Low-Grade Fibromyxoid Sarcoma of the External Auditory Canal: A Rare Pathology and Unusual Location

Kalpana Kumari¹ · Ramya Thota² · Heera Lal Chaudhary³ · Mehar C. Sharma¹ · Alok Thakar² · Geetika Singh^{1,4}

Received: 11 October 2018 / Accepted: 13 March 2019 / Published online: 4 April 2019
© Springer Science+Business Media, LLC, part of Springer Nature 2019

Abstract

Low-grade fibromyxoid sarcoma (LGFMS) is an enigmatic soft tissue tumor. It frequently presents as a deeply seated mass in the proximal extremities and trunk. Superficial LGFMSs of the head and neck are exceedingly rare. Hyalinizing spindle cell tumor with giant rosettes (HSTGR) is an entity considered to be on the histologic spectrum of LGFMS. We present a case of a 44-year-old female who presented with a superficial, polypoid mass of the external auditory meatus. Microscopic examination revealed the classic histologic features of HSTGR. To our knowledge, this case is the first described at this extremely unusual location. Identification and reporting of such unusual cases is important to understand and compare the behavior of superficial LGFMS to that of the more common deeply seated tumors.

Keywords Low-grade fibromyxoid sarcoma · Hyalinizing spindle cell tumor with giant rosettes · Superficial · External auditory meatus

Introduction

Low-grade fibromyxoid sarcoma (LGFMS) is a rare soft tissue tumor of fibroblastic lineage [1]. Fewer than 350 cases are reported in literature. The majority of these were initially misdiagnosed as benign entities, such as a fibroma or fibromatosis, and later presented with metastases [2]. Hyalinizing spindle cell tumor with giant rosettes (HSTGR) is now considered to be part of the histological spectrum of low-grade fibromyxoid sarcoma (LGFMS) [3]. Studies have shown shared morphologic features and common cytogenetic alterations between these two tumors [3–5]. There is no sex predilection for either, and young adults are predominantly affected [2, 4].

The typical presentation is characterized by a slow-growing, deep seated mass located in the proximal extremities or trunk [4–6]. In rare instances, unusual sites including the head and neck region, abdominal wall, chest wall, axilla, and gastrointestinal tract are affected [7–12]. To date, only five cases of LGFMS located in head and neck region are reported in literature [9–12]. Recent studies show that superficial LGFMS may occur more frequently than previously believed and predominately affect the pediatric population [3]. This entity is now considered a grade 1 sarcoma with potential for local recurrences and distant metastases [2]. Here, we present a case of HSTGR presenting as a superficial, polypoid mass arising from the external auditory meatus. To the best of our knowledge, this case appears to be the first described at this extremely unusual location.

✉ Geetika Singh
ggmed22@gmail.com

¹ Department of Pathology, All India Institute of Medical Sciences, New Delhi, India

² Department of Otorhinolaryngology, All India Institute of Medical Sciences, New Delhi, India

³ Department of Radiology, All India Institute of Medical Sciences, New Delhi, India

⁴ Department of Pathology, All India Institute of Medical Sciences, Room No. 1048, First Floor, Teaching Block, New Delhi 110029, India

Case Report

A 44-year-old woman presented with a complaint of bilateral pain in her shoulders. She experienced difficulty with movement and associated headaches of 6 years duration. She also reported a swelling in the right external auditory canal (EAC) for the past 6 months with bleeding and occasional pus. On examination, there was right-sided facial weakness. High resolution computed tomography (HRCT) of the

temporal bone showed a well-defined, round to ovoid, non-enhancing soft tissue lesion measuring 10.6×11.4 mm. A small calcific focus was noted near its base. The lesion arose from the antero-superior wall of the cartilaginous aspect of the right EAC and extended medially to the margin of antero-superior bony aspect of the canal (Fig. 1). Laterally, it completely occluded the canal. No vascular invasion or bony erosion was identified. Bilateral pinna, middle ear cavities, and internal ears were normally seen. Carotid Doppler revealed no abnormality.

Fig. 1 Axial contrast CT sections show a well defined, heterogeneously enhancing mass (scale bar) in the cartilaginous part of right external auditory canal

Fine needle aspiration cytology (FNAC) showed scant fragments of dispersed, bland spindle cells embedded in a collagenous stroma. Mitoses or necrosis were absent. The possibility of a benign spindle cell lesion was suggested.

With this diagnosis, the patient underwent excisional biopsy under local anesthesia. A firm to soft, pedunculated tumor was excised with adequate margins from the antero-superior wall of EAC at its bony attachment. The surgical specimen was sent for histopathologic examination.

