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SYSTEMATIC REVIEWS

Systematic review of anorectal leiomyosarcoma: Current challenges and recent advances

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Abstract

BACKGROUND

The anorectal leiomyosarcoma (LMS) is an aggressive malignant neoplasm. Owing to the rarity of LMSs, an optimal treatment modality has yet to be determined.

AIM

To collect all published data on anorectal LMS characteristics, explore current treatment options, and review recent cases of postradiation LMS.

METHODS

A literature search of the PubMed electronic database was conducted using the MeSH terms "rectal neoplasms", "anus neoplasms" and "gastrointestinal neoplasms" combined with "leiomyosarcoma". The search was limited to English language and human studies. All available case reports and case series of anal or rectal LMSs that were published from the beginning of January 1996 to May 2017 were included if the diagnosis of LMS had been confirmed by histopathologic examination. Data were analyzed using simple statistics (mean, median, and standard deviation). Independent sample *t*-test was used to compare means for continuous variables.

RESULTS

A total of 27 articles reporting on 51 cases of anorectal LMS were identified. Among these cases, 11.7% had undergone previous pelvic radiotherapy (developing LMS at 13-35 years afterwards). Anorectal LMS affected the rectum in 92.2% of the cases, and no sex-based predominance was observed. Surgical resection with negative margins remains the mainstay of treatment, which can be accomplished with wide local excision or radical resection. The local recurrence rate was higher among cases who received wide local excision (30%), as compared to radical resection (20%); however, the overall rate of metastasis was

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51.61% regardless of the treatment approach. The use of neoadjuvant radiation lowers the risk of local recurrence compared to adjuvant radiotherapy, and facilitates R0 resection of the tumor. Cases treated with adjuvant chemotherapy showed better rates of distant recurrence and overall survival. Nonetheless, multidisciplinary team discussion is necessary to determine the optimal management plan whilst considering patient- and disease-related factors.

CONCLUSION
A multidisciplinary team approach, considering the underlying patient- and disease- related factors, is necessary for optimal management of these complex tumors.

Key words: Leiomyosarcoma; Rectal neoplasms; Anal neoplasms; Gastrointestinal neoplasms; Soft tissue neoplasms

Core tip: The current mainstay treatment of anorectal leiomyosarcoma is surgical resection with negative margins. Based on the published case series and reports, sphincter-preserving surgery followed by radiotherapy yields local recurrence rates that are comparable to radical resection. Moreover, neoadjuvant radiation improves local recurrence rates, as compared to adjuvant radiation. Adjuvant chemotherapy significantly improves rates of distant recurrence and overall survival; however, the choice to use chemotherapy in this setting should be determined according to a multidisciplinary team consideration of patient-related factors and treatment toxicity. Since local and distant tumor recurrences are common, even years after resection, post-surgery long-term follow-up is needed.

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INTRODUCTION

Leiomyosarcomas (LMSs) are malignant neoplasms of smooth muscle origin. They rarely arise in the anorectum, having an estimated incidence of < 0.1% among all cases of anorectal malignancies[1]. Diagnosis of anorectal LMS relies on identification of a characteristic profile of histological features and immunohistochemical markers. Typically, these tumors express the smooth muscle markers of smooth muscle actin, muscle-specific actin, desmin, and h-caldesmon, and are negative for KIT (CD117), CD34, and DOG-1[2]. Such markers also serve to facilitate the differentiation of LMSs from gastrointestinal stromal tumors, since both tumors have similar histological appearance. Microscopically, LMSs appear as spindle cell tumors. The presence of cellular atypia and high mitotic activity [> 50 per 50 high power field (HPF)] further supports the diagnosis of LMS, and allows for differentiation from benign leiomyoma[3-5]. Different treatment approaches, including radical resection, sphincter-preserving surgery, and adjuvant treatments, have been reported. However, owing to the rarity of LMSs, the optimal treatment modality is yet to be determined[6].

Despite the unique characteristics of anorectal LMSs, their features, management, and outcomes are usually reported in conjunction with data on colonic or other gastrointestinal LMSs in the literature[7]. Hatch *et al*[8] have periodically published literature reviews of all cases of anorectal soft tissue tumors independently; the latest published review was in the year 2000. However, their studies described anorectal LMSs prior to the introduction of immunohistochemistry, and since that time no further reviews have been published to describe the post-immunohistochemistry recent cases of anorectal LMSs.

To supplement and carry on the work of Hatch *et al*[8], we designed this study to collect all characteristic data regarding LMSs of the anorectum, to explore current treatment options and their outcomes, and to provide an overview of the recent

reports of radiation-induced LMSs of the anorectum.

MATERIALS AND METHODS

The study was approved by the ethics committee of our institution (Ref. No. 255-16).

Literature search

A literature search was conducted in the PubMed database using the MeSH terms "rectal neoplasms", "anus neoplasms", and "gastrointestinal neoplasms" combined with "leiomyosarcoma". The search was restricted to articles published between January 1996 and end of May 2017, in the English language, and on humans. All case reports and case series of anal or rectal LMSs were considered, and additional studies were identified by manually searching the reference lists of the selected articles. Two authors, working independently, screened the titles and abstracts of each retrieved article, and those which were relevant were selected for full-text review and assessment for inclusion. Cases that were confirmed to be anorectal LMS by histopathologic examination were included.

Statistical analysis

Statistical analyses were performed using SPSS version 23 (The Statistical Package for the Social Sciences software; IBM Corp., Armonk, NY, United States). Due to heterogeneity of the reported mitotic rates, studies that reported the mitotic rate per 10 HPF were multiplied by 5 to unify the mitotic rate. This strategy was chosen after discussion with multiple renowned pathologists specialized in the field. Studies that reported the mitotic rate in < 10 HPF were excluded from calculation of the mean. Data were analyzed using simple statistics, such as by mean, median, and standard deviation. Independent sample *t*-test was used to compare the means for continuous variables. P value < 0.05 was considered significant.

RESULTS

The literature search yielded 628 articles after removing duplicates, 570 of which were excluded because they did not meet the inclusion criteria (Figure 1). After a full-text review of the remaining 58 studies, 35 were further excluded and a total of 23 articles were compiled along with 4 additional articles identified by searching the reference lists. Finally, 27 articles were included in our review, reporting on a total of 51 cases of anorectal LMS. Of these cases, 47% (24/51) were confirmed by immunohistochemistry to be LMS, whereas the remaining were diagnosed by histopathologic examination alone. The tumors occurred mainly in the rectum 92% (47/51), and 8% (4/51) were located in the anal canal. Mean age at the time of diagnosis was 60 ± 17.1 years, affecting males and females equally. These tumors were commonly polypoid masses in appearance, with a median size of 6 cm [interquartile range (IQR) of 1.5-22 cm]. Moreover, 12% (6/51) of the patients reported a history of having undergone pelvic radiotherapy for tumors not related to anorectal LMSs. Rectal LMSs developed 13-35 years following the radiation. Additional clinicopathologic findings are summarized in Table 1.

Complete surgical resection with negative margins was the primary goal in the management of localized anorectal LMSs. The main surgical procedures performed were either wide local excision or radical excision (*i.e.*, low anterior resection or abdominoperineal resection). Extensive surgical procedures, including *en bloc* resection and pelvic exenteration, had been required when tumor invasion into adjacent organs was present, as evidenced by preoperative imaging or intraoperative findings.

Local excision was performed in 24% (11/45) of cases, only 2 of which received postoperative radiotherapy, and the largest size of these tumors measured 7 cm. The status of tumor margin was not reported in all cases. Patients treated with local excision had higher rate of local recurrence (30%, 3/10) than radical resection (20%, 3/15); however, distant metastasis was higher in those who underwent radical resection (53.3%, 8/15 *vs* 20%, 2/10 for local excision). There was no significant difference found for tumor size between local excision (mean: 4.1 cm) and radical resection (mean: 6.2 cm, P = 0.1). These tumors demonstrated similar mitotic rates as well (local excision; mean of 50.4/ 50 HPF *vs* radical resection; mean of 58.6/ 50 HPF, P = 0.63). Lymphadenectomy was performed in 15 cases, and only 1 case was positive for lymph node metastasis, which demonstrated a high mitotic rate of 10/1 HPF.

Among the patients with the relevant data reported, adjuvant radiotherapy was

Table 1 Patient characteristics, *n* (%)

Characteristic	Data
Location, *n* = 51%	
Rectal	47 (92.2)
Anal	4 (7.8)
Sex, *n* = 51%	
Female	26 (51)
Male	25 (49)
Mean age ± standard deviation, *n* = 51	60 ± 17.1 yr
Median tumor size (IQR), *n* = 38	6 (1.5-22) cm
Mean mitotic rate ± standard deviation of mitoses/50 HPF, *n* = 21	68.1 ± 40.42
Grade, *n* = 16%	
High	10 (62.5)
Intermediate	2 (12.5)
Low	4 (25)
Symptoms, *n* = 35%	
Rectal bleeding	17 (48.57)
Pain, rectal/abdominal	13 (37.14)
Weight loss	4 (11.43)
Constipation	4 (11.43)
Altered bowel motion	3 (8.57)
Protruding mass	3 (8.57)
Asymptomatic	3 (8.57)
Surgery, *n* = 45%	
Wide local excision	11 (24.4)
Abdominoperineal resection	14 (31.11)
Low anterior resection	12 (26.7)
Others	8 (17.8)
Outcome, *n* = 31%	
DOD	13 (41.94)
ANED	11 (35.48)
AWD	4 (12.9)
DDD	3 (9.68)

ANED: Alive with no evidence of disease; AWD: Alive with the disease; DDD: Died of a different disease; DOD: Died of disease(LMS); HPF: High power field; IQR: Interquartile range.

given in 40% (8/20), either to decrease the risk of local recurrence following wide local excision, to address positive resection margins (1 case), or to address large tumor size. Local recurrence occurred in 1 patient after 111 mo, and distant metastasis developed in 62.5% (5/8) of patients after a median of 14.5 mo (IQR: 5-111 mo) of follow-up.

Regardless of the treatment approach, the rate of local recurrence of the LMSs was 29% (9/31) and that of secondary metastasis was 52% (16/31). The most common site of distant metastasis was the liver, followed by the lung. At a median follow-up period of 24 mo (IQR: 1-325 mo), 42% (13/31) of the patients died of the disease and 35% (11/31) were alive with no evidence of the disease.

