Case Report

Low-grade fibromyxoid sarcoma in the middle ear as a rare location: a case report

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Background: Low-grade fibromyxoid sarcoma (LGFMS) is a rare soft tissue tumor with a misleadingly bland histological appearance and fully malignant behavior, typically occurring in the deep soft tissues of the proximal extremities or trunk of young adults. However, no cases of primary middle ear LGFMS have been reported previously. LGFMS is characterized by high rates of local recurrence and metastatic spread, which should be attached of great importance to clinical diagnosis and treatment.

Case Description: Herein, we report an unusual case of LGFMS occurring primarily in the middle ear of a 12-year-old boy, who presented with aural fullness and gradually progressive hearing loss in the left ear for 6 months, without other related symptoms and family history. Preoperative imaging examination suggested that the lesions were located in the tympanic cavity, tympanic antrum, and mastoid portion, with equisignal or hypointense on T1 weighted image (*T1WI*), apparent hyperintense on T2 weighted image (*T2WI*), and slight enhancement on *T1WI* following administration of gadolinium. A decision was made to perform mastoidectomy, as the lesion was limited to the middle ear and did not invade the facial nerve canal or the inner ear. During the surgery, the mass exhibited a hard texture and smooth surface that was approximately 1.0 cm × 1.5 cm in size, not easy to bleed, and non-adherent to surrounding tissues. After consultation, a diagnosis of LGFMS was made by postoperative pathology. The patient showed an excellent recovery from surgery without any complications. At present, the patient has been followed up for 24 months, and no local recurrence or distant metastasis has been observed.

Conclusions: The primary LGFMS in the middle ear is very rare, and the clinical manifestations and related examinations lack specificity, so a clinical diagnosis of LGFMS is very difficult, and the final diagnosis is mainly determined by pathological diagnosis. Due to its malignant behavior, clinical diagnosis and treatment should be vigilant against it. Treatment of LGFMS mainly requires extensive resection combined with radiotherapy and chemotherapy if necessary, and long-term follow-up is essential. Reporting and identification of this rare case are imperative to improving our understanding of LGFMS and reducing misdiagnosis.

Keywords: Low-grade fibromyxoid sarcoma (LGFMS); the middle ear; soft tissue tumor; case report

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Introduction

Low-grade fibromyxoid sarcoma (LGFMS) is a rare soft tissue tumor classified as a distinctive subtype of fibroblastic and myofibroblastic tumors, with a misleadingly bland histological appearance and fully malignant behavior. Currently, less than 500 cases of LGFMS have been reported in the literature worldwide (1-7). It was first proposed by Evans *et al.* (7) in 1987 and was characterized by alternating fibrous and mucinous regions, with stellate cells or bland spindles that exhibit swirling, spiraling growth patterns. Subsequent genetic analysis studies revealed that about 90% of LGFMSs harbor a *FUS-CREB3L2* fusion gene

resulting from a recurrent (7;16)(q34;p11) translocation (8), and a few harbor *FUS-CREB3L1* or *EWSR1-CREB3L1* fusion genes (9,10). However, the above three fusion genes were not detected in occasional cases. Meanwhile, diffuse cytoplasmic immunohistochemical expression of MUC4 was a consistent finding, which is useful for identifying morphological suspicion (11). Extensive radical surgery is the primary choice for LGFMS treatment, supplemented by radiotherapy and chemotherapy when necessary to reduce local recurrence.

LGFMS tends to occur in the deep soft tissues of the proximal extremities, trunk, and abdomen of young adults (12). However, head and neck involvement is relatively rare, and there are no reported cases of primary middle ear involvement in the literature. Herein, we report an unusual case of LGFMS occurring primarily in the middle ear of a 12-year-old boy who presented with gradually progressive hearing loss in the left ear for 6 months. To the authors' knowledge, the present case represents the first reported instance of a middle ear LGFMS. We present the following article in accordance with the CARE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-196/rc).