Grossly, it comprised a circumscribed, globular mass tissue measuring $2 \times 1.5 \times 1$ cm. The cut surface was firm with areas of pinpoint hemorrhages. Microscopic examination showed a hyperkeratotic and mildly acanthotic epidermis surfacing an unencapsulated tumor in the reticular dermis. The cellularity was variable. More cellular areas displayed oval to plump spindled cells arranged in short intersecting fascicles. Focal whirling and dispersed arteriole-sized vessels with peripheral hyalinization were present. Intervening paucicellular areas showed collagenized stroma. Focally, collagen rosettes with central hyalinization and scattered dystrophic calcifications were present. Nuclear atypia, mitoses, and necrosis were absent (Fig. 2).

By immunohistochemistry (IHC), the tumor cells were immunopositive for vimentin, epithelial membrane antigen (EMA), S100 (focally), and bcl2, and immunonegative for cytokeratin (CK), smooth muscle actin (SMA), and desmin (Fig. 3). MUC4 demonstrated a strong and diffuse

Fig. 2 Photomicrograph depicting overlying acanthotic epidermis with an underlying unencapsulated dermal tumor displaying variable cellularity (a), $\times 100$. Cellular bland tumor comprising spindle cells embedded in collagenous stroma. Focal dystrophic calcification and an abrupt transition to myxoid area are identified (b), $\times 100$. Cellu-

lar zone displaying whirling arrangement of tumor cells. No nuclear atypia or mitosis (c), $\times 200$. Classic collagen rosettes surrounded by tumor cells (d), $\times 200$. Focal area of larger collagen nodules (e), $\times 400$. Heavily collagenized stroma with curvilinear blood vessels (f), $\times 100$

Fig. 3 Photomicrograph showing strong and diffuse immunopositivity of spindle cells for vimentin (a), $\times 200$. Membranous positivity for EMA (b), $\times 200$. Immunonegative for CK (c), $\times 200$. Focal nuclear positivity for S100 (d), $\times 200$. Immunonegative for SMA and desmin (e, f), $\times 200$

Fig. 4 Photomicrograph displaying cytoplasmic immunopositivity for MUC4 in the tumor cells

cytoplasmic staining which helped to confirm the diagnosis (Fig. 4). The MIB-1 labelling index was 0%. Based on the presence of bland spindled cells, collagen rosettes, and the IHC results, a final diagnosis of HSTGR was rendered. The patient is on follow up and does not show evidence of recurrence 36 months post-surgery.

Discussion

LGFMS is a rare sarcoma which was first described by Evans in 1987 [1]. Increasing understanding of the histomorphologic features of LGFMS has led to a rising number

of cases reported in literature. Cases initially misdiagnosed as fibromatosis with later presentation of lung metastases have led to the reevaluation of this entity [2]. HSTGR and LGFMS share histologic features as well as a translocation, $t(7;16)(q34;p11)$, that results in a chimeric fusion protein [2, 3]. Therefore, they are believed to represent different morphological spectra of a single entity.

Tumors more frequently present as deeply seated intramuscular masses of the lower extremities and trunk [3]. The rare superficial tumors are subfascial or arise from subcutis or dermis [3]. Two cases of LGFMS have originated from the mesentery and stomach [7, 8].

In the present case, a superficial polypoid mass was attached to the antero-superior wall of the cartilaginous part of right EAC. The rarity of these tumors at superficial locations may lead to the erroneous diagnosis of a benign tumor. This mistake may delay biopsy or excision.

These tumors mostly occur in young- to middle-aged adults but can affect a wide age range including pediatric population [2, 3, 5, 6]. Billings et al., in a series of 19 cases, showed that superficial LGFMS are more common than previously recognized and children are more often affected [3]. Tumor size can range from 1 cm to more than 20 cm [2]. Four cases of head and neck LGFMS were described in thyroid gland, parotid gland, and masseter muscle [9–12]. These cases were predominantly diagnosed in elderly [9–12]. One of the four cases metastasized, demonstrating the malignant potential for local and distant metastases [10].