DISCUSSION

The mainstay treatment of anorectal LMS is surgical resection with negative margins, which can be accomplished with local excision or radical resection. In the literature, wide local excision has been found to be associated with a higher rate of local recurrence (55%) compared to radical resection (24%), and the rate of distant metastasis was similar between the two operations[6]. Similarly, in our review the rate of local recurrence was not significantly different between the two operations (30% *vs* 20%), although a higher rate of distant metastasis was observed with radical resection,

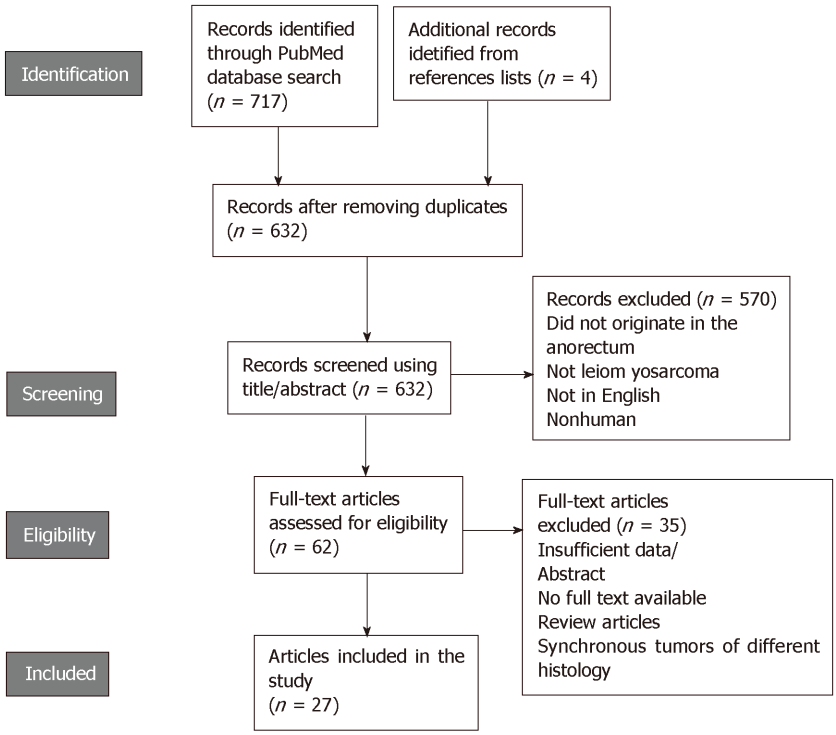

Figure 1 Flow diagram of the study selection.

even though the tumors' sizes and mitotic rates were similar between the two treatment approaches. This could be due to surgery selection bias as these cases would be more advanced locally and/or invading nearby structures, necessitating a radical excision.

Sphincter-preserving surgery followed by brachytherapy and/or external beam radiation has been investigated as an alternative to abdominoperineal resection. Grann *et al*[9] reported on 8 patients with tumors of 5 cm or less in size managed with this approach. The rate of local recurrence was 25% after 53 mo of follow up. These results were comparable to LMSs treated with abdominoperineal resection, where (19.5%) of patients developed local recurrence, and superior to those treated with wide local excision alone (67.5%) as described in another study. Although, it is important to note that tumor sizes ranged from 1 cm to 20 cm in that study[1]. There are a limited number of studies that have explored the outcomes of sphincter-preserving surgery that are nonrandomized and retrospective in nature, and have wide variation in histological grades and margin status across the reported cases[9-11]. Therefore, further randomized controlled trials (commonly known as RCTs) are needed to establish the benefit and criteria of patients eligible for this treatment approach.

Studies investigating the role of radiotherapy in anorectal LMS exclusively are lacking due the rarity of these tumors. However, the benefit of radiation therapy has been explored in retroperitoneal sarcomas by several studies who have reported improved local control rates after neoadjuvant radiotherapy. A meta-analysis including 11 studies with 1 RCT showed significantly improved local recurrence risk with preoperative compared to postoperative radiotherapy in resectable retroperitoneal sarcoma (odds ratio: 0.03, P = 0.02)[12]. Two prospective trials have reported favorable 5-year local recurrence- free survival rate of 60%, disease-free survival rate of 46%, and overall survival rate of 61% in patients with localized operable retroperitoneal sarcoma who underwent neoadjuvant radiotherapy[13]. Another RCT evaluating the benefit of neoadjuvant radiotherapy and complete surgical resection *vs* surgery alone in retroperitoneal sarcoma is underway (European Organisation for Research and Treatment of Cancer: EORTC 62092 STRASS Trial)[14].

LMSs rarely metastasize to lymph nodes, as shown in our study. Therefore, lymphadenectomy is not indicated unless regional lymph nodes are found to be enlarged in preoperative imaging. Leaving a positive margin should be avoided, since it is an independent predictor of local recurrence, and re-excision is indicated in cases of R1 or R2 resection whenever feasible[15]. Management of local or distant recurrence of LMSs is carried out by surgical resection or palliative chemoradiation. Surgical resection of liver metastases from a primary resectable colorectal LMS has been found

to be associated with prolonged overall survival, with a median of 47 mo (range: 7-135 mo) in 5 patients[16].

Regarding the role of adjuvant chemotherapy, different regimens have been assessed in multiple trials; none of which, however, have been specific for abdominal LMSs. Doxorubicin-based regimens remain the standard first-line chemotherapy for metastatic or locally advanced soft tissue sarcoma, with an overall response rate of 14% (31/228) and a median overall survival of 12.8 mo[17]. For resectable soft tissue sarcomas, multiagent combination chemotherapy has shown promising results compared to single-agent regimens; this includes the combination of doxorubicin and ifosfamide, that resulted in significant reduction in distant recurrence rate (odds ratio of 0.61, 95% confidence interval of 0.41-0.92, P = 5.02) as well as reduced mortality with a hazard ratio of 0.56 (95% confidence interval of 0.36-0.85, P = 5.01). However, no significant changes were reported for local recurrence rates[18]. In addition, combination of doxorubicin and olaratumab showed significantly improved overall survival compared to doxorubicin alone (26.5 mo *vs* 14.7 mo, P = 0.003), having an acceptable safety profile[19]. Moreover, second-line agents that have been found to be effective against LMSs are trabectedin and pazopanib[20,21].

The prognosis of anorectal LMSs remains poor, even after surgical resection. Yeh *et al*[6] reported 5-year overall survival and disease-free survival rates of 75% and 46%, respectively, in 40 patients after tumor resection. A high mitotic rate (≥ 10/10 HPF), large tumor size (> 10 cm), and high tumor grade were found to be consistently associated with worse survival and higher risk of metastasis[6,15,22]. For radiation-induced sarcoma, a study[23] found that LMSs had a favorable outcome compared to other histological types, with 5-year disease-specific survival of 68%. However, that study included abdominal, extremity, and trunk LMSs. Moreover, LMSs developed after a median duration of 23.5 years following radiation, which was the longest latency period upon comparison to other sarcomas. Regardless of histological type, though, the 5-year disease-specific survival was significantly less in the radiation-induced sarcoma cases than in those of sporadic sarcoma. Margin status, tumor size, and histological type were independent predictors of disease-specific survival.

One of the limitations of our study is that it included cases of LMSs that were not proven by immunohistochemistry to be of smooth muscle origin. Also, there was wide variation in the reported follow-up periods and incomplete information in the included cases, both of which precluded survival analysis.

In conclusion, the current mainstay treatment of anorectal LMS is surgery. Neoadjuvant radiotherapy may improve local control after resection; however, local and distant recurrence are common, which may develop years after resection. Therefore, long- term follow-up is needed after the surgery.

ARTICLE HIGHLIGHTS

Research background

Anorectal leiomyosarcomas (LMSs) are rare and complex tumors, known to present a therapeutic dilemma and having a high tumor recurrence risk after resection. Prior to application of immunohistochemistry to their diagnosis, LMSs were often misdiagnosed as gastrointestinal stromal tumors, which have a different treatment approach and prognosis. Additionally, owing to the rarity of anorectal LMSs, they are usually reported collectively with LMSs in other locations of the gastrointestinal tract.

Research motivation

To conduct a recent and comprehensive review of anorectal LMS in the time following the advent of immunohistochemistry use to highlight the tumor characteristics, treatment approach, role of adjuvant chemoradiation, and tumor prognosis as well as to review postradiation LMS of the anorectum.

Research objectives

To conduct a recent and comprehensive review of anorectal LMS in the time following the advent of immunohistochemistry use to highlight the tumor characteristics, treatment approach, role of adjuvant chemoradiation, and tumor prognosis as well as to review postradiation LMS of the anorectum.

Research methods

A systematic literature search of the PubMed electronic database was conducted using the MeSH terms "rectal neoplasms", "anus neoplasms" and "gastrointestinal neoplasms" combined with "leiomyosarcoma". The search was limited to English language and studies on humans. All available case reports and case series of anorectal LMSs that were published from January 1996 to May 2017 were included if the diagnosis of LMS had been confirmed by histopathologic examination.

Research results

We identified a total of 27 articles, reporting on 51 cases of anorectal LMS. Of these, 6 reported on cases of previous pelvic radiotherapy who had developed LMS 13-35 years after the radiation. Anorectal LMS affected the rectum in 92.2% of the cases, and no sex-based predominance was observed. Surgical resection with negative margins remains the mainstay of treatment, which can be accomplished by wide local excision or radical resection. The rate of local recurrence was higher in wide local excision (30%) compared to radical resection (20%), and the overall rate of metastasis was 51.61% regardless of the treatment approach. Use of neoadjuvant radiation lowers the risk of local recurrence, as compared to adjuvant radiotherapy, and facilitates R0 resection of the tumor. The use of adjuvant chemotherapy has shown improvement in distant recurrence and overall survival rates; however, multidisciplinary team discussion is necessary to determine the optimal management plan whilst considering patient and disease-related factors.

Research conclusions

The mainstay treatment of anorectal LMS is surgical resection with negative margins. Sphincter-preserving surgery followed by radiotherapy showed comparable local recurrence rates to radical resection based on case series and reports. Neoadjuvant radiation improved local recurrence rates compared to adjuvant radiation. Adjuvant chemotherapy showed significant improvement in distant recurrence and overall survival rates; however, use of chemotherapy in this setting should be assessed by a multidisciplinary team and with consideration to patient-related factors and treatment toxicity. Nevertheless, local and distant tumor recurrence are common and may develop years after the resection. Therefore, long-term follow-up is needed after surgery.

Research perspectives

Anorectal LMSs are rare tumors and further randomized controlled trials are needed to outline the criteria for patients' eligibility for sphincter-preserving surgery compared to radical resection. A multidisciplinary team approach is necessary for optimal management.

REFERENCES

1 **Khalifa AA**, Bong WL, Rao VK, Williams MJ. Leiomyosarcoma of the rectum. Report of a case and review of the literature. *Dis Colon Rectum* 1986; **29**: 427-432 [PMID: 3709322 DOI: 10.1007/BF02555068]

2 **Nassif MO**, Trabulsi NH, Bullard Dunn KM, Nahal A, Meguerditchian AN. Soft tissue tumors of the anorectum: rare, complex and misunderstood. *J Gastrointest Oncol* 2013; **4**: 82-94 [PMID: 23450454 DOI: 10.3978/j.issn.2078-6891.2012.042]

3 **Yamaguchi U**, Hasegawa T, Masuda T, Sekine S, Kawai A, Chuman H, Shimoda T. Differential diagnosis of gastrointestinal stromal tumor and other spindle cell tumors in the gastrointestinal tract based on immunohistochemical analysis. *Virchows Arch* 2004; **445**: 142-150 [PMID: 15232741 DOI: 10.1007/s00428-004-1055-8]

4 **Aggarwal G**, Sharma S, Zheng M, Reid MD, Crosby JH, Chamberlain SM, Nayak-Kapoor A, Lee JR. Primary leiomyosarcomas of the gastrointestinal tract in the post-gastrointestinal stromal tumor era. *Ann Diagn Pathol* 2012; **16**: 532-540 [PMID: 22917807 DOI: 10.1016/j.anndiagpath.2012.07.005]

5 **Miettinen M**, Furlong M, Sarlomo-Rikala M, Burke A, Sobin LH, Lasota J. Gastrointestinal stromal tumors, intramural leiomyomas, and leiomyosarcomas in the rectum and anus: a clinicopathologic, immunohistochemical, and molecular genetic study of 144 cases. *Am J Surg Pathol* 2001; **25**: 1121-1133 [PMID: 11688571 DOI: 10.1097/00000478-200109000-00002]

