier than seen for patients without dysplasia[3]. There are many challenges in considering THA in patients with DDH including patient factors such as young age, distorted anatomy[4], and documented higher failure and revision rates[5].

ANATOMY

Although every patient with DDH has unique anatomy, there are well described trends seen for the acetabulum and the proximal femur. The acetabulum usually is characterized by deficiencies anterolaterally and superiorly. The proximal femur has been characterized by increased anteversion, decreased intramedullary canal size, straight contour, and either coxa vara or valga. Recent computed tomography (CT) studies have demonstrated that dys-

plastic femurs had consistently increased anteversion, shorter necks, and smaller canals than non-dysplastic femurs, and that the anterior bow of the femur displaced further distally with increasing degree of dysplasia[6]. The decreased canal width and thinner cortical diameters in dysplastic hips also may make them more prone to fracture[7]. Hence, particular attention to detail to each patient's anatomic factors need to be made prior to proceeding with THA.

Soft tissue considerations in patients with DDH are also important. Patients with severe DDH often have inefficient abductor musculature leading to limp or frank trendelenburg gait. Musculature around the hip including the adductors, hip flexors, and hip extensors are shortened due to chronic dislocation. The sciatic nerve also is prone to injury if excessive limb lengthening occurs greater than 3 cm. Sciatic nerve palsy has been reported to range from 5.2% to 13% for patients with hip dysplasia treated with arthroplasty[8].

DIAGNOSIS AND CLASSIFICATION

Patients with DDH commonly present as young patients who develop an insidious onset of activity related groin pain or lateral hip pain. Many patients have a leg length discrepancy, and the development of a limp is the most commonly reported functional loss in this population[9]. Patients with high dislocation have a decreased lever arm for the hip abductors which reduces gait efficiency and can lead to a limp. The development of advanced osteoarthritis secondary to abnormal biomechanics including acetabular rim overload eventually leads to significant pain and functional limitations necessitating THA. Radiographic evaluation confirms diagnosis and the characteristic anatomic abnormalities of the acetabulum and proximal femur.

Radiographic evaluation of the patient with DDH is essential for surgical planning. Standard radiographic series include an AP view of the pelvis and a false profile view of the hip, which conveys information regarding the amount of lateral and anterior acetabular coverage of the femoral head respectively. The center edge angle, normally > 25°, is measured as the angle between a vertical line through the center of the femoral head and a line going through the center of the head and the lateral edge of the acetabulum on an AP view of the hip. The vertical-center-anterior angle, normally > 25°, is measured similarly as the angle between a vertical line through the center of the femoral head and a line going through the center of the head and the anterior edge of the acetabulum on a false profile view of the hip[10]. An AP view of the hip also provides a general assessment of neck shaft angle of the proximal femur. CT scans are also helpful for assessment of acetabular bone stock and anteversion.

Several classification systems exist that are helpful for considering surgical treatment. The most commonly used classification scheme is that of Crowe *et al*[11] which characterizes severity based on the amount of femoral head displacement from the acetabulum as follows: Type Ⅰ: < 50% femoral head subluxation, Type Ⅱ: 50%-75% subluxation, Type Ⅲ: 75%-100% subluxation, Type IV: > 100% subluxation. This classification scheme can be used as a general guideline for the acetabular component reconstruction in THA. The Hartofilakidis classification describes three characteristic types: dysplasia in which the femoral head is contained in the true acetabulum, low dislocation in which the femoral head articulates with a false acetabulum that partially covers the true acetabulum, and high dislocation in which the femoral head does not articulate with a true or false acetabulum[12]. Many surgeons find this classification to be more practical in guiding surgical treatment.

SURGICAL TECHNIQUES

Approach

The surgical approach is often dictated by the surgeon's preference. In mildly dysplastic hips in which extensive exposure of the acetabulum is not necessary, standard approaches including anterior, anterolateral, and posterior approaches of the hip can be utilized. In cases of severe dysplasia with significant subluxation of the femoral head, a posterior approach is favored in order to gain enough exposure to the femoral head and acetabulum. Furthermore, in cases of severe dysplasia, a subtrochanteric shortening osteotomy is often needed for which a direct approach to the proximal femur can be extended from the posterior approach. Another option for severe dysplasia is a trochanteric slide osteotomy that provides excellent exposure to the acetabulum, and allows for trochanteric advancement to improve the biomechanics of the abductor mechanism.

ACETABULAR RECONSTRUCTION

In Crowe Ⅰ hips, the acetabular component can usually be placed in the true acetabulum without augmentation (Figure 1). If necessary, medialization of the cup can generally provide adequate coverage. Garvin *et al*[13] suggested that approximately 20% of the superolateral aspect of the acetabular cup could be left uncovered without significant risk for failure. However, no clear guideline exists regarding the amount of adequate acetabular cup coverage. Although cemented and press fit acetabular components can be considered in Crowe Ⅰ hips, cemented fixation is associated with higher rates of mechanical failure as discussed later.

In Crowe Ⅱ and Ⅲ dysplastic hips, the superolateral acetabular deficiency prevents placement of a standard cup due to inadequate coverage. These hips are the most challenging for reconstruction. Special components including extra small cups and metal augments may be necessary to address inadequate osseous coverage of the acetabulum. The acetabular deficiency can be addressed in one of several methods: (1) Acetabular reconstruction

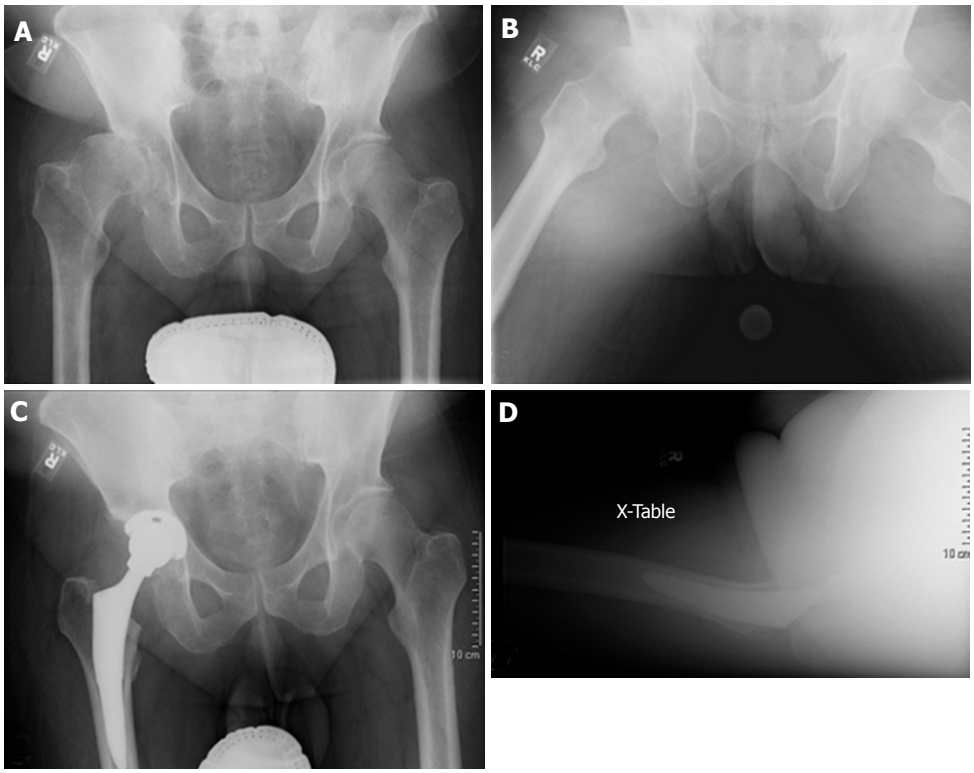

Figure 1 Treatment of Crowe I hip using an anatomic hip center. A and B: Pre-op X-rays; C and D: Post-op X-rays.

at the anatomic hip center with augmentation using bone graft or augments; (2) Medialization of the anatomic hip joint to obtain sufficient lateral coverage (Figure 2); or (3) Acetabular reconstruction at a high hip center in a false acetabulum. Acetabular augmentation with bone graft allows for more anatomic position of the cup as well as increased bone stock for future revisions. However, the use of bone grafts for acetabular augmentation is associated with significant complications including bone graft resorption, nonunion, mechanical failure of the graft, and cup loosening[14-17]. The use of bulk femoral head autograft from the resected femoral head is an effectively utilized technique in which the deficient acetabulum bone is reamed to prepare a vascular bed of bone, and the cancellous portion of the femoral head is shaped to match the convexity of the prepared area of deficient acetabulum then impacted and secured by two or more screws into the ilium[18]. With this technique, no grafts were observed to fail at 10 years. To prevent mechanical graft failure, Mulroy and Harris[14] recommended > 70% coverage of the cup by host bone, while Rodriguez *et al*[19] suggested that < 60% of structural support of the cup should be from the graft.

Medialization of the anatomic hip joint involves controlled reaming of the acetabulum through the medial acetabular wall to create enough coverage for the cup. The cortical edge of the cotyloid notch is palpated. Any intervening soft tissue in the acetabulum is removed. The anterior wall is protected during the reaming as it is hypoplastic and prone to fracture. Undersized reamers are used first to create a hemispheric acetabulum, with the appropriate degree of anteversion. The protrusio technique involves careful reaming through the medial wall until the medial periostium is seen[20]. Successful medialization allows for the use of a porous coated press fit component and avoids the use of bone graft augmentation.

It may not be feasible to recreate the anatomic hip center during reconstruction due to excessive acetabular deficiencies. In these situations, placement of the acetabular component at a high hip center in a false acetabulum can be performed using a small cementless cup affixed with screws. This technique is biomechanically unfavorable compared to anatomic hip center reconstruction, as it leads to increased joint contact forces, less mechanical advantage of the abductors, and increased rates of acetabular component loosening[21,22]. Superolateral displacement of hip center decreases the abductor moment arm by 28%[23]. If a high hip center is chosen for reconstruction, it is recommended to avoid lateral positioning of the hip center, with which Kaneuji *et al*[24] showed no acetabular loosening in their series at 10 years follow up.

In Crowe Ⅳ hips, the acetabulum is also hypoplastic, however the superior rim is less eroded than Crowe Ⅱ-Ⅲ hips. Therefore, placement of the hip in the anatomic hip center is possible using a small uncemented acetabular cup in the anatomic hip center. Augmentation with bone graft is usually not needed.