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient's parents for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

A 12-year-old boy presented with gradually progressive hearing loss in the left ear for 6 months. He also reported aural fullness during the disease course, but without otorrhea, otalgia, and tinnitus. There was no family history of deafness and no history of any treatment for hearing loss. Upon examination, the left tympanic membrane appeared porcelain white and granulation tissue was visible in the anterior inferior quadrant of the tympanic membrane (*Figure 1A*). Pure tone audiometry (PTA) showed moderate to severe conductive hearing loss in the left ear, and air and bone conduction thresholds disclosed an approximately 50 dB HL air-bone gap (*Figure 1B*). High-resolution computed tomography (HRCT) of the temporal bone revealed an irregular soft tissue density mass with significant strip calcification in the tympanic cavity, tympanic antrum, and mastoid portion. The lesions resulted in a slightly rough surface of the bone in the inferior tympanic cavity and also contributed to utterly unclear air compartments in the inferior tympanic cavity (*Figure 1C*,*1D*). Magnetic resonance imaging (MRI) indicated that the mass was equisignal or hypointense on T1 weighted image (*T1WI*), with apparent hyperintense on T2 weighted image (*T2WI*), and slight enhancement on *T1WI* following administration of gadolinium (*Figure 2*).

A decision was made to perform mastoidectomy since the lesion was limited to the middle ear and did not invade the facial nerve canal or the inner ear. During the surgery, the mass exhibited a hard texture and smooth surface that was approximately 1.0 cm × 1.5 cm in size, not easy to bleed, and non-adherent to surrounding tissues. Intraoperative pathological results suggested that the tumor was more likely to be benign, so extended resection was not performed.

After surgery, the specimen was sent for histopathologic examination. Macroscopically, the tumor measured 1.0 cm × 1.4 cm × 0.9 cm, with a lobulated appearance and smooth surface. Also, the cut surface was tough with pinpoint hemorrhages in the central area. Microscopically, the tumor was characterized by less cellular and shallower myxoid areas alternating with fibrous areas with increased atypia cells where eosinophilic collagen fibers and hyalinization were present. The tumor cells were morphologically consistent, mainly composed of slender spindle cells with small nuclei and inconspicuous nucleoli. Nuclear atypia was not obvious and mitosis was rare. Immunohistochemical examination exhibited that the tumor cells were immunopositive for vimentin and MUC4, and immunonegative for Ki-67, CD34, smooth muscle actin (SMA), epithelial membrane antigen (EMA), and desmin (*Figure 3*). MUC4 with strong and diffuse immunoreactivity is considered key evidence for a diagnosis of LGFMS. Ultimately, a diagnosis of LGFMS was made by postoperative pathology after consultation.

Postoperative follow-up was achieved via telephone and outpatient at regular intervals (3- to 6-monthly intervals for up to 2 years and annually thereafter). At present, the patient has been followed up for 24 months, and no local recurrence or distant metastasis has been observed.

Discussion

LGFMS is a rare fibroblastic and myofibroblastic tumor that was first proposed by Evans *et al.* in 1987. The age