6 **Yeh CY**, Chen HH, Tang R, Tasi WS, Lin PY, Wang JY. Surgical outcome after curative resection of rectal leiomyosarcoma. *Dis Colon Rectum* 2000; **43**: 1517-1521 [PMID: 11089585 DOI: 10.1007/bf02236730]

7 **Hilal L**, Barada K, Mukherji D, Temraz S, Shamseddine A. Gastrointestinal (GI) leiomyosarcoma (LMS) case series and review on diagnosis, management, and prognosis. *Med Oncol* 2016; **33**: 20 [PMID: 26786155 DOI: 10.1007/s12032-016-0730-3]

8 **Hatch KF**, Blanchard DK, Hatch GF, Wertheimer-Hatch L, Davis GB, Foster RS, Skandalakis JE. Tumors of the rectum and anal canal. *World J Surg* 2000; **24**: 437-443 [PMID: 10706916 DOI: 10.1007/s002689910069]

9 **Grann A**, Paty PB, Guillem JG, Cohen AM, Minsky BD. Sphincter preservation of leiomyosarcoma of the rectum and anus with local excision and brachytherapy. *Dis Colon Rectum* 1999; **42**: 1296-1299 [PMID: 10528767 DOI: 10.1007/BF02234218]

10 **Minsky BD**, Cohen AM, Hajdu SI, Nori D. Sphincter preservation in rectal sarcoma. *Dis Colon Rectum* 1990; **33**: 319-322 [PMID: 2323283 DOI: 10.1007/BF02055476]

11 **Minsky BD**, Cohen AM, Hajdu SI. Conservative management of anal leiomyosarcoma. *Cancer* 1991; **68**: 1640-1643 [PMID: 1893364 DOI: 10.1002/1097-0142(19911001)68:7<1640::AID-CNCR2820680729>3.0.CO;2-6]

12 **Albertsmeier M**, Rauch A, Roeder F, Hasenhütl S, Pratschke S, Kirschneck M, Gronchi A, Jebsen NL, Cassier PA, Sargos P, Belka C, Lindner LH, Werner J, Angele MK. External Beam Radiation Therapy for Resectable Soft Tissue Sarcoma: A Systematic Review and Meta-Analysis. *Ann Surg Oncol* 2018; **25**: 754-767 [PMID: 28895107 DOI: 10.1245/s10434-017-6081-2]

13 **Pawlik TM**, Pisters PW, Mikula L, Feig BW, Hunt KK, Cormier JN, Ballo MT, Catton CN, Jones JJ, O'Sullivan B, Pollock RE, Swallow CJ. Long-term results of two prospective trials of preoperative external beam radiotherapy for localized intermediate- or high-grade retroperitoneal soft tissue sarcoma. *Ann Surg Oncol* 2006; **13**: 508-517 [PMID: 16491338 DOI: 10.1245/ASO.2006.05.035]

14 **European Organisation for Research and Treatment of Cancer - EORTC**. Surgery With or Without Radiation Therapy in Untreated Nonmetastatic Retroperitoneal Sarcoma (STRASS). [Accessed on 6 August, 2019]. In ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine.

Available from: https://clinicaltrials.gov/ct2/show/NCT01344018
15 **Gladdy RA**, Qin LX, Moraco N, Agaram NP, Brennan MF, Singer S. Predictors of survival and recurrence in primary leiomyosarcoma. *Ann Surg Oncol* 2013; **20**: 1851-1857 [PMID: 23354568 DOI: 10.1245/s10434-013-2876-y]
16 **Faraj W**, El-Kehdy J, Nounou GE, Deeba S, Fakih H, Jabbour M, Haydar A, El Naaj AA, Abou-Alfa GK, O'Reilly EM, Shamseddine A, Khalife M, Mukherji D. Liver resection for metastatic colorectal leiomyosarcoma: a single center experience. *J Gastrointest Oncol* 2015; **6**: E70-E76 [PMID: 26487954 DOI: 10.3978/j.issn.2078-6891.2015.044]
17 **Judson I**, Verweij J, Gelderblom H, Hartmann JT, Schöffski P, Blay JY, Kerst JM, Sufliarsky J, Whelan J, Hohenberger P, Krarup-Hansen A, Alcindor T, Marreaud S, Litière S, Hermans C, Fisher C, Hogendoorn PC, dei Tos AP, van der Graaf WT; European Organisation and Treatment of Cancer Soft Tissue and Bone Sarcoma Group. Doxorubicin alone versus intensified doxorubicin plus ifosfamide for first-line treatment of advanced or metastatic soft-tissue sarcoma: a randomised controlled phase 3 trial. *Lancet Oncol* 2014; **15**: 415-423 [PMID: 24618336 DOI: 10.1016/S1470-2045(14)70063-4]
18 **Pervaiz N**, Colterjohn N, Farrokhyar F, Tozer R, Figueredo A, Ghert M. A systematic meta-analysis of randomized controlled trials of adjuvant chemotherapy for localized resectable soft-tissue sarcoma. *Cancer* 2008; **113**: 573-581 [PMID: 18521899 DOI: 10.1002/cncr.23592]
19 **Tap WD**, Jones RL, Van Tine BA, Chmielowski B, Elias AD, Adkins D, Agulnik M, Cooney MM, Livingston MB, Pennock G, Hameed MR, Shah GD, Qin A, Shahir A, Cronier DM, Ilaria R, Conti I, Cosaert J, Schwartz GK. Olaratumab and doxorubicin versus doxorubicin alone for treatment of soft-tissue sarcoma: an open-label phase 1b and randomised phase 2 trial. *Lancet* 2016; **388**: 488-497 [PMID: 27291997 DOI: 10.1016/S0140-6736(16)30587-6]
20 **van der Graaf WT**, Blay JY, Chawla SP, Kim DW, Bui-Nguyen B, Casali PG, Schöffski P, Aglietta M, Staddon AP, Beppu Y, Le Cesne A, Gelderblom H, Judson IR, Araki N, Ouali M, Marreaud S, Hodge R, Dewji MR, Coens C, Demetri GD, Fletcher CD, Dei Tos AP, Hohenberger P; EORTC Soft Tissue and Bone Sarcoma Group; PALETTE study group. Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet* 2012; **379**: 1879-1886 [PMID: 22595799 DOI: 10.1016/S0140-6736(12)60651-5]
21 **Demetri GD**, von Mehren M, Jones RL, Hensley ML, Schuetze SM, Staddon A, Milhem M, Elias A, Ganjoo K, Tawbi H, Van Tine BA, Spira A, Dean A, Khokhar NZ, Park YC, Knoblauch RE, Parekh TV, Maki RG, Patel SR. Efficacy and Safety of Trabectedin or Dacarbazine for Metastatic Liposarcoma or Leiomyosarcoma After Failure of Conventional Chemotherapy: Results of a Phase III Randomized Multicenter Clinical Trial. *J Clin Oncol* 2016; **34**: 786-793 [PMID: 26371143 DOI: 10.1200/JCO.2015.62.4734]
22 **Delaney TF**, Kepka L, Goldberg SI, Hornicek FJ, Gebhardt MC, Yoon SS, Springfield DS, Raskin KA, Harmon DC, Kirsch DG, Mankin HJ, Rosenberg AE, Nielsen GP, Suit HD. Radiation therapy for control of soft-tissue sarcomas resected with positive margins. *Int J Radiat Oncol Biol Phys* 2007; **67**: 1460-1469 [PMID: 17394945 DOI: 10.1016/j.ijrobp.2006.11.035]
23 **Gladdy RA**, Qin LX, Moraco N, Edgar MA, Antonescu CR, Alektiar KM, Brennan MF, Singer S. Do radiation-associated soft tissue sarcomas have the same prognosis as sporadic soft tissue sarcomas? *J Clin Oncol* 2010; **28**: 2064-2069 [PMID: 20308666 DOI: 10.1200/JCO.2009.25.1728]

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CASE REPORT

Acute epiploic appendagitis at the tip of the appendix mimicking acute appendicitis: A rare case report with literature review

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Abstract

BACKGROUND

Acute epiploic appendagitis of the appendix (AEAA) is a rare self-limiting inflammatory disorder of the epiploic appendages (EA) close to the vermiform appendix, which often times mimicking the presentation of acute appendicitis (AA). To date, very few cases of AEAA have been reported. We report a case of a 52-year old man with the clinical suspicion of AA, but post-operative specimen examination confirmed AEAA as the final diagnosis.

CASE SUMMARY

A 52-year-old morbidly obese man presented to the emergency department with a 1-d history of the right lower quadrant (RLQ) abdominal pain. Physical examination revealed localized RLQ tenderness mimicking AA. The computed tomography abdomen was inconclusive, and a decision was made to perform laparoscopic appendectomy (LA). During the LA, an infarcted epiploic appendage at the tip of appendix and adherent to the abdominal wall was found, which was entirely excised. Final pathology showed congested and hemorrhagic epiploic appendage without any accompanied acute inflammatory changes in the wall of the appendix. Postoperative course was uneventful and he was doing well at seven months follow-up.

CONCLUSION

The possibility of AEAA should be considered in patients clinically suspected of having AA. Surgery is considered for those refractory to conservative management, with inconclusive diagnosis or develop complications at presentation.

Key words: Acute epiploic appendagitis of the appendix; Acute epiploic appendagitis; Acute appendicitis; Case report

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Core tip: Acute appendiceal epiploic appendagitis is very rare condition challenging to differentiate from acute appendicitis clinically. Computed tomography abdomen plays a crucial role in diagnosis, while pain control with anti-inflammatory drugs is the treatment of choice. Surgery is only considered for those refractory to conservative management or develop complications at presentation.

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NTRODUCTION

Acute epiploic appendagitis of the appendix (AEAA) is a benign, mostly non-surgical inflammatory disorder of the epiploic appendages (EA), which are usually located adjacent to the tenia coli[1]. Although the actual incidence of AEAA is not well known, however, it has been reported in 0.3%-1% of patients initially suspected of having acute appendicitis (AA)[2]. The most common mechanism resulting in AEAA is the acute torsion of abnormally elongated and large appendages, which leads to ischemia and necrosis of appendages[3]. Also, the primary thrombosis of the epiploic appendage central draining vein has also been related to the development of AEAA[4]. It most commonly presents as acute, constant, and non-radiating right lower quadrant (RLQ) abdominal pain[5].

Moreover, computed tomography (CT) scan of the abdomen is considered as the diagnostic modality of choice for AEAA, while ultrasound abdomen is reserved for patients with equivocal finding on CT abdomen[2,6,7]. Additionally, conservative management with oral anti-inflammatory medications is the most appropriate management for AEAA patients, while those who fail the conservative management, those with new or worsening symptoms and those with complications are best treated with the surgical interventions[6,8-10]. Current knowledge regarding AEAA is limited and only rare case reports exist. In order to better understand and add our contribution to the available literature on this rare condition, we report a unique case of a 52-year-old male patient initially suspected of having AA, but post-operative specimen evaluation was significant for AEAA.

CASE PRESENTATION

Chief complaints

A 52-year-old man with a basal metabolic index: 43.4 kg/m^2, presented to the emergency department complaining of acute RLQ abdominal pain of 18 hours duration.

History of present illness

His pain was severe, constant, non-radiating, and aggravated with movement, without any history of associated symptoms including nausea, vomiting, diarrhea, anorexia, fever, and chills. He denies any recent history of trauma.