FEMORAL RECONSTRUCTION

Crowe Ⅰ and Ⅱ hips do not require femoral shortening

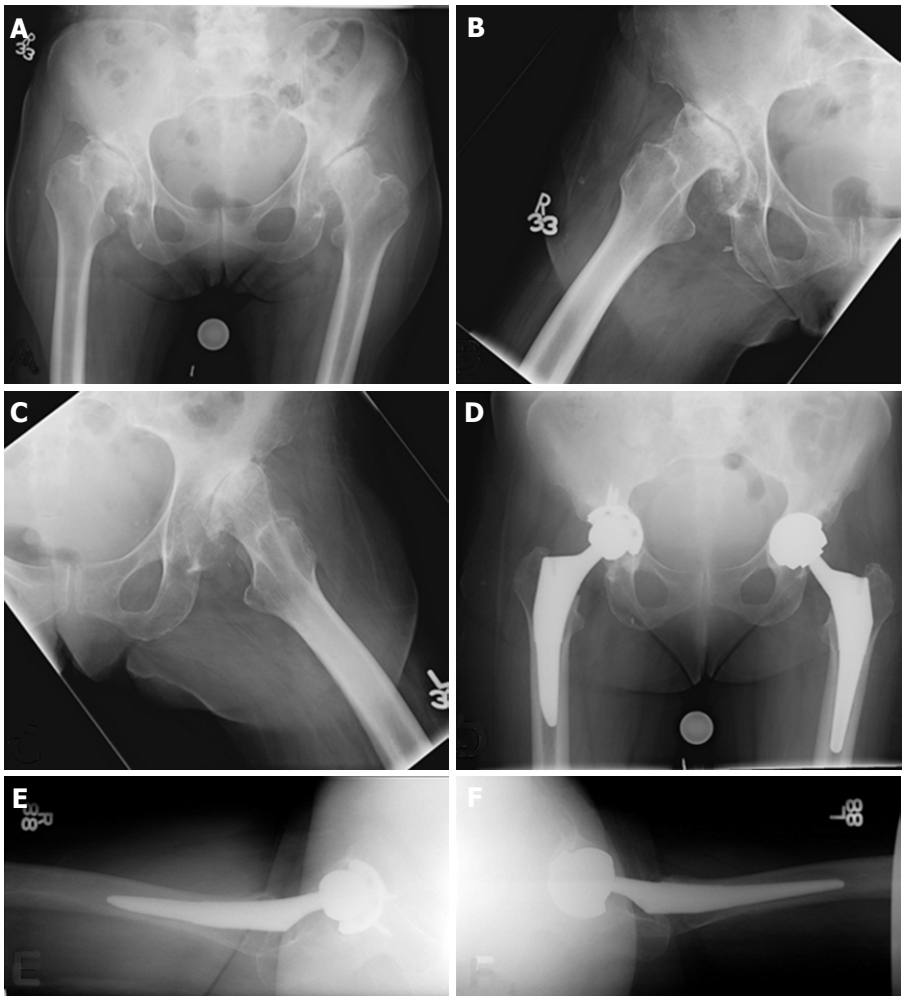

Figure 2 Treatment of Crowe II (right) and III (left) hips using an anatomic hip center with medialization. A, B and C: Pre-op X-rays; D, E and F: Post-op X-rays.

for safe positioning into the anatomic hip center. Due to the narrow medullary canal and commonly observed anteversion of the femur in hip dysplasia, both cemented narrow DDH specific femoral stems and uncemented stems can be utilized. Narrow stemmed cemented components allow for improved surgeon control of anteversion. If an uncemented press fit component is used, the surgeon must be careful to avoid excessive anteversion of the femoral component as the femur already carries some degree anteversion. Often the proximal femoral anatomy is significantly distorted, or biomechanically inadequate for fixation. In these situations, diaphyseal fixed components as well as modular components can be used. Modular components allow for easier control of anteversion. Techniques regarding use of modular systems are described elsewhere in this specific topic highlight symposium.

Femoral reconstruction of Crowe Ⅲ hips follows the same general principles as in Crowe Ⅰ and Ⅱ hips, however some may require femoral shortening if the anatomic hip center is used for reconstruction. Femoral shortening is more often the norm in Crowe Ⅳ hips, for which one of two techniques are often utilized: (1) subtrochanteric femoral shortening osteotomy with the use of an uncemented component (Figure 3); or (2) greater trochanteric osteotomy with proximal femoral shortening with the use of a cemented DDH specific stem. Recently, the second technique has fallen out of favor as subtrochanteric femoral shortening osteotomy preserves the proximal femoral metaphysis, which allows for the use of an uncemented component due to inherent rotational stability when affixed proximally. Furthermore, subtrochanteric osteotomy allows for correction of rotation, and obviates the need for trochanteric osteotomy which can be subject to nonunion. Kyrch *et al*[25] described a technique in which a subtrochanteric shortening osteotomy is considered when templating leads to limb lengthening of more than 3-4 cm. Based on templating, the osteotomy site is planned at a level distal to the metaphyseal flare of the implant though proximal enough for distal stem engagement. The femur is reamed or broached prior to the osteotomy. A lateral approach is made to the subtrochanteric femur, and a transverse osteotomy is created. A trial component is inserted to the proximal fragment, and the hip is reduced. The amount of femoral shortening can be verified intraoperatively by overlapping the two fragments, and a second cut is made on the distal fragment. The proximal edge of the

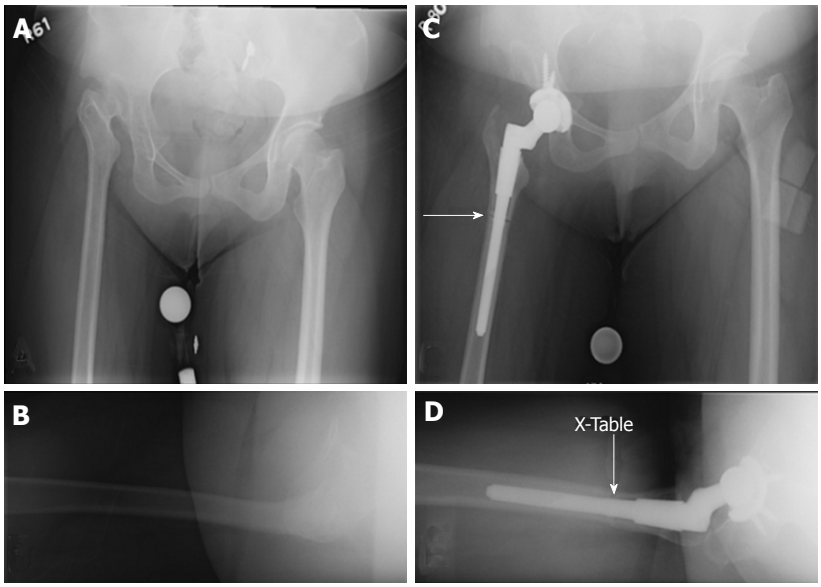

Figure 3 Treatment of Crowe IV hip using an anatomic hip center with subtrochanteric shortening osteotomy (arrow) and a modular femoral component. A and B: Pre-op X-rays; C and D: Post-op X-rays.

distal fragment is then prepared to create well opposed edges. The end of the trial component is then inserted and reduced into the distal fragment while adjusting for anteversion.

POST-OPERATIVE CARE

Postoperative care generally follows routine care for hip arthroplasty. Prophylactic anticoagulation should be initiated postoperatively to reduce the risk of deep venous thrombosis. A plan for an adequate pain control regimen to allow for postoperative mobilization should be made. Physical therapists are essential to help safely mobilize the patient after surgery. If femoral or trochanteric osteotomy was not required, then patients can bear weight as tolerated after surgery with hip restrictions based on the surgical approach. If a trochanteric osteotomy was used in Crowe IV hips for proximal femoral shortening or during the approach, trochanteric precautions should include limitations in active hip abduction for at least six weeks or until trochanteric union has been achieved. If a subtrochanteric osteotomy was used in Crowe IV hips for proximal femoral shortening, it is recommended to keep the patient toe touch weight bearing for 6-8 wk to allow for healing of the osteotomy.

OUTCOMES

Total hip arthroplasty improves both Harris hip scores and pain levels in patients with hip dysplasia. The outcomes for mildly dysplastic Crowe I and II hips are generally good, and are similar to results seen for THA in patients without dysplasia. Revision rates for THA in severely dysplastic hips, however, are significantly higher than revision rates for THA in non-dysplastic hips[2,26,27]. Patients with severe DDH may continue to walk with a limp after surgery due to the inherent abductor weakness, although overall function including walking distance, hip pain, range of motion generally improves after hip replacement. There are only a few large studies that directly compare THA outcomes in dysplastic and non-dysplastic patients. Recent studies show that short-term THA outcomes (6 mo follow-up) are similar for dysplastic and non-dysplastic hips with regards to Oxford hip score and revision rate[28]. At 15 year follow-up, however, THA revisions are 1.5-2.0 times more likely in dysplastic hips than in non-dysplastic hips[5].

Cemented acetabular reconstruction has fallen out of favor because of reported revision rates up to 37%[29-31]. Uncemented acetabular reconstruction without acetabular augmentation is now the standard of care in mildly dysplastic hips with lower rates of aseptic loosening and revision at mid to long term follow-up. When acetabular augmentation is necessary, uncemented acetabular components with augmentation have revision rates of 0-5% and aseptic loosening of up to 26% at short term follow up[15,32], while cemented components have revision rates of 10%-35% at long term follow-up[14,19,33]. The longest term follow-up of uncemented acetabular fixation in combination with bulk femoral allograft showed 94% survival at 10 years[18]. Overall, there is strong support in the literature for uncemented acetabular fixation, even when acetabular augmentation is required.

There are few reports on the outcomes of using a high hip center, which is limited by small sample size. Nevertheless, these reports show a wide range of acetabular component mechanical failure or loosening rates from 16%-83.3%[22,34,35]. Higher rates of loosening were correlated with lateral displacement of the hip center[22]. A recent report of 30 hips treated with slight elevation of the hip center without lateralization using an uncemented cup showed no evidence of loosening at

average 15.2 year follow up, which implies the potential importance of preventing lateralization when using this technique[24].

Cemented femoral reconstruction has shown more favorable results compared to acetabular reconstruction, though the results are inconsistent. Two studies with favorable results with long term follow up of at least 9.9 years showed femoral revision due to mechanical failure or loosening to range from 3%-10%[29,31]. One other study reported a 15%-40% incidence of radiographic loosening of cemented femoral components at 16 year follow-up when used in dysplastic hips[36].

Uncemented femoral components have had excellent survivorship in patients without DDH[37,38]. Nevertheless, definitive long term results in hip dysplasia are lacking. Mortazavi *et al*[39] evaluated the outcome of cementless femoral reconstruction in patients with proximal femoral deformity and found that the overall mechanical failure rate was 9% at an average four years follow up in 58 hips, though only 48.5% of hips evaluated had deformity due to dysplasia. The use of proximally fit uncemented components in hip dysplasia is challenging due to significant deformity, and often osteotomies and modular components are necessary to achieve an optimal fit.

Femoral shortening *via* proximal femoral osteotomy and distal greater trochanteric advancement can be associated with significant complications. Anwar *et al*[40] reported up to 29% nonunion of the greater trochanter, as well as increased frequency of Trendelenburg gait. Hence, recent attention has been directed towards subtrochanteric osteotomy which allows for maintenance of abductor mechanism as well as more flexibility in correcting for rotational deformities.

Short to medium term results of patients with Crowe IV hips treated with femoral shortening subtrochanteric osteotomy using uncemented components and anatomic hip center reconstruction generally show excellent healing rates of the osteotomy, ranging from 0-7%[41,42]. The overall outcome of reconstruction in these patients showed a 75% survivorship rate at 14 years follow up, with failure mostly attributable to polyethylene wear and osteolysis likely secondary to the use of older generation polyethylene components as well as thin liners[42]. A ten year follow up study also revealed improved lasting Harris hip scores in patients with dysplasia treated with modular femoral components and subtrochanteric osteotomy compared to preoperatively[43]. Long term results using newer generation highly cross linked polyethylene components need to be evaluated for this technique.

CONCLUSION

THA in patients with DDH is a complex procedure that requires an understanding of the complex acetabular and proximal femoral anatomy of each patient. The complex anatomy dictates what surgical techniques are necessary to create a mechanically stable and functional outcome. Patients can expect significant improvement in function and quality of life after THA, although complication rates are understandably higher in this patient group due to their increased complexity.