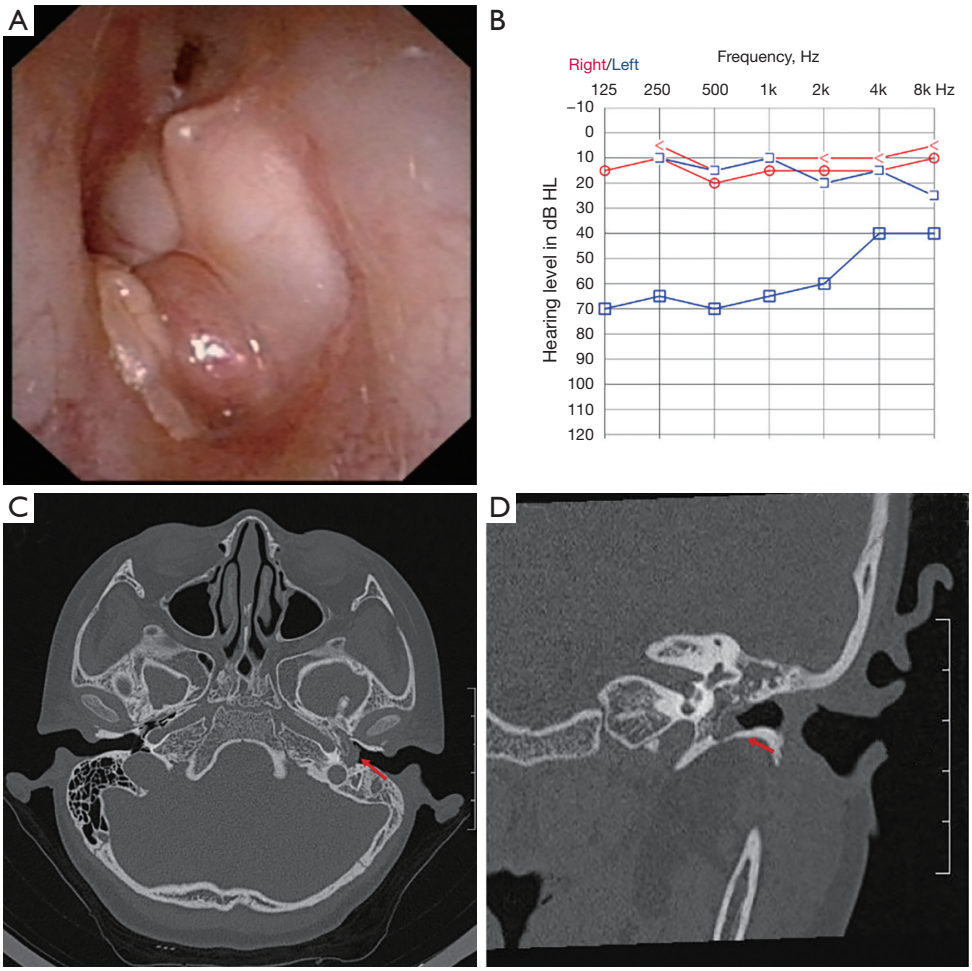

Figure 1 Otoscopy, audiograms, and preoperative HRCT. (A) The outcome of otoscopy in the left ear. (B) Audiograms of the patient. The air conduction results are represented by the blue "□" in the left ear and the red "○" in the right ear. The bone conduction results are represented by the blue "]" in the left ear and the red "<" in the right ear. (C) In the axial images, the red arrow represents an irregular soft tissue density mass with significant strip calcification. (D) In the coronal images, the red arrow represents a slightly rough surface of the bone in the inferior tympanic cavity. HRCT, high-resolution computed tomography.

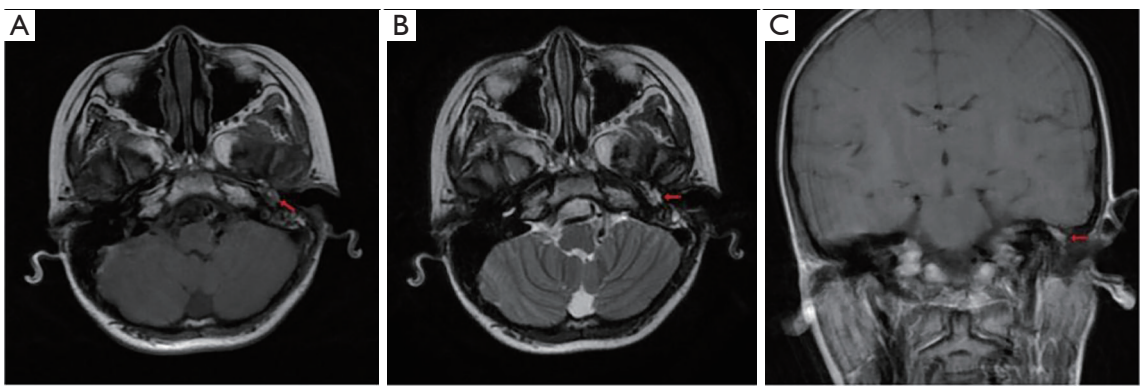

Figure 2 Preoperative MRI. (A) *T1WI*, axial. (B) *T2WI*, axial. (C) Enhanced *T1WI*, coronal. The red arrow indicates the lesion site. MRI, magnetic resonance imaging; T1WI, T1 weighted image; T2WI, T2 weighted image.