History of past illness

His past medical history was significant for hypertension, laparoscopic cholecystectomy and open umbilical hernia repair.

Personal and family history

Personal and family history was unremarkable.

Physical examination upon admission

On admission, his vitals were: temperature (T) = 36.5 °C, pulse (P) = 71, beats per minute, respiratory rate = 18/min, and blood pressure = 174/74 mmHg. Physical exam revealed severe tenderness in the abdominal RLQ, no peritoneal sign, although

Rovsing sign and Psoas signs were negative.

Laboratory examinations

Routine pre-operative laboratory testing indicated mild leukocytosis white blood count = 11200/m^3 with no left shift, and procalcitonin < 0.05 ng/mL). Basic metabolic panel was unremarkable.

Imaging examinations

Patient had an abdominal CT without contrast in the emergency room (ER), which showed a 1.0 cm × 1.8 cm focus of oval inflammatory changes surrounding central fat density adjacent to the tip of the appendix and inferior aspect of the cecum. This is likely due to epiploic appendagitis. Possibility of very early acute distal tip appendicitis cannot be entirely excluded but felt to be less likely.

FINAL DIAGNOSIS

Although these radiological findings are highly suspicious for AEAA, the possibility of very early acute distal tip appendicitis could not be entirely excluded at that moment (Figure 1). Despite the aggressive management with IV fluids and antibiotics, his abdominal pain persisted.

TREATMENT

Based on the suspicious of early appendicitis, and the fact that the patient decided to choose surgery after our length discussion, a decision was made to perform an emergent laparoscopic appendectomy. During the laparoscopic appendectomy, mild hyperemic changes were noted in the vermiform appendix which was intensely adhered to the RLQ abdominal pain. Also noted was an infarcted epiploic appendage which was also attached to the tip of the appendix (Figure 2). At this moment, a complete laparoscopic appendectomy was performed, and the specimen was retrieved. Pathology report showed a tubular appendix measuring 42 mm in length and 6 mm in diameter on macroscopic examination. The congested and hemorrhagic appendage measured 6.3 cm × 1.6 cm × 1 cm. On microscopic examination, the tip of appendix had partial fibrous obliteration with perpendicular fibrin, and no acute inflammation identified in the appendiceal wall confirming the AEAA as the final diagnosis (Figure 3).

OUTCOME AND FOLLOW-UP

The postoperative course was uneventful, and the patient was discharged on the following day. Patient was doing well at seven months follow-up.

DISCUSSION

Acute epiploic appendagitis (AEA), first described by Lynn *et al* in 1956, is one of the rare causes of acute abdomen secondary to the inflammation of the EA, which are 0.5-5 cm long and 1-2 cm thick serosa-covered fat pad pouches of the colonic wall[11,12]. Although the EA are distributed along the entire colon (50-100 in total), they are mostly populated in the rectosigmoid junction (57%), ileocecal region (26%), ascending colon (9%), transverse colon (6%) and descending colon (2%)[12].

AEA may be primary or secondary. Primary acute epiploic appendagitis (PAEA) is caused by torsion or spontaneous venous thrombosis of the involved epiploic appendage, while secondary epiploic appendagitis (SEA) is associated with inflammation of adjacent organs, such as diverticulitis, appendicitis or cholecystitis[13]. Moreover, the PAEA presents mostly in 2-5 decades of life without any sexual predominance, while SEA affects mostly middle-aged obese male population[3,11-13]. Also, the most common parts of the colon affected by AEA in decreasing order of frequency are the sigmoid colon, descending colon, cecum and the ascending colon[13].

AEAA is an even extremely rare form of AEA accounting for only 3% of all AEA cases. Shiryajev *et al*[14] described a case of AEAA secondary to underlying appendicitis, while Hambury *et al*[15] described an actual case of torsed EA of the vermiform appendix, which mimicked AA. Surprisingly, the luminal diameter of the EA near the vermiform appendix is usually smaller compared to those around the

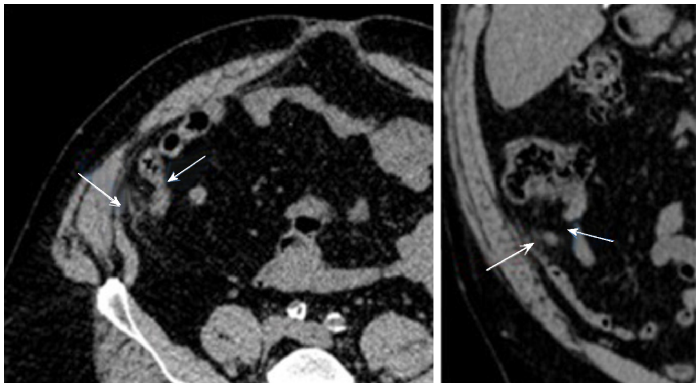

Figure 1 Abdominal computed tomography scan. A 1.0 cm × 1.8 cm focus of oval inflammatory changes surrounding central fat density visualized adjacent to the tip of the appendix and inferior aspect of the cecum noted. This is likely due to epiploic appendagitis. Possibility of very early acute distal tip appendicitis cannot be entirely excluded but felt to be less likely (Short arrow: Appendix; Long arrow: Epiploic appendagitis).

colon, making them susceptible to the early infarction after the torsion. Additionally, AEAA typically presents in the middle-aged male population with acute onset of right lower quadrant pain usually without associated symptoms such as fever, anorexia, nausea, vomiting, diarrhea, or constipation.

Given the non-specific clinical presentation of AEAA, the use of imaging technology plays a critical role in the diagnosis of this rare entity. Advances in imaging techniques made it possible to radiologically describe the first report of EA using CT scan abdomen in 1986[16]. The hallmark CT abdomen findings for AEAA include; fat attenuating oval lesion usually less than 2 cm with the hyper-attenuated rim located near the tip of the appendix[17]. Other less specific findings include localized edema, described at streaky fluid attenuation or fat stranding around the appendage[18]. Additionally, the appendix is usually normal in caliber without any enhancement or thickness of appendiceal wall[18].

Furthermore, AEAA is a self-limiting disease, and most of the patients recover within 1-14 d after the analgesic medication[12] Conservative management using non-steroidal anti-inflammatory drugs (NSAID) is currently considered the standard management for radiologically confirmed AEAA[3,19]. Antibiotics and surgery are reserved for those with worsening symptoms, or those who do not respond to conservative management, or those who develop complications such as the abscess or intestinal obstruction, new or worsening symptoms[12].

To comment further on the complex nature of the AEAA, we performed a literature search which yielded only seven case reports specifically for AEAA (Table 1). Based on the results of our literature search, we can conclude that most of the AEAA cases reported so far were an accidental finding in patients who underwent emergent appendectomy with a clinical diagnosis of AA in the absence of radiologic confirmation. Also, our literature search yielded AEAA effects mostly middle-aged population (32-63 years; mean = 42.7 years), mostly male (4/7, 62.5%), presents with RLQ pain, with normal or mild elevated white count (normal-13.3/mm^3). Also, the maximum diameter of lesions was 1.3 to 1.8cm. It was found near the tip of the appendix (3/7), proximal appendix (1/7) and middle and distal one third (2/7).

CONCLUSION

AEAA is a rare cause of abdominal RLQ pain that can easily mimic the clinical presentation of AA. The advances in the diagnostic modalities have permitted the better radiological delineation of this rare entity, and have also reduced the burden of un-necessary surgeries on the United States economy. In the clinical settings of the non-specific clinical presentation of AA, CT abdomen should be ordered in order to rule out AEAA as the possible cause of acute abdominal pain. Additionally, in the absence of other complication, conservative management with NSAID should be considered as the initial management for AEAA before making decision for the invasive approaches.

Table 1 Acute appendiceal epiploic appendagitis and literature review

Author	Age (yr)	Sex	Symptom	Lab results	Size of the lesion	Location of the lesion	CT appearance	Outcomes
Hambury *et al*[4]	34	F	RLQ pain	Not mentioned	1.3 cm	Junction of the middle and distal one-third of the appendix	N/A	Surgically confirmed
Sand *et al*[5]	50	M	RLQ pain	Leukocytosis (WBC 12/nL) Elevated CRP (1 mg/dL)	Not mentioned	Not mentioned	N/A	Surgically confirmed
Aslam *et al*[3]	57	M	RLQ pain	Leukocytosis	Not mentioned	Near the tip of appendix	N/A	Surgically confirmed
Magnuson*et al*[6]	36	F	RLQ pain	Within normal range	Not mentioned	Proximal appendix	N/A	Surgically confirmed
Purysko *et al*[2]	38	M	RLQ pain	Not mentioned	Not mentioned	Near the tip of appendix	Periappendiceal fatty oval lesion with hyperattenuating rim	Surgically confirmed
Jung *et al*[8]	32	M	RLQ pain	Leukocytosis(WBC 10950/mm^3) Elevated ESR (14 mm/h)	1.5 cm	Near the tip of appendix	Periappendiceal fatty oval lesion with hyperattenuating rim and central linear hyperattenuation	Surgically confirmed
Sahin *et al*[7]	63	F	RLQ pain	Leukocytosis (WBC 13300/mm^3	Not mentioned	Near the middle of appendix	N/A	Surgically confirmed

WBC: White blood cell; RLQ: Right lower quadrant; CT: Computed tomography.

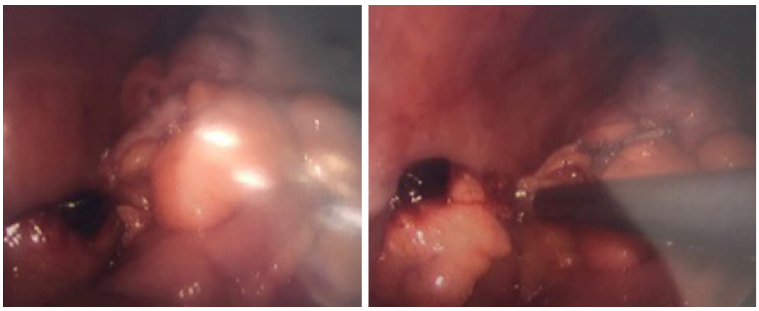

Figure 2 Infarcted appendiceal epiploic appendage at the tip of the appendix (Intraoperative).

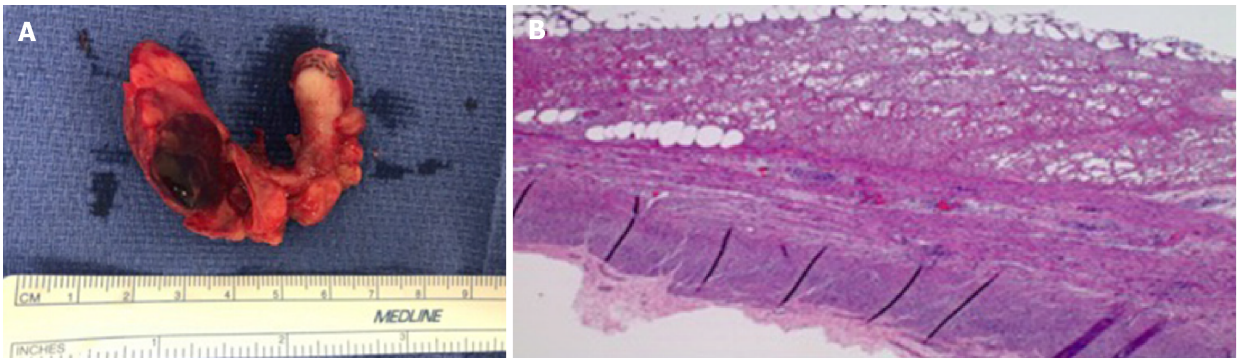

Figure 3 The Congested and hemorrhagic appendage. A: The congested and hemorrhagic appendage measures 6.3 cm × 1.6 cm × 1 cm; B: Serosal surface with fibrin and few acute inflammatory cells. Muscular layer with no inflammatory cells. High power.