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REFERENCES

1 **Sanchez-Sotelo J**, Trousdale RT, Berry DJ, Cabanela ME. Surgical treatment of developmental dysplasia of the hip in adults: I. Nonarthroplasty options. *J Am Acad Orthop Surg* 2002; **10**: 321-333
2 **Sanchez-Sotelo J**, Berry DJ, Trousdale RT, Cabanela ME. Surgical treatment of developmental dysplasia of the hip in adults: II. Arthroplasty options. *J Am Acad Orthop Surg* 2002; **10**: 334-344
3 **Brand RA**. Hip Osteotomies: A Biomechanical Consideration. *J Am Acad Orthop Surg* 1997; **5**: 282-291
4 **Argenson JN**, Flecher X, Parratte S, Aubaniac JM. Anatomy of the dysplastic hip and consequences for total hip arthroplasty. *Clin Orthop Relat Res* 2007; **465**: 40-45
5 **Engesaeter LB**, Furnes O, Havelin LI. Developmental dysplasia of the hip--good results of later total hip arthroplasty: 7135 primary total hip arthroplasties after developmental dysplasia of the hip compared with 59774 total hip arthroplasties in idiopathic coxarthrosis followed for 0 to 15 years in the Norwegian Arthroplasty Register. *J Arthroplasty* 2008; **23**: 235-240
6 **Noble PC**, Kamaric E, Sugano N, Matsubara M, Harada Y, Ohzono K, Paravic V. Three-dimensional shape of the dysplastic femur: implications for THR. *Clin Orthop Relat Res* 2003; **417**: 27-40
7 **Perka C**, Fischer U, Taylor WR, Matziolis G. Developmental hip dysplasia treated with total hip arthroplasty with a straight stem and a threaded cup. *J Bone Joint Surg Am* 2004; **86-A**: 312-319
8 **Lewallen DG**. Neurovascular injury associated with hip arthroplasty. *Instr Course Lect* 1998; **47**: 275-283
9 **Nunley RM**, Prather H, Hunt D, Schoenecker PL, Clohisy JC. Clinical presentation of symptomatic acetabular dysplasia in skeletally mature patients. *J Bone Joint Surg Am* 2011; **93** Suppl 2: 17-21
10 **Delaunay S**, Dussault RG, Kaplan PA, Alford BA. Radiographic measurements of dysplastic adult hips. *Skeletal Radiol* 1997; **26**: 75-81
11 **Crowe JF**, Mani VJ, Ranawat CS. Total hip replacement in congenital dislocation and dysplasia of the hip. *J Bone Joint Surg Am* 1979; **61**: 15-23
12 **Hartofilakidis G**, Stamos K, Karachalios T, Ioannidis TT, Zacharakis N. Congenital hip disease in adults. Classification of acetabular deficiencies and operative treatment with acetabuloplasty combined with total hip arthroplasty. *J Bone Joint Surg Am* 1996; **78**: 683-692
13 **Garvin KL**, Bowen MK, Salvati EA, Ranawat CS. Long-term results of total hip arthroplasty in congenital dislocation and dysplasia of the hip. A follow-up note. *J Bone Joint Surg Am* 1991; **73**: 1348-1354
14 **Mulroy RD**, Harris WH. Failure of acetabular autogenous grafts in total hip arthroplasty. Increasing incidence: a follow-up note. *J Bone Joint Surg Am* 1990; **72**: 1536-1540
15 **Morsi E**, Garbuz D, Gross AE. Total hip arthroplasty with shelf grafts using uncemented cups. A long-term follow-up

study. *J Arthroplasty* 1996; **11**: 81-85
16 **Gross AE**, Catre MG. The use of femoral head autograft shelf reconstruction and cemented acetabular components in the dysplastic hip. *Clin Orthop Relat Res* 1994; **298**: 60-66
17 **Gerber SD**, Harris WH. Femoral head autografting to augment acetabular deficiency in patients requiring total hip replacement. A minimum five-year and an average seven-year follow-up study. *J Bone Joint Surg Am* 1986; **68**: 1241-1248
18 **Kim M**, Kadowaki T. High long-term survival of bulk femoral head autograft for acetabular reconstruction in cementless THA for developmental hip dysplasia. *Clin Orthop Relat Res* 2010; **468**: 1611-1620
19 **Rodriguez JA**, Huk OL, Pellicci PM, Wilson PD. Autogenous bone grafts from the femoral head for the treatment of acetabular deficiency in primary total hip arthroplasty with cement. Long-term results. *J Bone Joint Surg Am* 1995; **77**: 1227-1233
20 **Dorr LD**, Tawakkol S, Moorthy M, Long W, Wan Z. Medial protrusio technique for placement of a porous-coated, hemispherical acetabular component without cement in a total hip arthroplasty in patients who have acetabular dysplasia. *J Bone Joint Surg Am* 1999; **81**: 83-92
21 **Linde F**, Jensen J. Socket loosening in arthroplasty for congenital dislocation of the hip. *Acta Orthop Scand* 1988; **59**: 254-257
22 **Stans AA**, Pagnano MW, Shaughnessy WJ, Hanssen AD. Results of total hip arthroplasty for Crowe Type III developmental hip dysplasia. *Clin Orthop Relat Res* 1998; **348**: 149-157
23 **Delp SL**, Wixson RL, Komattu AV, Kocmond JH. How superior placement of the joint center in hip arthroplasty affects the abductor muscles. *Clin Orthop Relat Res* 1996; **328**: 137-146
24 **Kaneuji A**, Sugimori T, Ichiseki T, Yamada K, Fukui K, Matsumoto T. Minimum ten-year results of a porous acetabular component for Crowe I to III hip dysplasia using an elevated hip center. *J Arthroplasty* 2009; **24**: 187-194
25 **Krych AJ**, Howard JL, Trousdale RT, Cabanela ME, Berry DJ. Total hip arthroplasty with shortening subtrochanteric osteotomy in Crowe type-IV developmental dysplasia: surgical technique. *J Bone Joint Surg Am* 2010; **92** Suppl 1 Pt 2: 176-187
26 **Thillemann TM**, Pedersen AB, Johnsen SP, Søballe K. Implant survival after primary total hip arthroplasty due to childhood hip disorders: results from the Danish Hip Arthroplasty Registry. *Acta Orthop* 2008; **79**: 769-776
27 **Charnley J**, Feagin JA. Low-friction arthroplasty in congenital subluxation of the hip. *Clin Orthop Relat Res* 1973; **91**: 98-113
28 **Boyle MJ**, Frampton CM, Crawford HA. Early results of total hip arthroplasty in patients with developmental dysplasia of the hip compared with patients with osteoarthritis. *J Arthroplasty* 2012; **27**: 386-390
29 **MacKenzie JR**, Kelley SS, Johnston RC. Total hip replacement for coxarthrosis secondary to congenital dysplasia and dislocation of the hip. Long-term results. *J Bone Joint Surg Am* 1996; **78**: 55-61
30 **Sochart DH**, Porter ML. The long-term results of Charnley low-friction arthroplasty in young patients who have congenital dislocation, degenerative osteoarthrosis, or rheumatoid arthritis. *J Bone Joint Surg Am* 1997; **79**: 1599-1617
31 **Numair J**, Joshi AB, Murphy JC, Porter ML, Hardinge K. Total hip arthroplasty for congenital dysplasia or dislocation of the hip. Survivorship analysis and long-term results. *J Bone Joint Surg Am* 1997; **79**: 1352-1360
32 **Silber DA**, Engh CA. Cementless total hip arthroplasty with femoral head bone grafting for hip dysplasia. *J Arthroplasty* 1990; **5**: 231-240
33 **Lee BP**, Cabanela ME, Wallrichs SL, Ilstrup DM. Bone-graft augmentation for acetabular deficiencies in total hip arthroplasty. Results of long-term follow-up evaluation. *J Arthroplasty* 1997; **12**: 503-510
34 **Schutzer SF**, Harris WH. High placement of porous-coated acetabular components in complex total hip arthroplasty. *J Arthroplasty* 1994; **9**: 359-367
35 **Russotti GM**, Harris WH. Proximal placement of the acetabular component in total hip arthroplasty. A long-term follow-up study. *J Bone Joint Surg Am* 1991; **73**: 587-592
36 **Klapach AS**, Callaghan JJ, Miller KA, Goetz DD, Sullivan PM, Pedersen DR, Johnston RC. Total hip arthroplasty with cement and without acetabular bone graft for severe hip dysplasia. A concise follow-up, at a minimum of twenty years, of a previous report. *J Bone Joint Surg Am* 2005; **87**: 280-285
37 **Kim YH**. The results of a proximally-coated cementless femoral component in total hip replacement: a five- to 12-year follow-up. *J Bone Joint Surg Br* 2008; **90**: 299-305
38 **Hallan G**, Lie SA, Furnes O, Engesaeter LB, Vollset SE, Havelin LI. Medium- and long-term performance of 11,516 uncemented primary femoral stems from the Norwegian arthroplasty register. *J Bone Joint Surg Br* 2007; **89**: 1574-1580
39 **Mortazavi SM**, Restrepo C, Kim PJ, Parvizi J, Hozack WJ. Cementless femoral reconstruction in patients with proximal femoral deformity. *J Arthroplasty* 2011; **26**: 354-359
40 **Anwar MM**, Sugano N, Masuhara K, Kadowaki T, Takaoka K, Ono K. Total hip arthroplasty in the neglected congenital dislocation of the hip. A five- to 14-year follow-up study. *Clin Orthop Relat Res* 1993; **295**: 127-134
41 **Krych AJ**, Howard JL, Trousdale RT, Cabanela ME, Berry DJ. Total hip arthroplasty with shortening subtrochanteric osteotomy in Crowe type-IV developmental dysplasia. *J Bone Joint Surg Am* 2009; **91**: 2213-2221
42 **Bernasek TL**, Haidukewych GJ, Gustke KA, Hill O, Levering M. Total hip arthroplasty requiring subtrochanteric osteotomy for developmental hip dysplasia: 5- to 14-year results. *J Arthroplasty* 2007; **22**: 145-150
43 **Biant LC**, Bruce WJ, Assini JB, Walker PM, Walsh WR. Primary total hip arthroplasty in severe developmental dysplasia of the hip. Ten-year results using a cementless modular stem. *J Arthroplasty* 2009; **24**: 27-32

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TOPIC HIGHLIGHT

Quanjun Cui, MD, *Series Editor*

Osteonecrosis of the femoral head: An update in year 2012

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Abstract

Osteonecrosis is a phenomenon involving disruption to the vascular supply to the femoral head, resulting in articular surface collapse and eventual osteoarthritis. Although alcoholism, steroid use, and hip trauma remain the most common causes, several other etiologies for osteonecrosis have been identified. Basic science research utilizing animal models and stem cell applications continue to further elucidate the pathophysiology of osteonecrosis and promise novel treatment options in the future. Clinical studies evaluating modern joint-sparing procedures have demonstrated significant improvements in outcomes, but hip arthroplasty is still the most common procedure performed in these affected younger adults. Further advances in joint-preserving procedures are required and will be widely studied in the coming decade.

Key words: Osteonecrosis; Avascular necrosis; Femoral head; Total hip arthroplasty; Core decompression; Hip

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INTRODUCTION

Osteonecrosis of the femoral head, also referred to as avascular necrosis, is a pathological state with multiple possible etiologies that causes decreased vascular supply to the subchondral bone of the femoral head, resulting in osteocyte death and collapse of the articular surface. The ischemic injury upregulates tartrate-resistant acid phosphatase (TRAP)-positive osteoclasts to resorb dead trabeculae of subchondral bone[1]. These trabeculae eventually fail under the repetitive loads of weight bearing during walking and other activities[2-4].

Total hip arthroplasty (THA) is commonly utilized as a definitive treatment for high-grade osteonecrosis with articular collapse. However, as this disorder is commonly seen in young adults, joint-sparing therapeutic techniques have been studied extensively in the past decade and will be a major focus of orthopaedic research in the coming years. Osteonecrosis is undoubtedly a challenging condition to treat, but ongoing basic science and clinical investigations are progressing toward effective future treatment options.

EPIDEMIOLOGY

Approximately 5%-18% of all hip arthroplasties are completed on patients with a primary diagnosis of osteonecrosis[4-6]. Patients are generally younger adults age

35 years to 45 years, and risk factors for 75%-90% of cases include chronic steroid use, alcoholism, smoking, hip trauma including femoral neck fractures and hip dislocations, and prior hip surgery. Other potential etiologies for osteonecrosis include childhood history of slipped capital femoral epiphysis (SCFE), deep sea diving or other hyperbaric conditions, systemic lupus erythematosus (SLE) and other connective tissue disorders, autoimmune diseases causing vasculitis, sickle cell anemia, coagulopathy such as thrombophilia or disseminated intravascular coagulation, human immunodeficiency virus (HIV) infection, hyperlipidemia, fat embolus syndrome, treatment of developmental hip dysplasia, chemotherapy and/or radiation, organ transplantation, chronic liver disease, Gaucher disease, gout, and metabolic bone disease[3,4,6-10]. Males are affected up to three times more than females, and bilateral femoral head osteonecrosis is found in up to 75% of cases[3,5]. Incidence in the late 1990's was reported to be 10 000 to 20 000 new patients per year, but this incidence has almost certainly increased over the past decade[4].