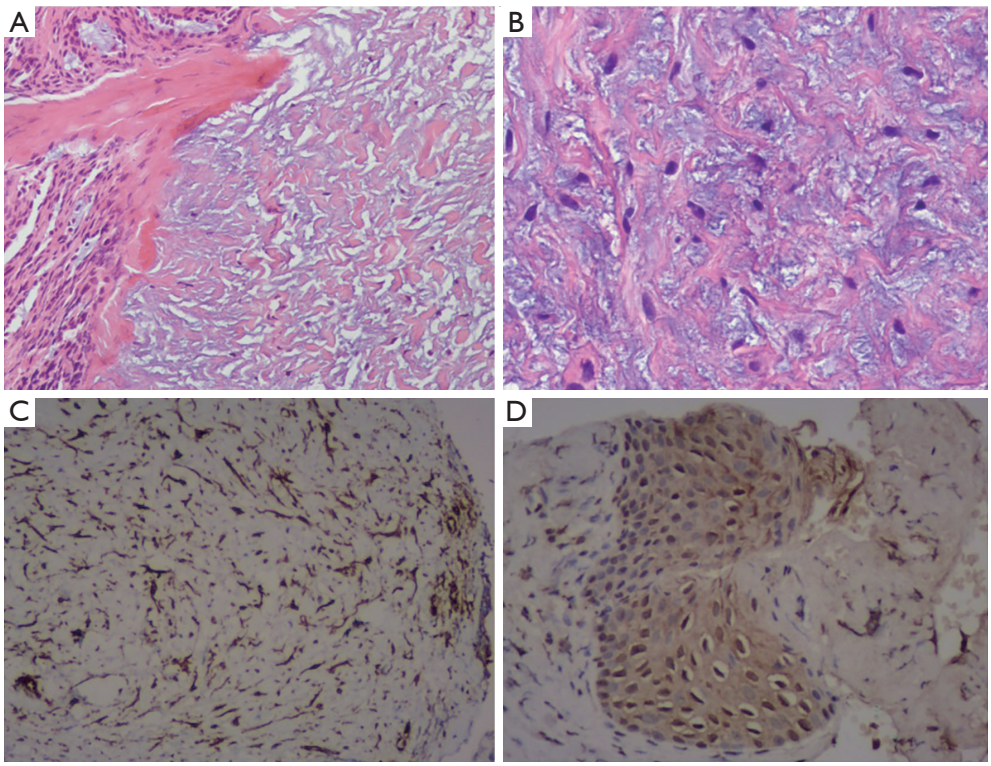

Figure 3 The pathology images of the lesion. (A) Myxoid areas alternate with fibrous areas (HE, ×200). (B) Slender spindle cells with small nuclei and scant, wispy cytoplasm (HE, ×400). (C,D) The tumor cells were immunopositive for vimentin immunostaining (×200) and MUC4 immunostaining (×200). HE, hematoxylin-eosin staining.

of onset of LGFMS ranges from 6 to 74 years old, but it mainly occurs in young and middle-aged adults, with a mean onset age of 34 years old and a median onset age of 29 years old (5,12). It tends to occur in the deep soft tissues of the proximal extremities, trunk, and abdomen, while other primary sites, including retroperitoneum, intracranial, mesentery, kidney, head, and neck, have also been reported (1,5,12-16). In this paper, we reported an unusual case of LGFMS occurring primarily in the middle ear of a 12-year-old boy. To the authors' knowledge, no cases of primary middle ear LGFMS have been reported previously. A portion of mucosal cells in the middle ear cavity is derived from neural crest cells, and cartilage tissue is derived from the mesoderm, which is the histomorphological basis for LGFMS origination in the middle ear.