Microscopic examination from different tumor areas can show variable morphology. Tumors show mild to moderate

Table 1 Differential diagnoses

Differential diagnosis	Common location	Histology	Collagen rosettes	EMA	CK	S100	Desmin	SMA	CD34	MUC4	Cytogenetics	Behavior
HSTGR	Proximal extremities, trunk	Heavily collagenized hypocellular myxoid and cellular areas with bland spindle cells	30% of cases	Positive	Negative	Focal in rosettes	Negative	Negative	Negative	Positive	FUS-CREB3L2 or FUS-CREB3L1 gene fusion	Prolonged follow up showed recurrences and metastases
Desmoid fibromatosis	Shoulder, chest wall, thigh, head & neck, back	Infiltrative border, bland spindled to stellate cells, in fascicles, slit like vessels, keloid like collagen	Absent	Negative	Negative	Negative	Negative	Positive	Negative	Negative	Trisomies chromosome 8 and/or 20 (< 30%), mutation in APC gene and CTNNB1	Locally aggressive
Soft tissue perineurioma	Lower limbs, upper limbs, head & neck rare	Storiform growth pattern, elongated spindle cells, collagenous and myxoid stroma	Absent	Positive (weak to strong, focal to diffuse)	Focal	Negative	Negative	Focal	Positive (60%)	Negative	Chromosome 22 deletions and monosomies	Benign rarely recurrences
Neurofibroma	Skin in association with small nerves	Infiltrative, spindle-shaped cells in myxoid stroma and collagen fibres	Absent	Positive in perineurial cells	Negative	Positive	Negative	Negative	Positive	Negative	Inactivating mutations in NF1	Benign
Myxoid DFSP	Trunk, proximal extremities, head and neck region	Infiltrative, spindled cells in storiform/whorled pattern, blood vessels in collagenized stroma	Absent	Weak	Negative	Negative	Negative	Positive	Positive	Negative	Supernumerary ring chromosomes	Locally aggressive

Table 1 (continued)

Differential diagnosis	Common location	Histology	Collagen rosettes	EMA	CK	S100	Desmin	SMA	CD34	MUC4	Cytogenetics	Behavior
Dermatofibroma	Limbs, trunk, neck and face	Dermal can involve subcutis and pseudoepitheliomatous hyperplasia, interlacing fascicles of spindle cells in loose collagenous stroma, inflammatory & foam cells. Variants; myxoid, cellular, epithelioid, hemosiderotic, clear etc.	Absent	Negative	Negative	Negative	Negative	Focal	Peritumoral	Negative	t(17;22) (q22;q13), supernumerary ring chromosome some from translocation r(17;22)	Benign rarely recurrences
Nodular fasciitis	Subcutaneous/intramuscular, upper extremity, trunk, head and neck	Spindle-shaped fibroblast, cellular, keloidal collagen bundle, blood vessels	Absent	Negative	Negative	Negative	Rare	Positive	Negative	Negative	MYH9-USP gene fusion	Recurrence rare
Myxoid solitary fibrous tumor	Any location, subcutaneous/deep tissue, head and neck etc	Hypo-and hypercellular areas, bland spindle cells, hyalinized collagen, HPC-like vessels	Absent	Positive (20–35%)	Focal	Focal	Focal	Positive (20–35%)	Positive	Negative	Gain of chromosomes 5, 8 and 21 Loss of 13q	Benign, 10% cases behaves aggressively

Table 1 (continued)

Differential diagnosis	Common location	Histology	Collagen rosettes	EMA	CK	S100	Desmin	SMA	CD34	MUC4	Cytogenetics	Behavior
Myoepithelioma	Limbs and limb girdles	Reticular/trabecular growth pattern, spindled/epithelioid cells, clear cytoplasm	Absent	Positive (2/3rd cases)	Positive	Positive	Negative	Can be positive	Negative	Negative	EWSR1 gene rearrangement	Benign

cellularity and often have abrupt transitions from myxoid to fibrous to paucicellular zones [2–6]. The paucicellular areas comprise bland spindled to oval to epithelioid cells with minimal nuclear atypia [2, 3, 5]. Myxoid zones predominantly show collagenized stroma with dispersed spindled cells and few curvilinear vessels [2, 3]. Collagen rosettes with a central zone of eosinophilic collagen surrounded by spindled to epithelioid cells may be a conspicuous finding and are characteristic of HSTGR [4, 5]. The varied growth patterns, ranging between swirled, storiform, and fascicular, may suggest a wide range of benign and malignant soft tissue tumors in the histologic differential diagnosis [2, 3]. Mitoses and necrosis are not usually identified in LGFMS [2, 3]. Up to 10% of cases, however, may show increased cellularity, nuclear atypia, or epithelioid morphology [2, 3].