PATHOPHYSIOLOGY

The blood supply to the femoral head originates primarily from the basicervical extracapsular articular ring and ascending branch of the medial femoral circumflex artery, as well as smaller secondary contributions from inferior and superior gluteal arteries and artery of the ligamentum teres[11]. The interruption of this blood supply can be multifactorial, either extravascular or intravascular. Extravascular disruption is commonly attributed to traumatic causes. Proximal femur fractures resulting in displacement of the neck affect the basicervical arterial ring, whereas hip dislocations can disrupt the ligamentum teres and cause intracapsular hematoma, making the integrity of the extracapsular ring an important factor in the survival of the femoral head. Intravascular embolic matter such as clots, lipids, immune complexes, or sickle cells can also occlude the terminal arterioles in the subchondral bone of the femoral head[2-4,12].

Regardless of the underlying etiology of osteonecrosis, several studies suggest a common pathogenic pathway involving apoptosis of osteoblasts and osteocytes[13-15]. Following infarction, oxygen- and nutrient-deprived osteocytes and marrow cells die unless they can receive blood supply from collateral circulation. As the collateral circulation supplying the epiphyses is limited, capillary arterialization may not restore sufficient blood flow to the tissues[16]. In addition to vascular compromise and programmed cell death, defective bone repair is also a key component of osteonecrosis[17]. Adipogenesis has been shown to be a causal factor in steroid- and alcohol-related osteonecrosis, as it leads to compression of venous sinusoids and congestion. The venous congestion increases intraosseous pressure, preventing adequate arterial blood flow, eventually leading to bone infarction[18,19]. In certain cases, genetic factors, such as mutations in the *COL2A1* gene, have been associated with the pathogenesis of osteonecrosis[20].

Weight bearing during walking generates loads 2 to 3 times body weight on the anterosuperior femoral head articular cartilage and superior acetabular dome and 5 to 6 times body weight during running or jumping[21]. Ischemic disruption of the weight-bearing surface in an osteonecrotic hip significantly affects a person's ability to complete pain-free activities of daily living. Infarcted subchondral bone has trabeculae that become thinned by osteoclastic activity, and the hypoxic environment does not allow for osteoblastic repair or remodeling. The area of bone necrosis becomes surrounded by a reactive, sclerotic rim, and the weakened cancellous bone eventually fails under the repetitive loads of weight bearing, leading to subchondral fracture (the "crescent sign" on radiographs). Subchondral collapse eventually leads to articular degeneration[2,22].

DIAGNOSIS AND CLASSIFICATION

Medial thigh or groin pain with limitation of hip motion in patients less than 50 years of age should raise the suspicion of osteonecrosis. Patients usually present with slow-onset, insidious groin pain that may be unilateral or bilateral. Symptoms are generally amplified with weight bearing and relieved with rest. The pain may also be in the buttocks, knees, or anterior and lateral thigh. Range of motion becomes limited, particularly hip abduction and internal rotation, and logrolling (passive internal and external rotation) elicits pain. Early stages of the disease can often be asymptomatic, and some patients present after articular surface collapse has already occurred. Hip prognosis can be significantly improved with early diagnosis, before articular collapse[4,22].

Laboratory values such as activated partial thromboplastin time (aPTT) and prothrombin time (PT) are generally normal in hip osteonecrosis, although more extensive workup of the etiology may reveal coagulopathy or inflammatory joint disease such as SLE[23]. Plain radiographs should include anteroposterior and frog-leg lateral views of both hips, as the pathology commonly also presents in the contralateral hip. Radiographs may demonstrate normal findings (Ficat stage Ⅰ) or subchondral cyst formation and sclerosis (Ficat stage Ⅱ), but more advanced disease involves femoral head flattening and subchondral collapse, as seen with the "crescent sign" (Ficat stage Ⅲ). Osteoarthritic joint space narrowing with osteophyte formation are findings of untreated osteonecrosis (Ficat stage Ⅳ)[24] (Table 1). Radiographs are highly specific for more advanced osteonecrosis (Ficat Ⅱ or Ⅲ) but not very sensitive for early changes (Ficat Ⅰ)[3].

The advent of magnetic resonance imaging (MRI) and its widespread use gave rise to the Steinberg or University of Pennsylvania osteonecrosis classification system[22,25], which differentiates subchondral collapse from femoral head articular cartilage collapse (flattening) (Table 1). Stages Ⅰ through Ⅳ are classified by percent of

Table 1 Osteoarthritic joint space narrowing with osteophyte formation findings of untreated osteonecrosis

	System		
	Ficat/Arlet	Steinberg/U Penn	ARCO
Stage Ⅰ	Normal radiographs	Normal radiographs	Normal radiographs
Stage Ⅱ	Subchondral cyst formation and sclerosis	Femoral head lucency/sclerosis	Demarcating sclerosis in femoral head, no collapse
Stage Ⅲ	Femoral head flattening, subchondral collapse, "crescent sign"	Subchondral collapse without femoral head flattening, "crescent sign"	Femoral head collapse, "crescent sign", no joint space narrowing
ⅢA			Collapse < 3 mm
ⅢB			Collapse > 3 mm
Stage Ⅳ	Osteoarthritic joint space narrowing, degenerative changes	Subchondral collapse, femoral head flattening, normal joint space	Osteoarthritic degenerative changes
Stage Ⅴ		Flattening with joint space narrowing, acetabular changes, or both	
Stage Ⅵ		Advanced degenerative changes, secondary osteoarthritis	

ARCO: Association Research Circulation Osseous.

femoral head involvement: A < 15%, B 15%-30%, C > 30%. These size modifiers are considered predictors of femoral head collapse. Small lesion size and more medial location are considered prognostically favorable[25].

Another commonly used classification system that utilizes MRI and other radiographic modalities is the Association Research Circulation Osseous (ARCO) staging system, which was introduced in 1992 and is summarized in Table 1[26].

MRI has become the imaging modality of choice, as it is highly sensitive and specific for osteonecrosis[3]. T1 images on MRI typically demonstrate a serpiginous "band-like" lesion with low signal intensity in the anterosuperior femoral head, and a "double-line sign" can be seen on T2 sequences, which depicts a high signal intensity reparative interface of vascular reactive bone adjacent to necrotic subchondral bone[3]. Radionuclide bone scans are less sensitive and specific than MRI but can be used to detect inflammatory activity in the femoral head when MRI is contraindicated. CT is also less sensitive than MRI in detecting osteonecrosis and has a significant radiation burden. Angiography and biopsy are invasive methods to confirm osteonecrosis and therefore are only used as research modalities[25,27].

CURRENT TREATMENT OPTIONS

Non-operative treatments for osteonecrosis include measures to offload force on the affected hip by limiting weight bearing with a cane or walker, activity modification, and physical therapy. However, these methods have no role in treatment of late stage osteonecrosis and show limited success in preventing disease progression, even in early stage (Steinberg stage Ⅰ and Ⅱ) disease[9,28]. Patients can be encouraged to abstain from or decrease alcohol consumption and smoking[29]. Other conservative options include lipid-reducing agents, bisphosphonates, and hyperbaric oxygen, but these therapies have minimal utility after subchondral collapse has occurred in the femoral head, as seen in a meta-analysis when compared with core decompression[30].

Core decompression is a commonly used prophylactic surgery used in pre-collapse osteonecrosis (prior to Ficat and ARCO stage Ⅱ, Steinberg stage Ⅲ), in which necrotic cancellous bone in the femoral head is drilled and removed from a lateral femoral cortical entry point (Figure 1). This is often stabilized with structural allograft or with autograft by harvesting cancellous bone from the greater trochanter and proximal femur. This cancellous graft contains osteoprogenitor cells that aid in healing. The results for core decompression alone generally deteriorate with more advanced lesions[27]. However, augmentation of the core decompression can be achieved with the addition of bone morphogenic proteins, electromagnetic stimulation, or demineralized bone matrix[27,31]. Although core decompression for Steinberg stage I disease was successful as a definitive procedure in > 80% of patients, Steinberg stage Ⅱ and Ⅲ osteonecrosis treated with decompression required further surgical reconstructive intervention in 37% and 71% of patients, respectively[28,30]. Multiple drilling of the femoral head osteonecrotic lesion can be an alternative, and comparable results have been reported[32]. Another biologic option that has met with some success is the harvesting and *in vitro* culture of autologous mesenchymal stem cells (MSCs) and reimplantation in the core decompression site[33,34]. Studies of the long-term success of using bone morphogenic proteins and autologous MSCs are still underway[35].

Vascularized fibular graft supplementation during core decompression and other salvage procedures has also been studied extensively and implemented for higher stages of osteonecrosis. These grafts deter progression of pre-collapse (Steinberg stage Ⅰ and Ⅱ) lesions and can also delay the development of end stage osteonecrosis after mild collapse (Steinberg stage Ⅲ through Ⅴ) has occurred. The cortical graft not only offers structural stability, but also biologic incorporation, as the vascularized bone promotes callus formation and remodeling in the femoral head[36-39]. Although certain methods such as the patient-specific Ioannina aiming device increase optimal graft placement in the anterosu-

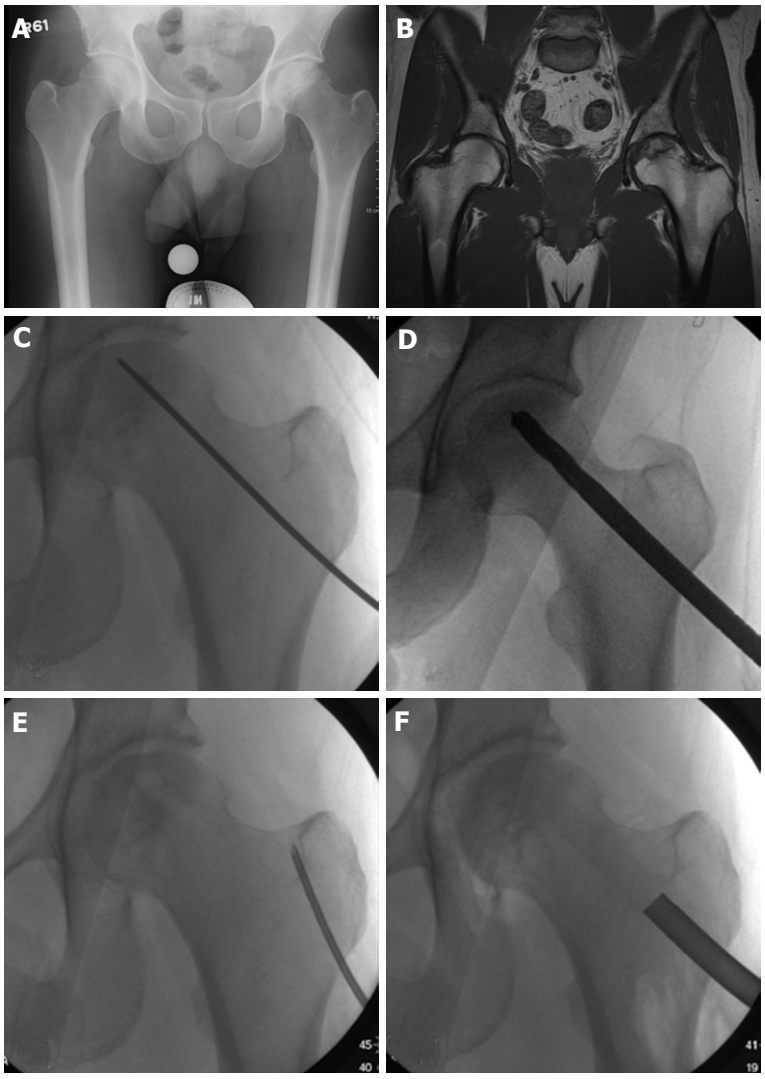

Figure 1 Forty-one year old male with pre-collapse osteonecrosis of left femoral head as evidenced by (A) plain radiograph and (B) magnetic resonance imaging of pelvis. Patient underwent core decompression: (C) Kirschner wire to localize to affected subchondral bone; D: Drilling of lesion; E: Aspiration of bone marrow from cancellous bone in greater trochanter; F: Insertion of bone graft mixed with bone marrow aspirate.

perior aspect of the femoral head, vascularized grafting still remains technically challenging[40]. Non-vascularized fibular grafts have also been studied as an alternative, but vascularized grafts appear to have better clinical results for prevention of femoral head collapse[41].