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REFERENCES

1 **Patel H**, Abdelbaki A, Steenbergen P, Chanana C, Li S. Know the name: acute epiploic appendagitis-CT findings and review of literature. *AME Case Rep* 2018; **2**: 8 [PMID: 30264004 DOI: 10.21037/acr.2018.02.02]
2 **Thomson GT**, Johnston JL, Baragar FD, Toole JW. Psoriatic arthritis and myopathy. *J Rheumatol* 1990; **17**: 395-398 [PMID: 2110253 DOI: 10.1038/nrgastro.2010.189]
3 **Aslam MB**, Hasan N. Torsion of an appendix epiploica present at the vermiform appendix: a rare cause of acute abdomen. *Ulus Travma Acil Cerrahi Derg* 2009; **15**: 509-510 [PMID: 19779995]
4 **Tabbara TA**, Alassaf OY, Kaouas MC. Acute epiploic appendigitis: Diagnostic and laparoscopic approach. *Int J Surg Case Rep* 2018; **44**: 157-160 [PMID: 29505992 DOI: 10.1016/j.ijscr.2018.02.003]
5 **Sandrasegaran K**, Maglinte DD, Rajesh A, Akisik FM. Primary epiploic appendagitis: CT diagnosis. *Emerg Radiol* 2004; **11**: 9-14 [PMID: 15278705 DOI: 10.1007/s10140-004-0369-9]
6 **Rioux M**, Langis P. Primary epiploic appendagitis: clinical, US, and CT findings in 14 cases. *Radiology* 1994; **191**: 523-526 [PMID: 8153333 DOI: 10.1148/radiology.191.2.8153333]
7 **Singh AK**, Gervais DA, Hahn PF, Rhea J, Mueller PR. CT appearance of acute appendagitis. *AJR Am J Roentgenol* 2004; **183**: 1303-1307 [PMID: 15505294 DOI: 10.2214/ajr.183.5.1831303]
8 **Desai HP**, Tripodi J, Gold BM, Burakoff R. Infarction of an epiploic appendage. Review of the literature. *J Clin Gastroenterol* 1993; **16**: 323-325 [PMID: 8331268 DOI: 10.1097/00004836-199306000-00012]
9 **Legome EL**, Belton AL, Murray RE, Rao PM, Novelline RA. Epiploic appendagitis: the emergency department presentation. *J Emerg Med* 2002; **22**: 9-13 [PMID: 11809550 DOI: 10.1016/S0736-4679(01)00430-9]
10 **Vinson DR**. Epiploic appendagitis: a new diagnosis for the emergency physician. Two case reports and a review. *J Emerg Med* 1999; **17**: 827-832 [PMID: 10499697 DOI: 10.1016/S0736-4679(99)00090-6]
11 **Almuhanna AF**, Alghamdi ZM, Alshammari E. Acute epiploic appendagitis: A rare cause of acute abdomen and a diagnostic dilemma. *J Family Community Med* 2016; **23**: 48-50 [PMID: 26929730 DOI: 10.4103/2230-8229.172234]
12 **Sand M**, Gelos M, Bechara FG, Sand D, Wiese TH, Steinstraesser L, Mann B. Epiploic appendagitis--clinical characteristics of an uncommon surgical diagnosis. *BMC Surg* 2007; **7**: 11 [PMID: 17603914 DOI: 10.1186/1471-2482-7-1]
13 **Subramaniam R**. Acute appendagitis: emergency presentation and computed tomographic appearances. *Emerg Med J* 2006; **23**: e53 [PMID: 16988291 DOI: 10.1136/emj.2005.033704]
14 **Shiryajev YN**, Glebova AV. Torsion of an epiploic appendage of the vermiform appendix. *Ulus Travma Acil Cerrahi Derg* 2013; **19**: 593 [DOI: 10.5505/tjtes.2013.82574]
15 **Hambury HJ**. Torsion of an appendix epiploica of the vermiform appendix. *Br J Surg* 1952; **40**: 176-177 [PMID: 12987654 DOI: 10.1002/bjs.18004016019]
16 **Danielson K**, Chernin MM, Amberg JR, Goff S, Durham JR. Epiploic appendicitis: CT characteristics. *J Comput Assist Tomogr* 1986; **10**: 142-143 [PMID: 3944300 DOI: 10.1097/00004728-198601000-00032]
17 **Almeida AT**, Melão L, Viamonte B, Cunha R, Pereira JM. Epiploic appendagitis: an entity frequently unknown to clinicians--diagnostic imaging, pitfalls, and look-alikes. *AJR Am J Roentgenol* 2009; **193**: 1243-1251 [PMID: 19843737 DOI: 10.2214/AJR.08.2071]
18 **Eberhardt SC**, Strickland CD, Epstein KN. Radiology of epiploic appendages: acute appendagitis, post-infarcted appendages, and imaging natural history. *Abdom Radiol (NY)* 2016; **41**: 1653-1665 [PMID: 27142382 DOI: 10.1007/s00261-016-0757-0]
19 **Ozdemir S**, Gulpinar K, Leventoglu S, Uslu HY, Turkoz E, Ozcay N, Korkmaz A. Torsion of the primary epiploic appendagitis: a case series and review of the literature. *Am J Surg* 2010; **199**: 453-458 [PMID: 19520357 DOI: 10.1016/j.amjsurg.2009.02.004]

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CASE REPORT

Doege-Potter syndrome by malignant solitary fibrous tumor of the liver: A case report and review of literature

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Abstract

BACKGROUND

Solitary fibrous tumor of the liver (SFTL) is a rare occurrence with a low number of cases reported in literature. SFTL is usually benign but, 10%-20% cases are reported to be malignant with a tendency to metastasize. The majority of malignant SFTL cases are associated with a paraneoplastic hypoglycaemia defined as Doege-Potter syndrome. Surgery is the best therapeutic treatment, however, long- life follow-up is recommended.

CASE SUMMARY

A 74-year-old man, was admitted to the emergency department after a syncopal episode with detection of hypoglycaemia resistant to medical treatment. The computed tomography revealed a solid mass measuring 15 cm of the left liver. An open left hepatectomy was performed with complete resection of tumor. Histopathological analyses confirmed a malignant SFTL.

CONCLUSION

Large series with long-term follow-up have not been published neither have clinical trials been undertaken. Consequently, the methodical long-term follow-up of surgically treated SFTLs is strongly recommended.

Key words: Solitary fibrous tumor; Malignant solitary fibrous tumor of the liver;

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Mesenchymal tumor; Hepatic tumor; Doege-Potter syndrome

Core tip: Solitary fibrous tumors (SFTs) are rare mesenchymal tumors first described in 1931 by Klemperer and Rabin. Usually, SFTs are benign, but 10%-20% of them are reported to be malignant with a tendency to metastasize. At present, 22 cases of liver malignant SFTs, including our patient, have been reported in literature. Some cases are associated with a paraneoplastic hypoglycaemia definied as Doege-Potter syndrome. Surgery is the best therapeutic modality and prolongs life, but also improves the clinical characteristics associated with Doege-Potter syndrome if present. Longlife follow-up is recommended.

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INTRODUCTION

Solitary fibrous tumors (SFTs) are rare mesenchymal tumors first described in 1931 by Klemperer and Rabin[1]. Originally the are usually found in pleura but they have also been reported in other serous cavities such as pericardium and peritoneum. Such tumours have also been described in other unusual organs such as the liver, orbit, retroperitoneum, maxillary sinus, pancreas, upper respiratory tract, lung, soft tissues, kidneys, thyroid gland, meninges, and prostatic gland[2,3].

SFTs of the liver (SFTLs) are some of the most uncommon SFT, with only approximately 84 reported cases in the English literature[1]. SFTs are usually benign, but 10%-20% cases are reported to be malignant with a tendency to metastasize[2]. Histologically, they are characterized by proliferation of spindle cells, and immunohistochemically are positive for CD34 and BCL2 and bland for CD99[4].

Clinico-radiological features are not specific, therefore the diagnosis can be made only on the basis of histopathological data[2]. Some cases of malignant SFTs are associated with a paraneoplastic hypoglycaemia defined as Doege-Potter syndrome, described in pleural and extrapleural tumors[5].

Surgery is considered the best therapeutic modality, with outcomes dependent on resectability. Resection prolongs life, but also improves the clinical characteristics associated with Doege-Potter syndrome if present[6]. Longlife follow-up is recommended. We reported a new case of malignant SFTL treated at our Institute and reviewed 22 cases of this rare tumor present in English scientific literature.

CASE PRESENTATION

History of present illness

A 74 years old man, was admitted to the emergency department for syncopal episode, with detection of hypoglycaemia resistant to medical treatment.

History of past illness

His past medical history included hypertension, benign prostatic hypertrophy and glaucoma.

Physical examination upon admission

Physical examination revealed a morbidly obese (body mass index = 35), painless hepatomegaly without weight loss.

Laboratory examinations

Investigations reported a marked hypoglycaemia, with capillary blood glucose measurements ranged from 30 to 70 mg/dL treated with continuous glucose infusion and a rich carbohydrate diet.

Laboratory tests revealed low levels of insulin: 0.3 mcrU/mL (range 5-25 mcrU/mL), low levels of C-peptide: < 0.10 ng/dL (range 0.9-4 ng/dL), low levels of GH: <0.02 ng/dL (range 0.02-1.23 ng/dL), normal level of cortisol: 8.9 mcg/dL (range 3.7-19.4 mcg/dL), normal level of insulin-like growth factor I (IGFI): 84 ng/mL (range 20-300 ng/mL) and normal level of insulin-like growth factor II (IGFII): 575.70 ng/mL (range 373-1000 ng/mL) in the patient's serum. The IGFII/IGFI ratios was 7:1. Liver functions, viral panel, tumor markers (alpha-fetoprotein, carcinoembryonic antigen and cancer antigen 19-9) were within the normal limits.

Imaging examinations

A total body computed tomography (CT) was performed and revealed a solid mass measuring 15 cm of the left liver. The intravenous contrast demonstrate an inhomogeneous enhancement for necrosis within the tumour as well as a thick capsule that enhances during the portal phase (Figure 1). Radiological findings on abdominal magnetic resonance (MR) were similar to ones described for abdominal TC with evidence of a voluminous liver mass measuring 15 cm × 13 cm (Figure 2). There was no evidence of metastatic disease

FINAL DIAGNOSIS

Doege-Potter syndrome by malignant solitary fibrous tumor of the liver.

TREATMENT

A left hepatectomy was performed with complete resection of tumor and free margin were obtained. Intraoperative ultrasound (IOUS) revealed a left liver tumor mass of 15 cm. There were no sign of contiguous organ invasion or other hepatic lesion. The parenchymal transection was performed with an ultrasonic dissector and bipolar sealers. On frozen section SFT present well circumscribed but unencapsulated border with infiltrative pattern and central necrosis (Figure 3).