The clinical manifestations of LGFMS are mostly slow-growing, painless single masses with a hard texture, which are easily misdiagnosed as benign tumors. CT scanning shows an uneven, slightly low-density or isodensity shadow with an unclear boundary with surrounding tissues. Enhanced scanning reveals a slight enhancement of lesions. MRI examination demonstrates that the fiber component manifests as hypointense on both *T1WI* and *T2WI*, while the myxoid component presents as hypointense on *T1WI* and hyperintense on *T2WI*. Since LGFMS is composed of mixed fibrous and myxoid components, *T1WI* tends to present as hypointense, and *T2WI* usually shows mixed signals of hyperintense and hypointense (17). In this case, the clinical manifestations lack specificity. The patient only presented with gradually progressive hearing loss without otorrhea, otalgia, tinnitus, and other related symptoms. Electronic otoscopy showed a porcelain white tympanic membrane with granulation tissue, which is easily confused with congenital cholesteatoma of the middle ear. Imaging examination was consistent with the characteristics of a fibromyxoid tumor, but cholesterol granuloma, tympanic bulbous tumor, and malignant tumor of the middle ear could not be excluded. Therefore, a clinical diagnosis of LGFMS is very difficult and clinicians should be vigilant when diagnosing and treating LGFMS middle ear lesions.

The definitive diagnosis of LGFMS mainly depends on the pathological diagnosis. LGFMS exhibits an infiltrative

growth pattern with mild tumor morphology, which is characterized by alternating fibrous and mucinous regions and a transition between the two regions as well as a clear boundary (18). In addition, arcuate vessels and perivascular hyaline degeneration are two other histological features of LGFMS, and rare central necrosis has been reported in individual cases. The tumor cells are morphologically consistent, mainly comprising slender spindle cells or stellate cells that exhibit spiraling growth patterns. The tumor cells have an irregular nuclear outline, with hyperchromatic nuclei but inconspicuous atypia. Furthermore, mitosis is rare, with mitotic counts less than 5/50 HPF in most cases. Immunohistochemically (19), the tumor cells are almost always positive for vimentin, CD99, BCL-2, and MUC4 to different degrees, among which MUC4 with strong and diffuse immunoreactivity is the key evidence for the diagnosis of LGFMS (11). Genetically, the majority of LGFMS cases are characterized by a *FUS-CREB3L2* fusion gene resulting from a recurrent (7;16)(q34;p11) translocation, with a few harboring *FUS-CREB3L1* or *EWSR1-CREB3L1* fusion genes (8-10). Due to the mild histological appearance and completely malignant behavior of LGFMS, pathological diagnosis is crucial, and attention should be paid to distinguish it from other benign soft tissue tumors or sarcomas with spindle cell proliferation and mucinous changes, including sclerosing epithelioid fibrosarcoma (SEF), low-grade myxoid fibrosarcoma (LGMF), solitary fibrous tumor (SFT), and invasive fibromatosis.

Treatment of LGFMS mainly requires extensive resection combined with radiotherapy and chemotherapy if necessary, and long-term follow-up is essential. The results of the long-term follow-up study reported by Evans *et al.* showed that the recurrence rate of LGFMS was 63.64%, the metastasis rate was 45.45%, and the fatality rate was 42.42% (5). Mastoidectomy was performed in our case, and no recurrence or metastasis was observed during the 24 months follow-up, which may be due to the limited lesions and the relatively good prognosis of LGFMS in children.