Several osteotomies have been studied for the treatment of pre-collapse and early post-collapse (Steinberg stage II to IV) osteonecrosis, with the goal of transferring weight-bearing forces away from necrotic subchondral bone toward other areas of the articular surface. These include flexion, extension, varus, valgus, rotation, or combined osteotomies, and subtrochanteric and intertrochanteric osteotomies have also been described[42-45]. These procedures have met with favorable success rates but can have a moderate risk of nonunion, and they can make conversion to total hip arthroplasty more difficult.

The emergence of hip arthroscopy has improved surgeons' ability to visualize and quantify or stage the degree of chondrosis in osteonecrosis[46]. Small-diameter core decompression has been described as an arthroscopic procedure for early stages[47], but arthroscopy is not considered an effective option to treat advanced osteonecrosis.

Advanced osteonecrosis with significant arthrosis is commonly treated with prosthetic replacement, including femoral resurfacing arthroplasty, hemiarthroplasty, and THA. THA has excellent clinical results for pain relief and functional improvement, but these reconstructive arthroplasties in young patients can be problematic, as they are often associated with early failure from loosening and other complications[48-51].

Femoral resurfacing can be used in younger patients with osteonecrosis involving less than one third of the femoral head, and this arthroplasty option has been studied and used more outside of the United States. Technical issues with these implants have been associated in the past with femoral neck fracture, high failure rate, and conversion to THA[48,52]. Newer designs and uncemented implants have yielded more favorable results, but other complications such as ionic metal wear in metal-on-

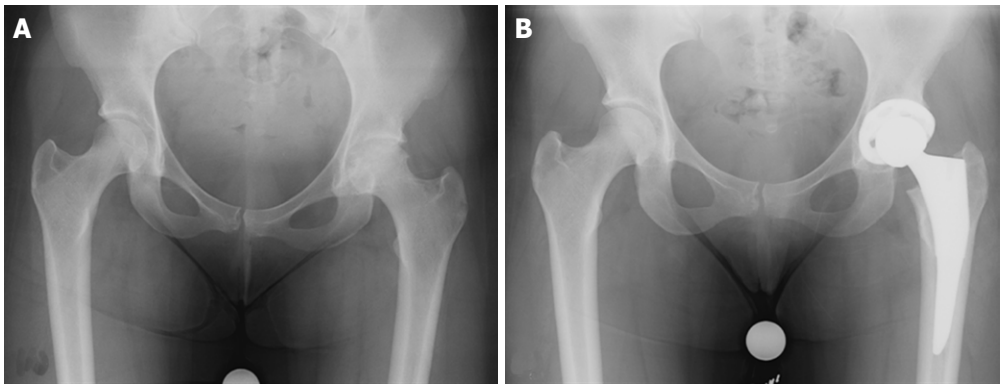

Figure 2 Forty-eight year old female with osteonecrotic left femoral head, with evidence of left hip osteoarthritis (A). Patient underwent left uncemented total hip arthroplasty (B).

metal implants can still occur[53]. Hemiarthroplasty with unipolar or bipolar implants have been utilized but by design do not address pathology at the acetabular surface in late-stage osteonecrosis and are also associated with wear, loosening, groin pain, and conversion to THA[48]; therefore hemiarthroplasty is not recommended.

Ultimately, advanced osteonecrosis and failure of the other aggressive interventions mentioned above may necessitate total hip arthroplasty. THA is the most commonly performed procedure for Ficat and ARCO stage Ⅲ and Ⅳ (Steinberg stage Ⅳ to Ⅵ) osteonecrosis and is highly successful for symptomatic improvement[49,50] (Figure 2). The durability of THA, however, is inferior to the same procedure performed for osteoarthritis, as patients with osteonecrosis are generally younger and have higher functional demands[54]. Associated comorbidities such as alcohol abuse and inflammatory disorders associated with steroid use such as SLE may also contribute to the inferior outcomes. Cemented THA has been documented to have higher complication rates relative to cementless prosthesis with improved modern press-fit designs[55]. THA complications in osteonecrosis include infection (particularly in SLE, sickle cell, and immunocompromised patients), high risk of dislocation (notably in alcohol abusers), compromise in soft tissue healing, and implant loosening. Despite these risk factors and potential complications, however, modern advancements in hip arthroplasty over the past decade have improved outcomes of THA in osteonecrosis, as seen in a recent meta-analysis by Myers *et al*[51].

In summary, there are several pre-collapse treatment options available for symptomatic osteonecrosis; however, the majority of patients progress to advanced stages with articular collapse, requiring total hip arthroplasty. The future of osteonecrosis treatment depends on finding alternative joint-sparing procedures and treatments to delay the need for hip arthroplasty. Basic science and clinical research in this field over the past decade has focused on developing animal models to understand pathophysiologic mechanisms, as well as testing novel growth factor- and cell-based therapeutic options that may prevent or postpone the progression of osteonecrosis.

UPDATE ON BENCH RESEARCH AND CLINICAL APPLICATIONS

As the research and development of new osteonecrosis treatments are continuously being explored, one of the limiting factors that prevents the systemic evaluation of the effectiveness of the treatments is the lack of an animal model that replicates the natural history and progression of osteonecrosis in humans. Nevertheless, several animal models have been developed to evaluate various treatment strategies. Vascular damage is a crucial event in trauma-induced osteonecrosis, and many animal models have attempted to mimic this injury by surgically inducing vascular deprivation. A rat osteonecrosis model in which the femoral head is temporarily dislocated after the ligamentum teres is cut is the most common surgical osteonecrosis model[56-58]. An adult rabbit model of traumatic osteonecrosis has been established by complete surgical removal of the hip joint capsule followed by circumferential cauterization of the periosteum and blood vessels covering the femoral neck to interrupt the blood supply to the femoral head[59]. Cryogenic and thermal insults have been used to induce osteonecrosis in quadrupeds such as canines[60] and bipeds such as emus[61]. Intramuscular injection of methylprednisolone has been used to develop steroid-induced osteonecrosis in mouse[62], rat[63], rabbit[64,65], pig[66], and chicken models[18], where the percent incidence of induced osteonecrosis is dependent on the amount of methylprednisolone injected. These animal models have been used to study the molecular mechanisms of osteonecrosis and assess the usefulness of several therapies over the last few decades.

Some of the more recent efforts in treatment development have focused on the use of cellular therapies for osteonecrosis. In one study, CD34+ cells, known to be both vasculogenic and osteogenic, were intravenously transplanted after G-CSF mobilization in a rat model, resulting in improved outcomes[67]. Since it has been reported that MSC proliferation is affected during

osteonecrosis[68], several studies have attempted to treat osteonecrosis by transplanting MSCs either systemically or locally in various animal models. Li *et al*[69] investigated the efficacy of giving allogeneic MSCs derived from the bone marrow to rabbits with heat-induced femoral head necrosis and showed the directional migration of GFP-labeled MSCs to the defect site. Yan *et al*[70] showed that transplanted MSCs differentiated into osteoblasts and aided in the repair process of traumatic osteonecrosis in a skeletally mature canine model. Another recent study evaluated the effectiveness of biphasic calcium phosphate (BCP) ceramic scaffolds seeded with MSCs on inducing osteointegration and new bone formation in a canine model[71]. These studies indicate the efficacy of exogenous stem cells in osteonecrosis treatment. Early trials outside the United States have also utilized MSCs in humans and preliminarily show good results. For instance, the percutaneous injection of autologous adipose-derived MSCs with hyaluronic acid, platelet-rich plasma, and calcium chloride demonstrate MRI evidence of improvement in osteonecrosis and cartilage regeneration[72]. However, this is an uncontrolled clinical trial, and further study is needed.

Another branch of osteonecrosis research has focused on the effectiveness of bisphosphonates, growth factors, lipid-lowering agents, and combined drug therapies. Lipid-lowering drugs such as statins decrease the incidence of steroid-induced osteonecrosis[73,74]. Other studies have also shown that the simultaneous use of anticoagulants along with lipid-lowering agents can decrease the prevalence of steroid-induced osteonecrosis in rabbits[75,76]. Bisphosphonates, used regularly for the treatment of osteoporosis and other pathologic conditions of bone, have been found to be promising for clinically treating osteonecrosis to postpone surgical interventions[77]. Lai *et al*[78] developed a randomized study that showed that alendronate delays or prevents progression of femoral head collapse in Steinberg stage Ⅱ and Ⅲ disease, and may ultimately reduce the need for joint arthroplasty, although longer term follow-up was needed. Agarwala *et al*[79] showed that a daily dose of alendronate resulted in improved hip function and decreased dependency on nonsteroidal antiinflammatory drugs over a period of 2.5 years. In addition, there was decreased femoral head edema on MRI, suggesting slower progression of osteonecrosis. Along with preservation, it is crucial that the bone undergoes remodeling during osteonecrosis. While bisphosphonates have been known to do the former, Vandermeer *et al*[80] show that combining these drugs with bone morphogenetic protein-2 improved the epiphyseal quotient and trabecular bone remodeling in immature pigs that had surgically-induced ischemic ON. The impact of such combination drug therapies is yet to be fully evaluated in human subjects.

On the surgical forefront, clinical studies have scrutinized older techniques and evaluated novel techniques for treatment of osteonecrosis. Transtrochanteric rotational osteotomy has historically demonstrated variable success for avoidance of femoral head collapse[43,45,81]. Exploration of the risk factors revealed that higher age, higher BMI, and higher stages of osteonecrosis were determinants of likelihood of conversion of osteotomies to THA[82]. These factors can be useful during patient selection for joint-sparing procedures. Advancements in hip resurfacing have made this procedure a viable option in younger patients under the age of 25 years and can help reduce the need for THA, but there are still risks of ionic wear, fracture, and loosening[83]. Total hip arthroplasty itself has undergone technical improvements over the last two decades, and implant survival is significantly higher. Uncemented ceramic-on-ceramic THA has demonstrated some promise for improved outcomes and implant durability in younger patients[84].

Improvements in microsurgical techniques have enhanced outcomes for free vascularized fibula grafting to the osteonecrotic hip. This procedure has been shown to be successful for younger patients in pre-collapse stages and generally delays the need for THA, even in post-collapse osteonecrosis[85]. Other grafting techniques, such as bone graft pedicled with quadratus femoris in a titanium mesh, have also been developed, but long-term effectiveness has not yet been studied[86]. Augmentation of core decompression with porous tantalum rods has also been explored as a treatment method for early stages of osteonecrosis, with some favorable results; however, the release of high-density metal particles as well as progression to femoral head collapse are frequent complications[87]. Other clinical trials involving the use of trabecular metal rods[88] and mesh cages[86] have also been published.

CONCLUSION

Osteonecrosis is a pathology commonly seen in younger adults, in which collapse of the femoral head and early onset of osteoarthritis may eventually necessitate hip arthroplasty when non-operative measures and joint-sparing procedures fail. Basic science research to understand the pathophysiology and to develop therapies that can be translated to clinical application has progressed rapidly, and these advances offer great promise for the future treatment of osteonecrosis. Similarly, technological improvements in surgical treatment methods have also improved outcomes over the past two decades and will continue to help patients recover from this functionally debilitating joint disease.