OUTCOME AND FOLLOW-UP

Immediately after surgery glucose serum levels returned to a physiologic daily profile. The patient was discharged on postoperative day four without complications. Histopathological analyses confirmed a malignant SFTL; microscopically, the tumours tissue showed a proliferation of spindle cells with infiltrative pattern of hepatic parenchyma, immunochemistry show strong positivity for CD34 and BCL2 and bland for CD99 and negative for ActinaML, Desmine, Cd117, CK pool, S100. The mitotic activity index Ki67 was 35% (Figure 4). Adjuvant protocol of chemiotherapy with Epirubicin and Ifosfamide was started. The patient was subjected to a strictly follow-up every 3-4 mo in the first 2-3 years after surgey, twice each year up to the 5th year and then once a year after the 5th year. Five months after surgery there were no signs of local recurrence or distant metastases.

DISCUSSION

An English literature search regarding "Solitary fibrous tumor of the liver", "Malignant solitary fibrous tumor of the liver", "Mesenchymal tumor", "Hepatic tumor", "Doege-Potter syndrome" was conducted using the common search engines and the relevant articles were reviewed and analysed. The reference list of each article was inspected searching for other articles reporting SFTL that were analysed and included in this report.

We selected all cases of malignant SFTL reported in the literature considering a total number of 19 articles and we excluded cases of benign SFTL or extrahepatic localization. At present, 22 cases of malignant SFTL, including including the patient described in this article, have been reported in literature (Table 1). All represent case reports except for one case series with three case series described by Maccio *et al*[7].

Malignant SFTL occurs with almost equal distribution between males (11, 50%) and female (11, 50%). It occurs more in the right lobe (14 cases, 64%) than the left one (6 cases, 27%). There was also two cases (9%) of bilateral localization. The average age of these patients was 61.1 years (range 24-80).

The clinical presentation was non-specific, ranging from weakness, fatigue,

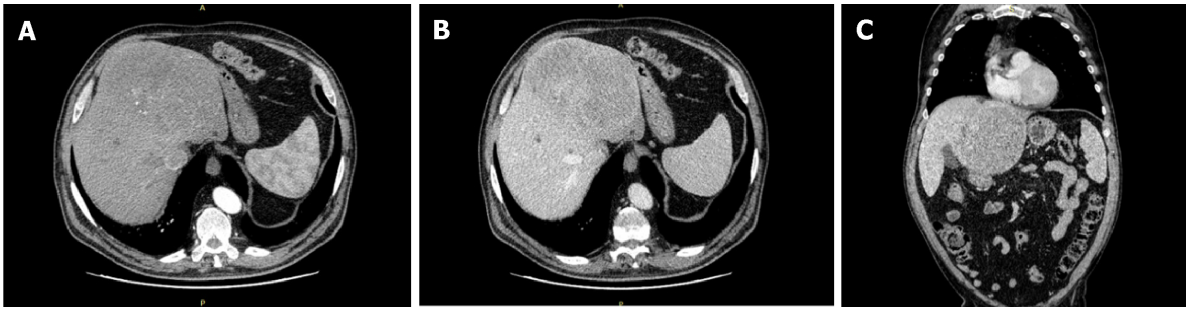

Figure 1 Abdominal computed tomography displaying the left liver mass. A: Arterial phase. B: Portal phase. C: Coronal view.

anorexia, vomiting, progressive jaundice, disorientation, incoherent speech, malaise abdominal bloating, abdominal discomfort, dyspnoea, abdominal pain, abdominal distension, weight loss. The syndrome of hypoglycaemia was seen in about 23%, five of 22 cases reported. There was no specific laboratory tests or tumor markers for malignant SFTL.

In our review 17 patients (77%) were treated with resection: 9 with unknown tumor margins and 8 with free tumor margins. One patient was treated with failed trans-arterial chemo embolization (TACE) and successful resection with unknown margins. Another case was subjected to TACE followed by resection. Two patient underwent to chemotherapy. One patient was treated with a right portal embolization and successful resection with free tumor margins.

Follow up was not available for 4 cases, no sign of local recurrence or distant metastasis in 7 cases (32%) with an average follow up duration of 17 mo. Local recurrence or distant metastasis were found in 11 patients (50%) with a averge time post-surgery of 27 mo.

SFT first described in the year 1931, is a rare neoplasm commonly located in the pleura and this tumor accounts for less than 2% of all soft tissue tumors[8,9]. SFT is considered a benign tumor with the potential for malignant transformation but the classification of this neoplasm is not yet clear in literature[4,10]. SFT of the liver (SFTL) is particularly rare, therefore the classification as a benign or malignant tumor remains controversial[11]. SFTL was reported for the first time in an article published in 1959 by Nevius and Friedman where three SFT in different localizations were described, one of them was a liver SFT and was clinically presented with hypoglycaemia[12].

England *et al*[13] established the criteria for malignant SFT: Mitotic changes (> 4/10 HPFs), tumor necrosis and hemorrhage, nuclear pleomorphism, and metastasis were the major criteria; large tumor size (> 10 cm) and cellular atypia were the minor criteria.

Wilky *et al*[14] classified the SFT into "benign" with no atypical features and no England's criteria, "borderline" with 1 or more England's criteria but final classification as benign, and "malignant." This report described that "borderline" SFT with any of England's criteria had been related to high risk of recurrence.

In the 2013 WHO classification of tumors of soft tissue and bone, extrapleural SFT was considered a fibroblastic/myofibroblastic neoplasm with uncertain biological behaviour, rarely metastasizing[15]. In the latest modified WHO classification of soft tissue tumors, SFT was divided into two categories: Solitary fibrous tumor and malignant solitary fibrous tumor[16]. However, according to the updated WHO classification of the digestive-system disorders, SFT is considered a benign tumor with the potential for malignant transformation, the benign or malignant classification of this neoplasm has not yet reached a consensus[4,10].

Chen *et al*[1] reported that 16 of 84 SFTL were malignant, which was similar to the intrapleural SFT recurrence rate of 20%-67% among malignant tumors. Histologically the tumour exhibits a hypercellular spindle-cell proliferation creating storiform arrays with hemangiopericytomatous branching vessels and a moderate to marked atypia. There was parenchymal invasion and no vascular infiltration. High mitotic count (12 per HPF) was observed.

Immunochemistry show strong positivity for CD34 and BCL2 and bland for CD99 and negative for EPAR1 Cytokeratin, CD117, DOG1, ActinaML and Desmine. The mitotic activity index Ki67 was in range from 15% to 20%. SFTL tendencies to be well circumscribed and encapsulated or partially encapsulated, with infiltrative pattern and central necrosis and a growth of > 20 cm in diameter. Malignant SFTL is rare with only 22 cases reported in literature including the present case (Table 1). Literature reported that SFTL usually occurs in female patient over 45 years of age, with no apparent predisposition, in either the right or left sides of the liver[1].

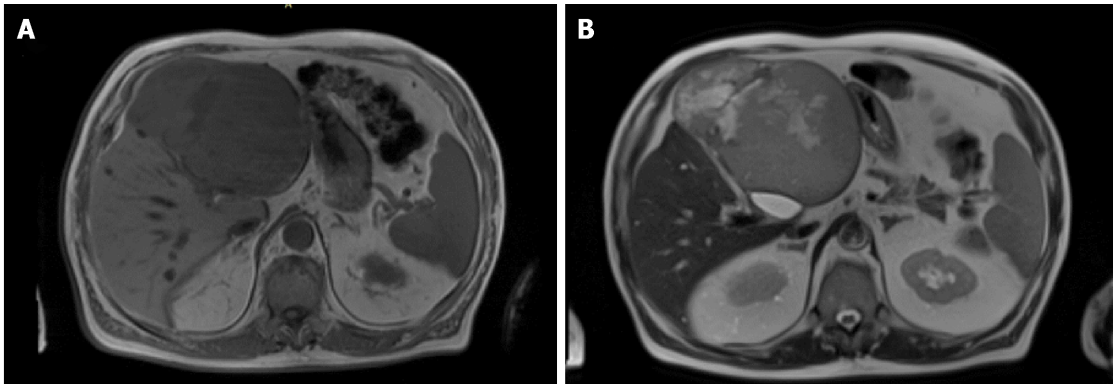

Figure 2 Abdominal magnetic resonance imaging displaying the left liver mass. A: T1. B: T2.

Clinical presentation of these tumors is usually non-specific and the majority of the patients are initially asymptomatic, with an incidental diagnosis, until the tumor attains a large size and presents with symptoms due to mass effect with compression of adjacent organs[2]. Clinical symptoms reported are non-specific, such as weight loss, right upper quadrant pain, fatigue, abdominal distension, gastric plenitude associated to nausea and postprandial vomit depending by tumor size[3]. The clinical presentation of malignant SFTL did not differ notably from the clinical presentation of benign SFTL, have described cases with intractable hypoglycemia[17], unspecific symptoms including abdominal pain and weight loss or muscular and neurological symptoms due to metastatic disease[18,19]. Hypoglycemia (diaphoresis, tremor, anxiety, and lost consciousness) accompanying SFT is the predominant symptom of Doege-Potter syndrome, generally is associated with malignant SFT and was first described in 1930 in a case report by Doege[20-22].

Our patient was conducted at our institution for a left liver mass and severe hypoglycaemia. The physical examination was not specific, in the literature the rare possibility of palpating a solid mass located above the right emmiabdomen and epigastrium is reported. In other cases, the abdominal circumference increases and peripheral edema develops[23]. We asked for an endocrinologist consultation, for the persistent hypoglycaemia, that rejected the insulinoma hypothesis for the low levels of insulin and C-peptide and confirmed that the hypoglycaemia was caused by the presence of insulin-like factors produced by the neoplasm. Although the serum values of IGF-I and IGF-II were normal, the IGFII/IGFI ratios was high.

The IGFII/IGFI ratio is considered a marker of high IGF-II concentration; a ratio of 3: 1 is normal, and in most IGFII-producing tumors the ratio is 10:1. In our case, the spontaneous symptomatic hypoinsulinemic hypoglycaemia, increased IGII/IGFI ratio (7:1), suppression of GH, and the associated clinical features made IGF-II-mediated hypoglycaemia the most likely aetiology.

The typical mechanism involves ectopic tumor production of insulin or other similar hormone such us insulin-like growth factor IGF-II, called "big IGF-II," which has insulin-like effects on the body, stimulating glucose uptake by insulin-sensitive tissues and the tumor itself[3]. IGF-II expression is high during fetal life and is relatively independent from growth hormone. That is the reason why its expression is coherent with the development of this primitive mesenchymal tumor[3]. It has been observed that the hypoglycemia intractable is associated with malignant transformation, suggesting that this phenomena is due to increased biologic activity in malignant SFTL cells[17]. No specific laboratory parameters findings for SFTL are currently available. Laboratory tests such as blood count or C reactive protein, serum tumor markers such as carcinoembryonic antigen (CEA), alpha-fetal-protein (AFP), and carbohydrate antigen 19-9 (CA19-9) are normal[3,23,24].

Radiological studies are unspecific and cannot be definitively distinguish between malignant or benign hepatic tumors. Ultrasound identifies the presence of a solid well-defined ovoid heterogeneous mass, in some cases homogenous and hyperechoic compared with the normal hepatic parenchyma. Computed tomography with intravenous contrast demonstrate a well-defined encapsulated hypervascular tumor and progressive heterogeneous enhancement, it is possible to identify cystic/necrotic areas within the mass. Radiological findings on abdominal MR are similar to the ones described for abdominal CT. The clinical utility of positron emission tomography (PET) in SFTL has not been established[2,9,25].