The histologic mimics of LGFMS include spindle cell lesions such as fibromatosis, nodular fasciitis, collagenous fibroma, benign nerve sheath tumors, collagenized neurofibroma, and myxofibrosarcoma (Table 1) [2, 3]. A panel of immunohistochemistry stains may aid to exclude entities on the differential diagnoses (Table 1). LGFMS shows consistent immunoreactivity for vimentin, focal immunoreactivity for smooth muscle actin, EMA, CD99, S100, bcl2, and CD68. Cytokeratins and CD34 are negative [2]. MUC4 is a highly sensitive and specific marker; however, Linos et al. described a case of *FUS-CREB3L2* rearranged LGFMS as negative for MUC4 [13, 14]. This finding suggests that classic histology with MUC4 negativity should not deter pathologists from making the diagnosis. Identification of t(7;16) (q33;p11) is recommended; however, the high cost and lack of fluorescent in situ probes may limit the capabilities for these tests in developing countries.

The bland histologic features of this tumor often do not correlate with clinical behavior. Wide local excision is the treatment of choice [2, 3]. Superficial LGFMS has a better prognosis as compared to deep seated LGFMS due to earlier detection and amenability for complete excision [3]. Studies have shown that both superficial and deep LGFMS have an approximate recurrence rate of 10%. Metastases have only been reported in cases of deep LGFMS (6%) [3, 5]. Late metastases are known to occur, and patients should be kept on long term follow-up. Our patient did not show any evidence of recurrence 36 months post-surgery.

Conclusion

LGFMSs are predominantly deep seated, intramuscular soft tissue tumors but can occasionally be superficial in location. Increasing knowledge of this entity has led to recognition of cases affecting unusual sites such as the EAC. Identification

and reporting of such unusual cases is necessary to understand their behavior.

Compliance with Ethical Standards

Conflict of interest All authors declare no potential conflicts of interest (financial or non-financial).

Informed Consent Informed consent was obtained from the patient. As article is in the form of case report with maintained patient anonymity, ethical clearance was not required.

References

1. 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.
2. Folpe AL. Low-grade fibromyxoid sarcoma: A review and update. *Pathol Case Rev.* 2002;7:139–45.
3. Billings SD, Giblen G, Fanburg-Smith JC. Superficial low-grade fibromyxoid sarcoma: a clinicopathological analysis of 19 cases with a unique observation in pediatric population. *Am J Surg Pathol.* 2005;29:204–10.
4. Lane KL, Shannon RJ, Weiss SW. Hyalinizing spindle cell tumor with giant rosettes: a distinctive tumor closely resembling low-grade fibromyxoid sarcoma. *Am J Surg Pathol.* 1997;21:1481–8.
5. Folpe AL, Lane KL, Paull G, Weiss SW. 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.
6. Goodlad JR, Mentzel T, Fletcher CD. Low grade fibromyxoid sarcoma: clinicopathological analysis of eleven new cases in support of a distinct entity. *Histopathology.* 1995;26:229–37.
7. Tsukamoto Y, Takahata H, Teramoto M, Nishimura R, Hato S, Nozaki I, et al. Primary gastric low-grade fibromyxoid sarcoma with FUS-CREB3L1 fusion: A hitherto undescribed origin of Evans tumor. *Human Pathol.* 2018;11:51–5.
8. Geramizadeh B, Zare Z, Dehghanian H, Bolandparvaz S, Marzbani M. Huge mesenteric low-grade fibromyxoid sarcoma: a case report and review of literature. *Rare Tumors.* 2018;10:1–4.
9. Merchant SH. Low grade fibromyxoid sarcoma: a report of a case with epithelioid cell morphology, masquerading as a papillary thyroid carcinoma. *Acta Cytol.* 2009;53:689–92.
10. Dong W, Zhang H. Low-grade fibromyxoid sarcoma of the thyroid: a case report. *Ann Acad Med Singapore.* 2013;42(1):55–6.
11. Botev B, Casale M, Vincenzi B, D’Ascanio L, Santini D, Esposito V, et al. A giant sarcoma of the parotid gland: a case report and review of the literature. *In Vivo.* 2006;20(6B):907–10.
12. Lee EJ, Hwang HJ, Byeon HK, Park HS, Choi HS. A low grade fibromyxoid sarcoma originating from the masseter muscle: a case report. *J Med Case Rep.* 2015;9:136.
13. Doyle LA, Wang WL, Dal Cin P, Fletcher CD, Mertens F, Hornick JL. Muc4 is a sensitive and extremely useful marker for sclerosing epithelioid fibrosarcoma: association with FUS gene rearrangement. *Am J Surg Pathol.* 2012;36:1444–51.
14. Linos K, Bridge JA, Edgar MA. MUC 4-negative FUS-CREB3L2 rearranged low-grade fibromyxoid sarcoma. *Histopathology.* 2014;65:722–30.

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.