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REFERENCES

1 **Li W**, Sakai T, Nishii T, Nakamura N, Takao M, Yoshikawa H, Sugano N. Distribution of TRAP-positive cells and ex-

pression of HIF-1alpha, VEGF, and FGF-2 in the reparative reaction in patients with osteonecrosis of the femoral head. *J Orthop Res* 2009; **27**: 694-700
2 **Lavernia CJ**, Sierra RJ, Grieco FR. Osteonecrosis of the femoral head. *J Am Acad Orthop Surg* 1999; **74**: 250-261
3 **Malizos KN**, Karantanas AH, Varitimidis SE, Dailiana ZH, Bargiotas K, Maris T. Osteonecrosis of the femoral head: etiology, imaging and treatment. *Eur J Radiol* 2007; **63**: 16-28
4 **Mont MA**, Hungerford DS. Non-traumatic avascular necrosis of the femoral head. *J Bone Joint Surg Am* 1995; **77**: 459-474
5 **Mankin HJ**. Nontraumatic necrosis of bone (osteonecrosis). *N Engl J Med* 1992; **326**: 1473-1479
6 **Vail TP**, Covington DB. The incidence of osteonecrosis. In: Osteonecrosis: Etiology, Diagnosis, Treatment. Rosemont, IL: American Academy of Orthopedic Surgeons; 1997: 43-49
7 **Larson AN**, McIntosh AL, Trousdale RT, Lewallen DG. Avascular necrosis most common indication for hip arthroplasty in patients with slipped capital femoral epiphysis. *J Pediatr Orthop* 2010; **30**: 767-773
8 **Luedtke LM**, Flynn JM, Pill SG. A review of avascular necrosis in developmental dysplasia of the hip and contemporary efforts at prevention. *Univ Penn Orthop J* 2000; **13**: 22-28
9 **Mont MA**, Zywiel MG, Marker DR, McGrath MS, Delanois RE. The natural history of untreated asymptomatic osteonecrosis of the femoral head: a systematic literature review. *J Bone Joint Surg Am* 2010; **92**: 2165-2170
10 **Morse CG**, Mican JM, Jones EC, Joe GO, Rick ME, Formentini E, Kovacs JA. The incidence and natural history of osteonecrosis in HIV-infected adults. *Clin Infect Dis* 2007; **44**: 739-748
11 **Grose AW**, Gardner MJ, Sussmann PS, Helfet DL, Lorich DG. The surgical anatomy of the blood supply to the femoral head: description of the anastomosis between the medial femoral circumflex and inferior gluteal arteries at the hip. *J Bone Joint Surg Br* 2008; **90**: 1298-1303
12 **Jones JP**. Fat embolism, intravascular coagulation, and osteonecrosis. *Clin Orthop Relat Res* 1993; **292**: 294-308
13 **Calder JD**, Buttery L, Revell PA, Pearse M, Polak JM. Apoptosis--a significant cause of bone cell death in osteonecrosis of the femoral head. *J Bone Joint Surg Br* 2004; **86**: 1209-1213
14 **Weinstein RS**, Nicholas RW, Manolagas SC. Apoptosis of osteocytes in glucocorticoid-induced osteonecrosis of the hip. *J Clin Endocrinol Metab* 2000; **85**: 2907-2912
15 **Youm YS**, Lee SY, Lee SH. Apoptosis in the osteonecrosis of the femoral head. *Clin Orthop Surg* 2010; **2**: 250-255
16 **Bejar J**, Peled E, Boss JH. Vasculature deprivation--induced osteonecrosis of the rat femoral head as a model for therapeutic trials. *Theor Biol Med Model* 2005; **2**: 24
17 **Assouline-Dayan Y**, Chang C, Greenspan A, Shoenfeld Y, Gershwin ME. Pathogenesis and natural history of osteonecrosis. *Semin Arthritis Rheum* 2002; **32**: 94-124
18 **Cui Q**, Wang GJ, Su CC, Balian G. The Otto Aufranc Award. Lovastatin prevents steroid induced adipogenesis and osteonecrosis. *Clin Orthop Relat Res* 1997; **344**: 8-19
19 **Wang GJ**, Sweet DE, Reger SI, Thompson RC. Fat-cell changes as a mechanism of avascular necrosis of the femoral head in cortisone-treated rabbits. *J Bone Joint Surg Am* 1977; **59**: 729-735
20 **Kannu P**, O'Rielly DD, Hyland JC, Kokko LA. Avascular necrosis of the femoral head due to a novel C propeptide mutation in COL2A1. *Am J Med Genet A* 2011; **155A**: 1759-1762
21 **van den Bogert AJ**, Read L, Nigg BM. An analysis of hip joint loading during walking, running, and skiing. *Med Sci Sports Exerc* 1999; **31**: 131-142
22 **Steinberg ME**. Avascular necrosis: diagnosis, staging, and management. *J Musculoskel Med* 1997; **14**: 13-25
23 **Jones LC**, Mont MA, Le TB, Petri M, Hungerford DS, Wang P, Glueck CJ. Procoagulants and osteonecrosis. *J Rheumatol* 2003; **30**: 783-791
24 **Arlet J**, Ficat P. [Non-traumatic avascular femur head necrosis. New methods of examination and new concepts]. *Chir Narzadow Ruchu Ortop Pol* 1977; **42**: 269-276
25 **Steinberg ME**. Diagnostic imaging and the role of stage and lesion size in determining outcome in osteonecrosis of the femoral head. *Techniques in Orthopaedics* 2001; **16**: 6-15
26 ARCO (Association Research Circulation Osseous): committee on terminology and classification. *ARCO News* 1992; **4**: 41-46
27 **McGrory BJ**, York SC, Iorio R, Macaulay W, Pelker RR, Parsley BS, Teeny SM. Current practices of AAHKS members in the treatment of adult osteonecrosis of the femoral head. *J Bone Joint Surg Am* 2007; **89**: 1194-1204
28 **Mont MA**, Carbone JJ, Fairbank AC. Core decompression versus nonoperative management for osteonecrosis of the hip. *Clin Orthop Relat Res* 1996; **324**: 169-178
29 **Hirota Y**, Hirohata T, Fukuda K, Mori M, Yanagawa H, Ohno Y, Sugioka Y. Association of alcohol intake, cigarette smoking, and occupational status with the risk of idiopathic osteonecrosis of the femoral head. *Am J Epidemiol* 1993; **137**: 530-538
30 **Castro FP**, Barrack RL. Core decompression and conservative treatment for avascular necrosis of the femoral head: a meta-analysis. *Am J Orthop (Belle Mead NJ)* 2000; **29**: 187-194
31 **Ciombor DM**, Aaron RK. Biologically augmented core decompression for the treatment of osteonecrosis of the femoral head. *Techniques in Orthopaedics* 2001; **16**: 32-38
32 **Song WS**, Yoo JJ, Kim YM, Kim HJ. Results of multiple drilling compared with those of conventional methods of core decompression. *Clin Orthop Relat Res* 2007; **454**: 139-146
33 **Gangji V**, Toungouz M, Hauzeur JP. Stem cell therapy for osteonecrosis of the femoral head. *Expert Opin Biol Ther* 2005; **5**: 437-442
34 **Hernigou P**, Beaujean F. Treatment of osteonecrosis with autologous bone marrow grafting. *Clin Orthop Relat Res* 2002; **405**: 14-23
35 **Hauzeur JP**, Gangji V. Phases 1-3 clinical trials using adult stem cells in osteonecrosis and nonunion fractures. *Stem Cells Int* 2010; **2010**: 410170
36 **Brannon JK**. Influence of acetabular coverage on hip survival after free vascularized fibular grafting for femoral head osteonecrosis. *J Bone Joint Surg Am* 2007; **89**: 448-49; author reply 448-49;
37 **Katz MA**, Urbaniak JR. Free vascularized fibular grafting of the femoral head for the treatment of osteonecrosis. *Techniques in Orthopaedics*. 2001; **16**: 44-60
38 **Malizos KN**, Soucacos PN, Beris AE. Osteonecrosis of the femoral head. Hip salvaging with implantation of a vascularized fibular graft. *Clin Orthop Relat Res* 1995; **314**: 67-75
39 **Urbaniak JR**, Coogan PG, Gunneson EB, Nunley JA. Treatment of osteonecrosis of the femoral head with free vascularized fibular grafting. A long-term follow-up study of one hundred and three hips. *J Bone Joint Surg Am* 1995; **77**: 681-694
40 **Beris AE**, Soucacos PN. Optimizing free fibular grafting in femoral head osteonecrosis: the Ioannina aiming device. *Clin Orthop Relat Res* 2001; **386**: 64-70
41 **Kim SY**, Kim YG, Kim PT, Ihn JC, Cho BC, Koo KH. Vascularized compared with nonvascularized fibular grafts for large osteonecrotic lesions of the femoral head. *J Bone Joint Surg Am* 2005; **87**: 2012-2018
42 **Atsumi T**, Muraki M, Yoshihara S, Kajihara T. Posterior rotational osteotomy for the treatment of femoral head osteonecrosis. *Arch Orthop Trauma Surg* 1999; **119**: 388-393
43 **Langlais F**, Fourastier J. Rotation osteotomies for osteonecrosis of the femoral head. *Clin Orthop Relat Res* 1997; **343**: 110-123
44 **Sugioka Y**. Transtrochanteric anterior rotational osteotomy of the femoral head in the treatment of osteonecrosis affect-