The majority of SFTL display benign clinical features, even if it should always be considered potentially malignant. R0 surgical resection remains the only therapeutic

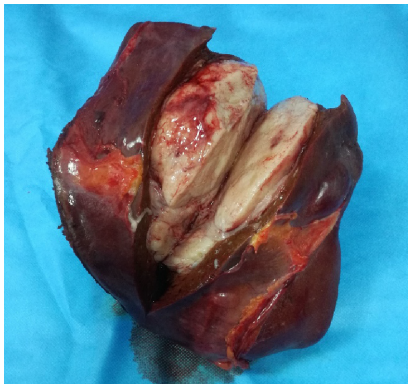

Figure 3 Macroscopic aspect of solitary fibrous tumor liver.

option and it has been proved to the solution to normalize glycaemia. In these patients lifelong follow-up is recommended for the high risk of recurrence[3,17,26]. Considering the literature, benefit of radio and chemotherapy is unknown, as well as prognosis due to the little experience and understanding of the biological nature of the disease[27].

CONCLUSION

Large series with long-term follow-up have not been published neither clinical trials have been undertaken. For all of these reasons, the methodical long-term follow-up of surgically treated SFTLs is strongly recommended.

Table 1 Solitary fibrous tumor liver cases with malignant features

No	Author (yr)	Age/Sex	Presentation	Lobe	Size	Treatment	Histopathology	Tumor-markers	IHC	Follow up
1	Fuksbrumera *et al*[28] (2000)	71/F	NA	R	14 × 17	Resection (UM)	Increased nuclear atypia, mitoses 8/10 HPF	NA	CD34+, Bcl2+, V+	NA
2	Yilmaz *et al*[18] (2000)	25/F	Weakness,fatigue, anorexia, vomiting and progressive jaundice	L + R	32 × 30	Resection (UM)	Cellularity ranged from 20%-60%, necrosis, hypervascularity	NAD	V+	Bone metastasis 1 mo postsurgery managed with 6 mo of chemo (cyclophosphamide, adriamycin)
3	Terkivatan *et al*[29] (2006)	74/M	Gastric fullness, postprandial nausea, and weight loss	L	24 × 21 × 15	Resection (FM)	A few highly cellular areas mitoses 10 - 13/10 HPF	NAD	CD34+, CD99+, Bcl2+, V+	12 mo no signs of local recurrence or distant metastases
4	Chan *et al*[16] (2007)	70/M	Hypoglycaemia, progressive jaundice	R	27 × 24 × 12	Failed TACE 6 wk preoperatively followed by successful resection (UM)	Mildly atypical spindle cells, highly cellular, plemorphia, necrosis, mitoses > 20 HPF	CA-125: 145 U/mL (normal< 35 U/mL)	CD34+, CD99+, bcl2+, V+	bilateral lung metastasis and bi-lobar recurrence at 9 mo
5	Brochard *et al*[30] (2010)	54/M	Abdominal pain, weight loss	R	17	Resection (FM)	Moderately cellular, polymorphic cells, mitoses < 5/10 HPF	NAD	CD34+, V+, desmin+, actin+	Patient died 1 mo after for Local recurrence 6 yr postsurgery, cranial base metastasis, Retroperitoneal and iliac bone metastasis
6	Fama *et al*[21] (2008)	68/M	Hypoglycaemic coma	R	15	Resection (FM)	Hypercellular, moderately atypical nuclei, mitoses 20/10 HPF	NAD	CD34+, Bcl2+	25 mo no signs of local recurrence or distant metastases
7	Peng *et al*[17] (2011)	24/F	Abdominal discomfort and distention	R	30 × 17 × 15	TACE few days prior to resection (FM)	Highly cellular, pleomorphic, necrosis, mitoses > 10/HPF	CA-125 augmented	CD34+, bcl2+, V+	Patient died 16 mo after initial surgery for skull base metastases, Vertebral metastasis
8	Belga *et al*[31] (2012)	66/F	Increase in abdominal girth	R	14	Resection (UM)	Mitoses > 4/10 HPF, necrosis, mild nuclear atypia	NAD	CD34+	30 mo no signs of local recurrence or distant metastases
9	Jakob *et al*[32] (2013)	62/F	Upper abdominal pain, weight loss	L	NA	Resection (UM)	High cellularity, cytological atypia, necrosis, mitoses 6/10 HPF	NAD	CD34+, CD99+, bcl2+	NA

10	Vythianathan and Yong[33] (2013)	78/M	Epigastric pain	L	17 × 13	Resection (UM)	Cellular pleomorphism, necrosis, mitoses > 4/10 HPF	NA	CD34+, CD99+, bcl2+, V+	NA
11	Song *et al*[34] (2014)	49/M	Abdominal pain	L+R	7.6 × 5 × 4.8	Resection (UM)	NAD	NA	CD34+, bcl2+, V+	NA
12	Du *et al*[4] (2015)	55/F	Hypoglycaemia, weight loss	L	15.3 × 15.5 × 15.4	Resection (UM)	NA	NAD	CD34+, bcl-2+	Local recurrence 5 yr postsurgery, resected
13	Feng *et al*[8] (2015)	52/F	NA	R	12	Resection (UM)	Haemorrhage, necrosis	NAD	CD34+	Local recurrence 2 yr postsurgery on L lobe managed with PEI. New lesion 6 mo after PEI
14	Silvanto *et al*[35] (2015)	65/M	Incidental finding	L	18	Resection (FM)	Myxoid changes, infarction, necrosis mitoses 5-7/10 HPF	NAD	CD34+, CD99+, Bcl2+	16 mo no signs of local recurrence or distant metastases
15	Maccio *et al*[26] (2015)	74/F	Right abdominal pain, distension	R	24 × 16	Resection (UM)	Nuclear pleomorphism, cytological atypia, necrosis, haemorrhage, mitoses 9/10 HPF	NA	CD34+, Bcl2+, V+, STAT6+	Lung, omentum, mesentery and abdominal wall metastasis at 9 mo. Patient died 4 mo later
16		80/F	Dyspnoea, cough, asthenia, abdominal pain	R	19 × 15	Palliative Chemotherapy	Highly cellular, pleomorphism, necrosis, haemorrhage, mitoses 7/10 HPF	NA	CD34+, Bcl-2+, V+, STAT6+	R lung metastasis. Patient died 5 mo later
17		65/M	Abdominal discomfort, vomiting and pain	R	3 × 2	Chemotherapy	Cytological atypia, necrosis, mitoses > 6/10 HPF	NA	CD34+, Bcl2+, V+, STAT6+	Bilateral lung metastasis. Patient died 5 mo later
18	Nelson *et al*[1] (2016)	61/M	Diarrhoea	R	15 × 11.5 × 7.5	Resection (FM)	Myxoid changes, mitoses > 9/10 HPF	NAD	CD34+, CD99+, Bcl2+	Extensive local recurrence and pleural metastases. Patient died 6 yr post-surgery
19	Esteves *et al*[7] (2018)	68/F	Incidental finding	R	13.3 × 11.6 × 13.5	Resection (FM)	Focal high-grade cytologic atypia, mitoses 25-27/10 HPF	NAD	CD34+, STAT6+	20-mo follow-up multiple bilateral pulmonary
20	De Los Santos-Aguilar *et al*[36] (2019)	61/M	hypoglycemia disorientation, incoherent speech	R	16 × 13 × 11	Right portal embolization. Six weeks after resection (FM)	High proliferation rate of 8/10 HPF Ki-67 15%	NAD	CD34+, Bcl2+, CD99+	No evidence of metastases
21	Yugawa *et al*[10] (2019)	49/F	Malaise abdominal bloating	R	14	Resection (FM)	Foci of hemorrhage and necrosis Mitosis 1/20 HPF)	NAD	STAT6+ V+	12mo no signs of local recurrence or distant metastases

22	Present case	74/M	Hypoglycemia	L	15 × 13	Resection (FM)	Moderately cellular, pleomorphism, necrosis, mitoses 4/10 HPF Ki-67 35%	CD34+, Bcl2+, CD99+	At the moment, 2 mo no signs of local recurrence or distant metastases

IHC: Immunohistochemistry; M: Male; F: Female; L: Left; R: Right; NA: Not available; UM: Unknown margins; FM: Free margins; HPF: High-power fields; TACE: Transarterial chemoembolization; NAD: No abnormality detected; PEI: Percutaneous ethanol injection; V: Viment.

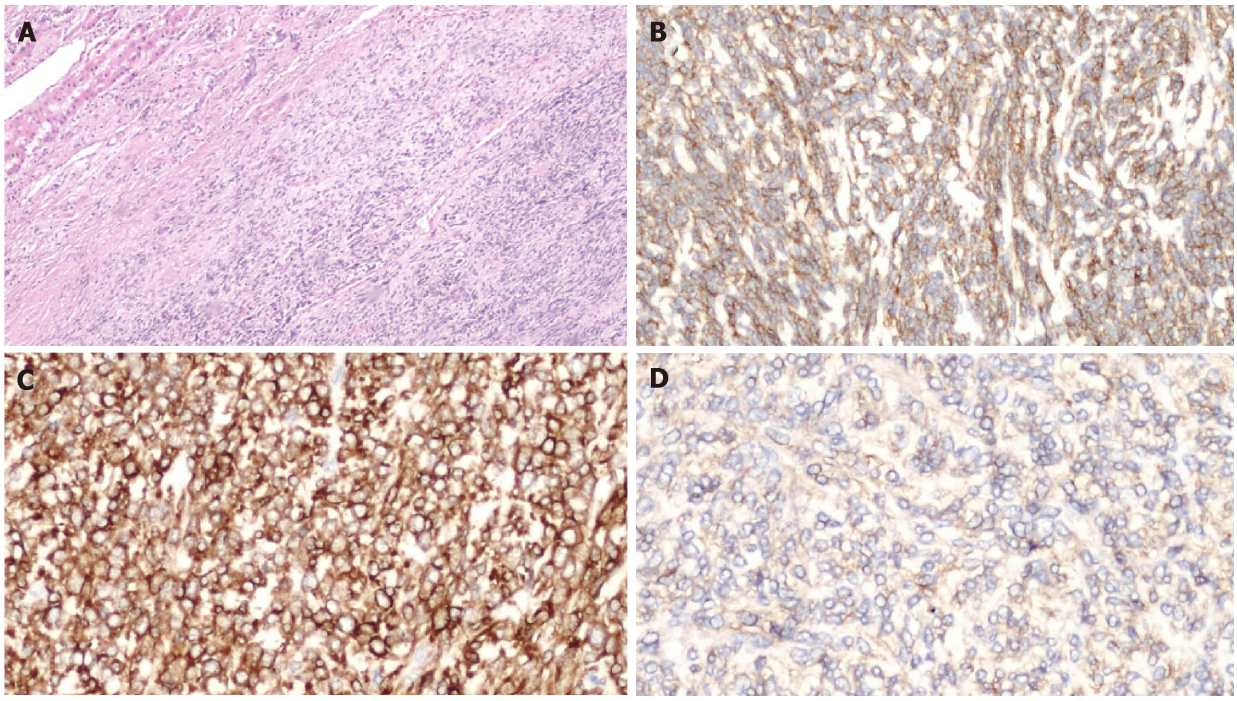

Figure 4 Microscopic findings of solitary fibrous tumor liver. A: Microscopically, the tumours tissue showed a proliferation of spindle cells with infiltrative pattern of hepatic parenchyma. Immunohistochemically, the tumour cells were strongly positive for CD34 (B) and for BCL2 (C). Weakly positive for CD99 (D).