Conclusions

LGFMS is a rare soft tissue tumor with a misleadingly bland histological appearance and fully malignant behavior, typically occurring in the deep soft tissues of the proximal extremities or trunk of young adults. However, no cases of the primary middle ear LGFMS have been previously reported in the literature. The present case represents the first reported instance of a middle ear LGFMS. The clinical manifestations and related examinations lack specificity, so a clinical diagnosis of LGFMS is very difficult, and the final diagnosis is mainly determined by pathological diagnosis. The treatment mainly requires extensive resection combined with radiotherapy and chemotherapy if necessary, and long-term follow-up is essential. Due to its malignant behavior, clinical diagnosis and treatment should be vigilant against it. Reporting and identification of this rare case are imperative to improving our understanding of LGFMS and reducing misdiagnosis.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-22-196/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-22-196/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient's parents for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. Yoshimura R, Nishiya M, Yanagawa N, et al. Low-grade fibromyxoid sarcoma arising from the lung: A case report. Thorac Cancer 2021;12:2517-20.
2. Dugalic V, Ignjatovic II, Kovac JD, et al. Low-grade fibromyxoid sarcoma of the liver: A case report. World J Clin Cases 2021;9:175-82.
3. Scheer M, Vokuhl C, Veit-Friedrich I, et al. Low-grade fibromyxoid sarcoma: A report of the Cooperative Weichteilsarkom Studiengruppe (CWS). Pediatr Blood Cancer 2020;67:e28009.
4. Rao R, Honavar SG, Mulay K, et al. Primary orbital low-grade fibromyxoid sarcoma - A case report. Indian J Ophthalmol 2019;67:568-70.
5. Evans HL. Low-grade fibromyxoid sarcoma: a clinicopathologic study of 33 cases with long-term follow-up. Am J Surg Pathol 2011;35:1450-62.
6. Evans HL. Low-grade fibromyxoid sarcoma. A report of 12 cases. Am J Surg Pathol 1993;17:595-600.
7. Evans HL. Low-grade fibromyxoid sarcoma. A report of two metastasizing neoplasms having a deceptively benign appearance. Am J Clin Pathol 1987;88:615-9.
8. Matsuyama A, Hisaoka M, Shimajiri S, et al. Molecular detection of FUS-CREB3L2 fusion transcripts in low-grade fibromyxoid sarcoma using formalin-fixed, paraffin-embedded tissue specimens. Am J Surg Pathol 2006;30:1077-84.
9. Mertens F, Fletcher CD, Antonescu CR, et al. Clinicopathologic and molecular genetic characterization of low-grade fibromyxoid sarcoma, and cloning of a novel FUS/CREB3L1 fusion gene. Lab Invest 2005;85:408-15.
10. Lau PP, Lui PC, Lau GT, et al. EWSR1-CREB3L1 gene fusion: a novel alternative molecular aberration of low-grade fibromyxoid sarcoma. Am J Surg Pathol 2013;37:734-8.
11. Doyle LA, Möller E, Dal Cin P, et al. MUC4 is a highly sensitive and specific marker for low-grade fibromyxoid sarcoma. Am J Surg Pathol 2011;35:733-41.
12. Sambri A, Righi A, Tuzzato G, et al. Low-grade fibromyxoid sarcoma of the extremities: a clinicopathologic study of 24 cases and review of the literature. Pol J Pathol 2018;69:219-25.
13. Modi MB, Pei S, Hedberg ML, et al. Clinical, pathologic, and molecular analyses of superficial low-grade fibromyxoid sarcoma in two young patients: A rare and deceptive mimic of benignancy. J Cutan Pathol 2022;49:638-44.
14. Koucky V, Kalfert D, Kodetova Novakova D, et al. Low-grade fibromyxoid sarcoma of the maxillary sinus. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2021;165:342-5.
15. White IK, Scherer AG, Baumanis MM, et al. Rapidly enlarging low-grade fibromyxoid sarcoma with intracranial extension in a 5-year-old girl: case report. J Neurosurg Pediatr 2015;16:372-6.
16. Gjorgova Gjeorgjievski S, Fritchie K, Thangaiah JJ, et al. Head and Neck Low-Grade Fibromyxoid Sarcoma: A Clinicopathologic Study of 15 Cases. Head Neck Pathol 2022;16:434-43.
17. Sargar K, Kao SC, Spunt SL, et al. MRI and CT of Low-Grade Fibromyxoid Sarcoma in Children: A Report From Children's Oncology Group Study ARST0332. AJR Am J Roentgenol 2015;205:414-20.
18. Fukunaga M, Ushigome S, Fukunaga N. Low-grade fibromyxoid sarcoma. Virchows Arch 1996;429:301-3.
19. Folpe AL, Lane KL, Paull G, et al. Low-grade fibromyxoid sarcoma and hyalinizing spindle cell tumor with giant rosettes: a clinicopathologic study of 73 cases supporting their identity and assessing the impact of high-grade areas. Am J Surg Pathol 2000;24:1353-60.

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