ing the hip: a new osteotomy operation. *Clin Orthop Relat Res* 1978; **130**: 191-201
45 **Sugioka Y**, Hotokebuchi T, Tsutsui H. Transtrochanteric anterior rotational osteotomy for idiopathic and steroid-induced necrosis of the femoral head. Indications and long-term results. *Clin Orthop Relat Res* 1992; **277**: 111-120
46 **Sekiya JK**, Ruch DS, Hunter DM, Pope TL, Koman LA, Poehling GG, Russell GB. Hip arthroscopy in staging avascular necrosis of the femoral head. *J South Orthop Assoc* 2000; **9**: 254-261
47 **Wang ZG**, Wang Y, Liu YJ, Li ZL, Cai X, Wei M. [Clinical evaluation of small diameter decompression and arthroscopy in the treatment of early avascular necrosis of femoral head]. *Zhonghua YiXue ZaZhi* 2007; **87**: 2041-2044
48 **Ivankovich DA**, Rosenberg AG, Malamis A. Reconstructive options for osteonecrosis of the femoral head. *Techniques in Orthopaedics* 2001; **16**: 66-79
49 **Lieberman JR**, Berry DJ, Mont MA, Aaron RK, Callaghan JJ, Rajadhyaksha AD, Urbaniak JR. Osteonecrosis of the hip: management in the 21st century. *Instr Course Lect* 2003; **52**: 337-355
50 **Mont MA**, Rajadhyaksha AD, Hungerford DS. Outcomes of limited femoral resurfacing arthroplasty compared with total hip arthroplasty for osteonecrosis of the femoral head. *J Arthroplasty* 2001; **16**: 134-139
51 **Myers TG**, Mihalko WM, Brown TE, Saleh KJ, Cui Q. Outcomes of total hip arthroplasty for osteonecrosis of the hip: systematic review and meta-analysis. *Curr Orthop Practice* 2010; **21**: 81-88
52 **Squire M**, Fehring TK, Odum S, Griffin WL, Bohannon Mason J. Failure of femoral surface replacement for femoral head avascular necrosis. *J Arthroplasty* 2005; **20**: 108-114
53 **DeSouza RM**, Parsons NR, Oni T, Dalton P, Costa M, Krikler S. Metal ion levels following resurfacing arthroplasty of the hip: serial results over a ten-year period. *J Bone Joint Surg Br* 2010; **92**: 1642-1647
54 **Xenakis TA**, Beris AE, Malizos KK, Koukoubis T, Gelalis J, Soucacos PN. Total hip arthroplasty for avascular necrosis and degenerative osteoarthritis of the hip. *Clin Orthop Relat Res* 1997; **341**: 62-68
55 **Ritter MA**, Helphinstine J, Keating EM, Faris PM, Meding JB. Total hip arthroplasty in patients with osteonecrosis. The effect of cement techniques. *Clin Orthop Relat Res* 1997; **338**: 94-99
56 **Levin D**, Norman D, Zinman C, Rubinstein L, Sabo E, Misselevich I, Reis D, Boss JH. Treatment of experimental avascular necrosis of the femoral head with hyperbaric oxygen in rats: histological evaluation of the femoral heads during the early phase of the reparative process. *Exp Mol Pathol* 1999; **67**: 99-108
57 **Peled E**, Bejar J, Zinman C, Boss JH, Reis DN, Norman D. Prevention of distortion of vascular deprivation-induced osteonecrosis of the rat femoral head by treatment with alendronate. *Arch Orthop Trauma Surg* 2009; **129**: 275-279
58 **Vadasz Z**, Misselevich I, Norman D, Peled E, Boss JH. Localization of vascular endothelial growth factor during the early reparative phase of the rats' vessels deprivation-induced osteonecrosis of the femoral heads. *Exp Mol Pathol* 2004; **77**: 145-148
59 **Hofstaetter JG**, Wang J, Yan J, Glimcher MJ. The effects of alendronate in the treatment of experimental osteonecrosis of the hip in adult rabbits. *Osteoarthritis Cartilage* 2009; **17**: 362-370
60 **Conzemius MG**, Brown TD, Zhang Y, Robinson RA. A new animal model of femoral head osteonecrosis: one that progresses to human-like mechanical failure. *J Orthop Res* 2002; **20**: 303-309
61 **Malizos KN**, Quarles LD, Seaber AV, Rizk WS, Urbaniak JR. An experimental canine model of osteonecrosis: characterization of the repair process. *J Orthop Res* 1993; **11**: 350-357
62 **Yang L**, Boyd K, Kaste SC, Kamdem Kamdem L, Rahija RJ, Relling MV. A mouse model for glucocorticoid-induced osteonecrosis: effect of a steroid holiday. *J Orthop Res* 2009; **27**: 169-175
63 **Han N**, Yan Z, Guo CA, Shen F, Liu J, Shi Y, Zhang Z. Effects of p-glycoprotein on steroid-induced osteonecrosis of the femoral head. *Calcif Tissue Int* 2010; **87**: 246-253
64 **Iwakiri K**, Oda Y, Kaneshiro Y, Iwaki H, Masada T, Kobayashi A, Asada A, Takaoka K. Effect of simvastatin on steroid-induced osteonecrosis evidenced by the serum lipid level and hepatic cytochrome P4503A in a rabbit model. *J Orthop Sci* 2008; **13**: 463-468
65 **Kuribayashi M**, Fujioka M, Takahashi KA, Arai Y, Ishida M, Goto T, Kubo T. Vitamin E prevents steroid-induced osteonecrosis in rabbits. *Acta Orthop* 2010; **81**: 154-160
66 **Drescher W**, Weigert KP, Bünger MH, Ingerslev J, Bünger C, Hansen ES. Femoral head blood flow reduction and hypercoagulability under 24 h megadose steroid treatment in pigs. *J Orthop Res* 2004; **22**: 501-508
67 **Terayama H**, Ishikawa M, Yasunaga Y, Yamasaki T, Hamaki T, Asahara T, Ochi M. Prevention of osteonecrosis by intravenous administration of human peripheral blood-derived CD34-positive cells in a rat osteonecrosis model. *J Tissue Eng Regen Med* 2011; **5**: 32-40
68 **Wang BL**, Sun W, Shi ZC, Lou JN, Zhang NF, Shi SH, Guo WS, Cheng LM, Ye LY, Zhang WJ, Li ZR. Decreased proliferation of mesenchymal stem cells in corticosteroid-induced osteonecrosis of femoral head. *Orthopedics* 2008; **31**: 444
69 **Li ZH**, Liao W, Cui XL, Zhao Q, Liu M, Chen YH, Liu TS, Liu NL, Wang F, Yi Y, Shao NS. Intravenous transplantation of allogeneic bone marrow mesenchymal stem cells and its directional migration to the necrotic femoral head. *Int J Med Sci* 2011; **8**: 74-83
70 **Yan Z**, Hang D, Guo C, Chen Z. Fate of mesenchymal stem cells transplanted to osteonecrosis of femoral head. *J Orthop Res* 2009; **27**: 442-446
71 **Peng J**, Wen C, Wang A, Wang Y, Xu W, Zhao B, Zhang L, Lu S, Qin L, Guo Q, Dong L, Tian J. Micro-CT-based bone ceramic scaffolding and its performance after seeding with mesenchymal stem cells for repair of load-bearing bone defect in canine femoral head. *J Biomed Mater Res B Appl Biomater* 2011; **96**: 316-325
72 **Pak J**. Regeneration of human bones in hip osteonecrosis and human cartilage in knee osteoarthritis with autologous adipose-tissue-derived stem cells: a case series. *J Med Case Reports* 2011; **5**: 296
73 **Pengde K**, Fuxing P, Bin S, Jing Y, Jingqiu C. Lovastatin inhibits adipogenesis and prevents osteonecrosis in steroid-treated rabbits. *Joint Bone Spine* 2008; **75**: 696-701
74 **Pritchett JW**. Statin therapy decreases the risk of osteonecrosis in patients receiving steroids. *Clin Orthop Relat Res* 2001; **386**: 173-178
75 **Kang P**, Gao H, Pei F, Shen B, Yang J, Zhou Z. Effects of an anticoagulant and a lipid-lowering agent on the prevention of steroid-induced osteonecrosis in rabbits. *Int J Exp Pathol* 2010; **91**: 235-243
76 **Motomura G**, Yamamoto T, Miyanishi K, Jingushi S, Iwamoto Y. Combined effects of an anticoagulant and a lipid-lowering agent on the prevention of steroid-induced osteonecrosis in rabbits. *Arthritis Rheum* 2004; **50**: 3387-3391
77 **Silverman SL**. Bisphosphonate use in conditions other than osteoporosis. *Ann N Y Acad Sci* 2011; **1218**: 33-37
78 **Lai KA**, Shen WJ, Yang CY, Shao CJ, Hsu JT, Lin RM. The use of alendronate to prevent early collapse of the femoral head in patients with nontraumatic osteonecrosis. A randomized clinical study. *J Bone Joint Surg Am* 2005; **87**: 2155-2159
79 **Agarwala S**, Jain D, Joshi VR, Sule A. Efficacy of alendronate, a bisphosphonate, in the treatment of AVN of the hip. A prospective open-label study. *Rheumatology (Oxford)* 2005;

44: 352-359

80 **Vandermeer JS**, Kamiya N, Aya-ay J, Garces A, Browne R, Kim HK. Local administration of ibandronate and bone morphogenetic protein-2 after ischemic osteonecrosis of the immature femoral head: a combined therapy that stimulates bone formation and decreases femoral head deformity. *J Bone Joint Surg Am* 2011; **93**: 905-913

81 **Biswal S**, Hazra S, Yun HH, Hur CY, Shon WY. Transtrochanteric rotational osteotomy for nontraumatic osteonecrosis of the femoral head in young adults. *Clin Orthop Relat Res* 2009; **467**: 1529-1537

82 **Ha YC**, Kim HJ, Kim SY, Kim KC, Lee YK, Koo KH. Effects of age and body mass index on the results of transtrochanteric rotational osteotomy for femoral head osteonecrosis: surgical technique. *J Bone Joint Surg Am* 2011; **93** Suppl 1: 75-84

83 **Sayeed SA**, Johnson AJ, Stroh DA, Gross TP, Mont MA. Hip resurfacing in patients who have osteonecrosis and are 25 years or under. *Clin Orthop Relat Res* 2011; **469**: 1582-1588

84 **Millar NL**, Halai M, McKenna R, McGraw IW, Millar LL, Hadidi M. Uncemented ceramic-on-ceramic THA in adults with osteonecrosis of the femoral head. *Orthopedics* 2010; **33**: 795

85 **Korompilias AV**, Beris AE, Lykissas MG, Kostas-Agnantis IP, Soucacos PN. Femoral head osteonecrosis: why choose free vascularized fibula grafting. *Microsurgery* 2011; **31**: 223-228

86 **Wang YS**, Zhang Y, Li JW, Yang GH, Li JF, Yang J, Yang GH. A modified technique of bone grafting pedicled with femoral quadratus for alcohol-induced osteonecrosis of the femoral head. *Chin Med J (Engl)* 2010; **123**: 2847-2852

87 **Liu G**, Wang J, Yang S, Xu W, Ye S, Xia T. Effect of a porous tantalum rod on early and intermediate stages of necrosis of the femoral head. *Biomed Mater* 2010; **5**: 065003

88 **Wang S**, Song X, Sun Y. [Short-term effect of trabecular metal rod implant on early avascular necrosis of the femoral head]. *Zhongguo Xiufu Chongjian Waike Zazhi* 2009; **23**: 562-565

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CASE REPORT

Scurvy: An unusual presentation of cerebral palsy

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Abstract

Scurvy is caused by prolonged severe dietary deficiency of ascorbic acid, in which the breakdown of intercellular cement substances leads to capillary hemorrhages and defective growth of fibroblasts, osteoblasts and odontoblasts, resulting in impaired synthesis of collagen, osteoid and dentine. It is characterized by hemorrhagic gingivitis, subperiosteal hemorrhages, perifollicular hemorrhages, and frequently petechial hemorrhages (especially on the feet). People with abnormal dietary habits, mental illness or physical disability are prone to develop this disease. Epiphyseal separation is known to occur in scurvy but is rarely seen now. Epiphyseal separation from the metaphysis is always through the zone of calcified cartilage, known as "scorbutic lattice", which in the radiographs is represented as "the white line of Frenkel". We report a case of multiple epiphyseal separations in a cerebral palsy child because of vitamin C deficiency. The child was treated with splintage of extremity and nutritional supplementation. All physeal separation healed completely without any deformity.

INTRODUCTION

Epiphyseal separations are known to occur in scurvy, but only a few such cases have been reported in children with cerebral palsy[1,2]. Even rarer is epiphyseal separation involving three or more epiphysis in a single patient. We report a case of epiphyseal separation of the bilateral proximal humerii and bilateral distal end of femur in a scurvy affected quadriplegic cerebral palsy child. The aim of this article is to underline the rarity and gravity of this disease and its possible more frequent appearance in children affected by cerebral palsy.

CASE REPORT

Clinical presentation

A 6 year old female child presented with a 15 d history of non traumatic sudden onset swelling of bilateral shoulders and bilateral knees. The child was a known case of spastic quadriplegic cerebral palsy with seizure disorder.

General and neurological examination

Gross Motor Function Classification System (GMFCS) score of child was level V. She was completely non ambulatory and had been on oral phenytoin for the last

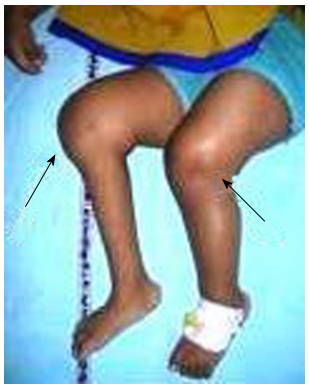

Figure 1 Clinical photo of patient showing swelling of bilateral knees (arrow).

four years; however, the onset of swelling was not related to an epileptic attack.

The child was lethargic but irritable and mildly febrile, was 91 cm in length and 11.5 kg in weight. Oral ulcers were evident. Bilateral upper limbs and lower limbs were spastic with poor power in all the extremities. Bilateral shoulders and knees were grossly swollen with overlying shiny skin (Figure 1).

On gentle palpation of the joints, the temperature was not raised and muffled crepitus was palpable in the affected joints. Any attempted movement of the affected joints was painful and restricted. There was no regional lymphadenopathy and the other joints were normal.