REFERENCES

1 **Chen N**, Slater K. Solitary fibrous tumour of the liver-report on metastasis and local recurrence of a malignant case and review of literature. *World J Surg Oncol* 2017; **15**: 27 [PMID: 28100235 DOI: 10.1186/s12957-017-1102-y]

2 **Shinde RS**, Gupta A, Goel M, Patkar S. Solitary fibrous tumor of the liver - An unusual entity: A case report and review of literature. *Ann Hepatobiliary Pancreat Surg* 2018; **22**: 156-158 [PMID: 29896577 DOI: 10.14701/ahbps.2018.22.2.156]

3 **Beltrán MA**. Solitary Fibrous Tumor of the Liver: a Review of the Current Knowledge and Report of a New Case. *J Gastrointest Cancer* 2015; **46**: 333-342 [PMID: 26490964 DOI: 10.1007/s12029-015-9769-1]

4 **Feng LH**, Dong H, Zhu YY, Cong WM. An update on primary hepatic solitary fibrous tumor: An examination of the clinical and pathological features of four case studies and a literature review. *Pathol Res Pract* 2015; **211**: 911-917 [PMID: 26601735 DOI: 10.1016/j.prp.2015.09.004]

5 **Du EH**, Walshe TM, Buckley AR. Recurring rare liver tumor presenting with hypoglycemia. *Gastroenterology* 2015; **148**: e11-e13 [PMID: 25529805 DOI: 10.1053/j.gastro.2014.09.036]

6 **Zafar H**, Takimoto CH, Weiss G. Doege-Potter syndrome: hypoglycemia associated with malignant solitary fibrous tumor. *Med Oncol* 2003; **20**: 403-408 [PMID: 14716039 DOI: 10.1385/MO:20:4:403]

7 **Maccio L**, Bonetti LR, Siopis E, Palmiere C. Malignant metastasizing solitary fibrous tumors of the liver: a report of three cases. *Pol J Pathol* 2015; **66**: 72-76 [PMID: 26017883 DOI: 10.5114/pjp.2015.51156]

8 **Dey B**, Gochhait D, Kaushal G, Barwad A, Pottakkat B. Solitary Fibrous Tumor of the Liver: A Rare Tumor in a Rarer Location. *Rare Tumors* 2016; **8**: 6403 [PMID: 27746883 DOI: 10.4081/rt.2016.6403]

9 **Esteves C**, Maia T, Lopes JM, Pimenta M. Malignant Solitary Fibrous Tumor of the Liver: AIRP Best Cases in Radiologic-Pathologic Correlation. *Radiographics* 2017; **37**: 2018-2025 [PMID: 29131777 DOI: 10.1148/rg.2017160200]

10 **Bosman FT**. *WHO classification of tumours of the digestive system-NLM Catalog-NCBI*. In: WHO classification of tumours of the digestive system 2010;

11 **Yugawa K**, Yoshizumi T, Mano Y, Kurihara T, Yoshiya S, Takeishi K, Itoh S, Harada N, Ikegami T, Soejima Y, Kohashi K, Oda Y, Mori M. Solitary fibrous tumor in the liver: case report and literature review. *Surg Case Rep* 2019; **5**: 68 [PMID: 31020464 DOI: 10.1186/s40792-019-0625-6]

12 **NEVIUS DB**, FRIEDMAN NB. Mesotheliomas and extraovarin thecomas with hypoglycemic and nephrotic syndromes. *Cancer* 1959; **12**: 1263-1269 [PMID: 14426759 DOI: 10.1002/1097-0142(195911/12)12:6<1263::AID-CNCR2820120620>3.0.CO;2-4]

13 **England DM**, Hochholzer L, McCarthy MJ. Localized benign and malignant fibrous tumors of the pleura. A clinicopathologic review of 223 cases. *Am J Surg Pathol* 1989; **13**: 640-658 [PMID: 2665534 DOI: 10.1097/00000478-198908000-00003]

14 **Wilky BA**, Montgomery EA, Guzzetta AA, Ahuja N, Meyer CF. Extrathoracic location and "borderline" histology are associated with recurrence of solitary fibrous tumors after surgical resection. *Ann Surg Oncol* 2013; **20**: 4080-4089 [PMID: 24046107 DOI: 10.1245/s10434-013-3241-x]

15 **Fisher C**. *Atlas of Soft Tissue Tumor Pathology*. New York: Springer 2013; [DOI: 10.1007/978-1-4614-7025-0]

16 **Jo VY**, Fletcher CD. WHO classification of soft tissue tumours: an update based on the 2013 (4th) edition. *Pathology* 2014; **46**: 95-104 [PMID: 24378391 DOI: 10.1097/PAT.0000000000000050]

17 **Chan G**, Horton PJ, Thyssen S, Lamarche M, Nahal A, Hill DJ, Marliss EB, Metrakos P. Malignant transformation of a solitary fibrous tumor of the liver and intractable hypoglycemia. *J Hepatobiliary Pancreat Surg* 2007; **14**: 595-599 [PMID: 18040628 DOI: 10.1007/s00534-007-1210-0]

18 **Peng L**, Liu Y, Ai Y, Liu Z, He Y, Liu Q. Skull base metastases from a malignant solitary fibrous tumor of the liver. A case report and literature review. *Diagn Pathol* 2011; **6**: 127 [PMID: 22192457 DOI: 10.1186/1746-1596-6-127]

19 **Yilmaz S**, Kirimlioglu V, Ertas E, Hilmioglu F, Yildirim B, Katz D, Mizrak B. Giant solitary fibrous tumor of the liver with metastasis to the skeletal system successfully treated with trisegmentectomy. *Dig Dis Sci* 2000; **45**: 168-174 [PMID: 10695631 DOI: 10.1023/A:1005438116772]

20 **Chamberlain MH**, Taggart DP. Solitary fibrous tumor associated with hypoglycemia: an example of the Doege-Potter syndrome. *J Thorac Cardiovasc Surg* 2000; **119**: 185-187 [PMID: 10612786 DOI: 10.1016/S0022-5223(00)70242-X]

21 **Heuer GJ**. Intrathoracic tumors: experiences with eight cases of tumor of the thoracic wall pleura and mediastinum. *Ann Surg* 1924; **79**: 670-686 [PMID: 17865026 DOI: 10.1097/00000658-192405000-00003]

22 **Famà F**, Le Bouc Y, Barrande G, Villeneuve A, Berry MG, Pidoto RR, Saint Marc O. Solitary fibrous tumour of the liver with IGF-II-related hypoglycaemia. A case report. *Langenbecks Arch Surg* 2008; **393**: 611-616 [PMID: 18418627 DOI: 10.1007/s00423-008-0329-z]

23 **Ji Y**, Fan J, Xu Y, Zhou J, Zeng HY, Tan YS. Solitary fibrous tumor of the liver. *Hepatobiliary Pancreat Dis Int* 2006; **5**: 151-153 [PMID: 16481304]

24 **Makino Y**, Miyazaki M, Shigekawa M, Ezaki H, Sakamori R, Yakushijin T, Ohkawa K, Kato M, Akasaka T, Shinzaki S, Nishida T, Miyake Y, Hama N, Nagano H, Honma K, Morii E, Wakasa K, Hikita H, Tatsumi T, Iijima H, Hiramatsu N, Tsujii M, Takehara T. Solitary fibrous tumor of the liver from development to resection. *Intern Med* 2015; **54**: 765-770 [PMID: 25832939 DOI: 10.2169/internalmedicine.54.3053]

25 **Soussan M**, Felden A, Cyrta J, Morère JF, Douard R, Wind P. Case 198: solitary fibrous tumor of the liver. *Radiology* 2013; **269**: 304-308 [PMID: 24062563 DOI: 10.1148/radiol.13121315]

26 **Weitz J**, Klimstra DS, Cymes K, Jarnagin WR, D'Angelica M, La Quaglia MP, Fong Y, Brennan MF, Blumgart LH, Dematteo RP. Management of primary liver sarcomas. *Cancer* 2007; **109**: 1391-1396 [PMID: 17315167 DOI: 10.1002/cncr.22530]

27 **Novais P**, Robles-Medranda C, Pannain VL, Barbosa D, Biccas B, Fogaça H. Solitary fibrous liver tumor: is surgical approach the best option? *J Gastrointestin Liver Dis* 2010; **19**: 81-84 [PMID: 20361081]

28 **Fuksbrumer MS**, Klimstra D, Panicek DM. Solitary fibrous tumor of the liver: imaging findings. *AJR Am J Roentgenol* 2000; **175**: 1683-1687 [PMID: 11090404 DOI: 10.2214/ajr.175.6.1751683]

29 **Terkivatan T**, Kliffen M, de Wilt JH, van Geel AN, Eggermont AM, Verhoef C. Giant solitary fibrous tumour of the liver. *World J Surg Oncol* 2006; **4**: 81 [PMID: 17118185 DOI: 10.1186/1477-7819-4-81]

30 **Brochard C**, Michalak S, Aubé C, Singeorzan C, Fournier HD, Laccourreye L, Calès P, Boursier J. A not so solitary fibrous tumor of the liver. *Gastroenterol Clin Biol* 2010; **34**: 716-720 [PMID: 20864281 DOI: 10.1016/j.gcb.2010.08.004]

31 **Belga S**, Ferreira S, Lemos MM. A rare tumor of the liver with a sudden presentation. *Gastroenterology* 2012; **143**: e14-e15 [PMID: 22841736 DOI: 10.1053/j.gastro.2012.02.045]

32 **Jakob M**, Schneider M, Hoeller I, Laffer U, Kaderli R. Malignant solitary fibrous tumor involving the liver. *World J Gastroenterol* 2013; **19**: 3354-3357 [PMID: 23745040 DOI: 10.3748/wjg.v19.i21.3354]

33 **Vythianathan M**, Yong J. A rare primary malignant solitary fibrous tumour of the liver. *Pathology* 2013 [DOI: 10.1097/01.PAT.0000426954.68370.26]

34 **Song L**, Zhang W, Zhang Y. (18)F-FDG PET/CT imaging of malignant hepatic solitary fibrous tumor. *Clin Nucl Med* 2014; **39**: 662-664 [PMID: 24686215 DOI: 10.1097/RLU.0000000000000431]

35 **Silvanto A**, Karanjia ND, Bagwan IN. Primary hepatic solitary fibrous tumor with histologically benign and malignant areas. *Hepatobiliary Pancreat Dis Int* 2015; **14**: 665-668 [PMID: 26663016 DOI: 10.1016/S1499-3872(15)60365-4]

36 **De Los Santos-Aguilar RG**, Chávez-Villa M, Contreras AG, García-Herrera JS, Gamboa-Domínguez A, Vargas-Sánchez J, Almeda-Valdes P, Reza-Albarrán AA, Iñiguez-Ariza NM. Successful Multimodal Treatment of an IGF2-Producing Solitary Fibrous Tumor With Acromegaloid Changes and Hypoglycemia. *J Endocr Soc* 2019; **3**: 537-543 [PMID: 30788455 DOI: 10.1210/js.2018-00281]

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