Laboratory data

Laboratory parameters revealed severe anemia (hemoglobin 4.4 g/dL) and normal serum calcium, phosphorus and alkaline phosphatase levels (Table 1).

Radiographic examination

Radiographs of bilateral shoulder and knee joints revealed complete separation of the proximal humerus epiphysis on the right side and the distal femoral epiphysis on the left side and partial separation of the left proximal humeral epiphysis and right distal femoral epiphysis (Figure 2).

Early subperiosteal hematoma was visible on all affected areas. Radiographs showed evidence of osteoporosis and thinning of cortices along with a distinctive radiological sign of scurvy, "Frenkel's white line".

The inability to reach a workable diagnosis prompted us to further enquire from the caregivers and it was revealed that the child was surviving on biscuits and pasteurized milk solely.

On the basis of clinical and radiological features, the child was diagnosed as a case of scurvy, confirmed after serum vitamin C level estimation, which was < 0.12 mg/dL (normal range 0.20-1.90 mg/dL).

Treatment

The child was splinted with high groin plaster slabs in both the lower limbs and cuff and collar slings in both the upper limbs after gentle attempt of closed reduction.

Table 1 Laboratory investigation of the patient

Blood/serum	Patient's value	Normal value
Hemoglobin	4.4 gm/dL	14.3-18.3 gm/dL
Total leucocytes count	7200	5.5-15.5 × 10^3 cells/μL
Differential count	Neutrophils 52.4%	54%-62%
	Lymphocytes 36.2%	25%-33%
Mean corpuscular volume	54.9	79.1-98.9 fL
Platelets	382 000	150-400 × 10^3 cells/μL
International normalised ratio	1.2	0.9-2.0
Serum calcium	9.8	8.4-10.8 mg/dL
Serum phosphorous	4.4	3.7-5.6 mg/dL
Serum alkaline phosphatase	197	145-420 IU/L

Vitamin C 200 mg per day along with hematinics was started. After 5 wk, as the pain and swelling subsided, plaster was removed and passive range of motion was started. All the slips healed within 4 mo. Even the completely displaced slips remodeled very well. At 6 mo of follow-up, all the slips were completely remodeled without obvious deformity (Figure 3).

DISCUSSION

The underlying basic biochemical defect in scurvy is failure to hydroxylate proline and lysine, an essential step in collagen formation (which is dependent on ascorbate).

Scurvy is rarely seen now because of the improvement in the nutritional and socioeconomic status of most populations. Children suffering from severe cerebral palsy are at increased risk for development of metabolic bone disease[3,4]. Various factors, including poor intake, oral motor dysfunction, feeding problems, non-ambulatory status and use of antiepileptics, contribute to deficiency of essential vitamins and minerals in this group of children.

Children with scurvy are irritable and lethargic, may have gum bleeding, petechiae, eccymosis, loosening of teeth, bone pains, weakness and poor wound healing. Early diagnosis requires a high degree suspicion as delay can result in jaundice, generalized edema, oliguria, neuropathy, fever, convulsions and eventually death may be seen. There are certain diseases that can mimic scurvy. Details of these diseases are given in Table 2.

Radiographic features include diminished bone density and cortical thinning. In addition, a white line of radiodensity is seen on the metaphyseal side of the physis, known as the white line of Frenkel[5]. This white line is due to an increase in the width and opacity of the zone of provisional calcification at the end of the metaphysis. Adjacent to this radiodense line is a radiolucent line which results in a very white appearance to this line.

Partial and complete separation of the epiphysis and fractures of calcified cartilage of the epiphyseal plate are known to occur in scurvy[6,7]. The usual locations of these epiphyseal injuries are the lower femur, upper humerus, osteochondral junction and lower tibia[5]. It is very rare to see epiphyseal separation involving three or

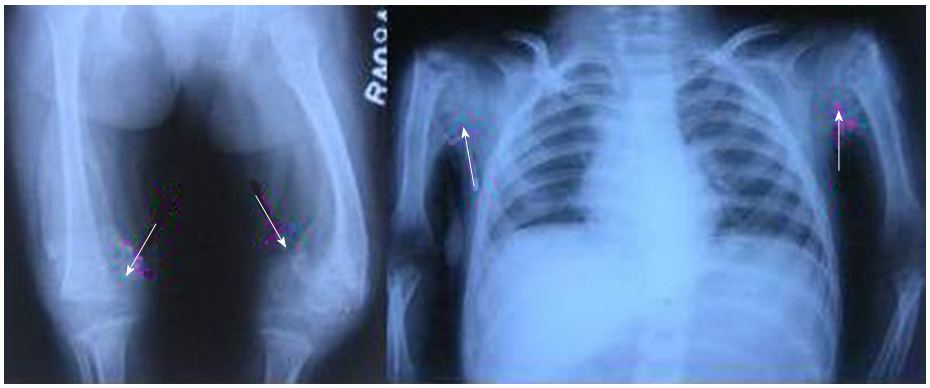

Figure 2 Plain radiograph of bilateral bilateral knees shoulder and showing epiphyseal separation (marked with arrow).

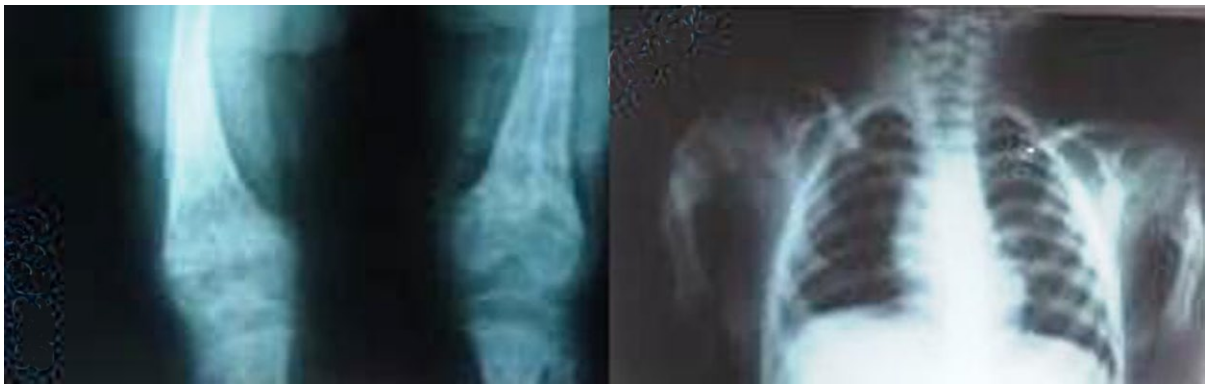

Figure 3 The follow-up radiograph shows normal alignment of epiphysis.

Table 2 Differential diagnosis of scurvy

Differential diagnosis
Child abuse and neglect
Medication side effects
Autoimmune diseases (e.g., henoch-schönlein purpura, systemic lupus erythematosus, sjogren syndrome)
Vitamin D deficiency and related disorders
Clotting factor deficiencies
Disseminated intravascular coagulation
Platelet dysfunction (e.g., immune thrombocytopenic purpura)
Senile purpura
Thrombophlebitis, deep venous thrombosis
Meningococcemia, rocky mountain spotted fever
Hematological malignancies (e.g., acute lymphoblastic leukemia)
Hypersensitivity vasculitis (leukocytoclastic vasculitis)
Necrotizing gingivitis
Osteomyelitis
Pediatric syphilis
Septic arthritis

more epiphyses. Aroojis *et al*[2] presented a series of four patients of cerebral palsy who had epiphyseal separation because of scurvy. In their series, diagnosis was based upon clinical and radiological features. Out of these four patients, only one patient had epiphyseal separation of both proximal humerii and both distal femurs. In our patient, there was separation of epiphyses of both proximal humerii and both distal femurs. The diagnosis was based upon clinical radiological features and was confirmed by assessment of vitamin C level.

Separation of the epiphysis from the metaphysis is always through the zone of calcified cartilage, known as "scorbutic lattice", which in the radiographs is represented as "the white line of Frenkel"[5]. A lattice fracture occurs in the zone of provisional calcification; because of this fracture, subperiosteal hemorrhages occur that leads to stripping of the periosteum from the shaft (particularly from the periphery of the epiphyseal plate)[5]. The epiphysis along with growth plate remains lined up to the denuded shaft with a periosteal sleeve containing a hematoma. Upon nutritional supplementation and administration of vitamin C, this subperiosteal hematoma begins to calcify. New bone is laid down on the side of the shaft where the epiphysis is displaced (and to a lesser degree on the opposite side). Thus, a new shaft is formed within the periosteal sleeve, while the protruding shaft undergoes rapid resorption. After subperiosteal bone formation, the epiphysis becomes centered on the widened metaphysic and remains in that position until the phase of remodeling[6-8].

So it can be inferred that separation of the epiphysis in scurvy is best treated conservatively by splintage and observation and a closed or open reduction of the displaced epiphysis is rarely required. Complete remodeling is the rule and residual deformity or disturbance in lon-

gitudinal bone growth is seldom seen.

The rarity of residual deformity in such epiphyseal separation can be explained by the blood supply to the growth plate. Trueta and associates have shown that the vessels on the epiphyseal side of the growth plate supply nourishment for resting and proliferative cartilage cells, which are primarily responsible for longitudinal growth of bone. In scurvy, epiphyseal separation occurs in the zone of provisional calcification so the blood vessels present on the epiphyseal side of growth plate are not damaged[7].

Deficiency of vitamin C is a common cause of epiphyseal separation in severely malnourished children and children with cerebral palsy appear to be more prone to this disease. Vitamin C supplementation along with immobilization for few weeks until the pain and swelling has subsided is sufficient for its management. Closed or open reduction is usually not required. Even in severe slips, healing with excellent remodeling is seen.

REFERENCES

1 **Nerubay J**, Pilderwasser D. Spontaneous bilateral distal femoral physiolysis due to scurvy. *Acta Orthop Scand* 1984; **55**: 18-20

2 **Aroojis AJ**, Gajjar SM, Johari AN. Epiphyseal separations in spastic cerebral palsy. *J Pediatr Orthop B* 2007; **16**: 170-174

3 **Henderson RC**, Lin PP, Greene WB. Bone-mineral density in children and adolescents who have spastic cerebral palsy. *J Bone Joint Surg Am* 1995; **77**: 1671-1681

4 **Shaw NJ**, White CP, Fraser WD, Rosenbloom L. Osteopenia in cerebral palsy. *Arch Dis Child* 1994; **71**: 235-238

5 **Scott W**. Epiphyseal dislocations in scurvy. *J Bone Joint Surg* 1941; **23**: 314–322

6 **Caffey J**. Paediatric Xray diagnosis. 7th ed. Chicago: Yearbook Publishers; 1978: 1459–1466

7 **Silverman FN**. Recovery from epiphyseal invagination: sequel to an unusual complication of scurvy. *J Bone Joint Surg Am* 1970; **52**: 384-390

8 **Aroojis A**, D'Souza H, Yagnik MG. Separation of the proximal humeral epiphysis. *Postgrad Med J* 1998; **74**: 752-755

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In press

3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

Organization as author

4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMCID:2516377 DOI:10.1161/01.HYP.0000035706.28494.09]

Both personal authors and an organization as author

5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

No author given

6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

Volume with supplement

7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/j.1526-4610.42.s2.7.x]

Issue with no volume

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No volume or issue

9 Outreach: Bringing HIV-positive individuals into care. *HRSA Careaction* 2002; 1-6 [PMID: 12154804]

Books

Personal author(s)

10 **Sherlock S**, Dooley J. Diseases of the liver and billiary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

Chapter in a book (list all authors)

11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

Author(s) and editor(s)

12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

Conference proceedings

13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

Conference paper

14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

Electronic journal (list all authors)

15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: http://www.cdc.gov/ncidod/eid/index.htm

Patent (list all authors)

16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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Write as mean ± SD or mean ± SE.

Statistical expression

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