Limbal, low-grade myofibroblastic sarcoma: Case report and literature review

Kaustubh Mulay, Mrittika Sen[1], Santosh G Honavar[1]

Low-grade myofibroblastic sarcoma is a relatively recently-described neoplasm of the myofibroblasts having a predilection for the head and neck region. Ophthalmic involvement is extremely rare. Limbal involvement has not yet been documented in the literature. We describe one such case involving the limbus of a 48-year-old Asian male.

Key words: Limbus, myofiboblastic, myofibroblast, ocular surface, sarcoma, SMA

Low-grade myofibroblastic sarcoma (LGMS) is an uncommon, malignant tumor of mesenchymal origin with predilection for the head and neck region. Classified by the World Health Organisation (WHO) as a distinct entity in 2002, LGMS comprises of atypical myofibroblasts.[1] Ophthalmic LGMS is rare.[2] To the best of our knowledge, involvement of the ocular surface by LGMS has not yet been reported in the literature.

Case Report

A 48-year-old male presented with a gradually progressive conjunctival swelling in the right eye of 2 years duration; initially observed and later, in view of the continued growth, was excised elsewhere. Slides/tissue were not available for review. A month later, following a recurrence, he was referred to our clinic. On examination, his BCVA was 20/40 and intraocular pressure was elevated (30 mm Hg) in the affected eye. Slit-lamp evaluation showed a 9 × 4 mm nodular, fleshy, reddish-pink and highly vascular limbal mass extending from 2 to 6 clock hours [Fig. 1a]. On palpation, the lesion was firm with its base fixed to the sclera. AS-OCT and UB-M showed angle involvement from 2 to 6 clock hours with maximum height and radial dimension of 3.4 mm and 8.3 mm, respectively, at 5 O'clock [Fig. 1b and c]. A provisional diagnosis of squamous cell carcinoma was made. An excision biopsy with a 4 mm clearance was performed. Plaque brachytherapy using a notched Ruthenium-106 plaque was performed in the same sitting to treat the base and angle involvement, with 6000 cGy dose to the tumor apex. Light microscopy showed a poorly circumscribed tumor in the substantia propria with infiltrative margins, composed of spindle-shaped cells in a sheet-like, fascicular or focally storiform pattern separated by a variably cellular, fibrocollagenous stroma with ropey collagen [Fig. 2a-c]. Ovoid to fusiform nuclei displayed mild to moderate atypia [Fig. 2b]. Mitoses were present, but sparse. The tumor cells were positive for smooth muscle actin [Fig. 2d] and vimentin [Fig. 2e], and negative for S100, CD34 and pan-cytokeratin. The Ki67-labeling index was approximately 13% [Fig. 2f]. Resected margins were tumor-free. Considering the morphological features and immunohistochemical findings, the diagnosis of limbal LGMS was confirmed. Systemic examination was normal. At 3-months follow-up, our patient continues to be disease-free [Fig. 1d].

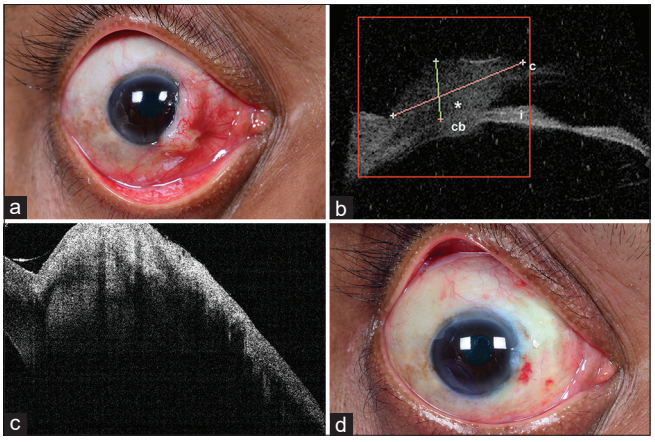

Figure 1: Clinicoradiological features of low-grade myofibroblastic sarcoma. (a) Right eye showing a fleshy mass extending from 2-6 O'clock at the limbus with intrinsic vascularity and episcleral feeder vessels. (b) Low magnification of ultrasound biomicroscopy showing full thickness scleral involvement and extension into the angle (Asterix). (CB - ciliary body, I - iris, C - cornea) (c) Anterior segment OCT through the lesion showing full-thickness scleral involvement with shadowing. (d) Post-operative clinical picture showing a healthy ocular surface and no residual lesion

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National Reporting Centre for Ophthalmic Pathology, Centre for Sight, Hyderabad, [1]Oculoplastics, Facial Aesthetics and Ocular Oncology, Centre for Sight, Hyderabad, Telangana, India

Correspondence to: Dr. Kaustubh Mulay, Centre for Sight, Ashoka Capitol Building, Road No. 2, Banjara Hills, Hyderabad - 500 034, Telangana, India. E-mail: kaustubh.m@hotmail.com

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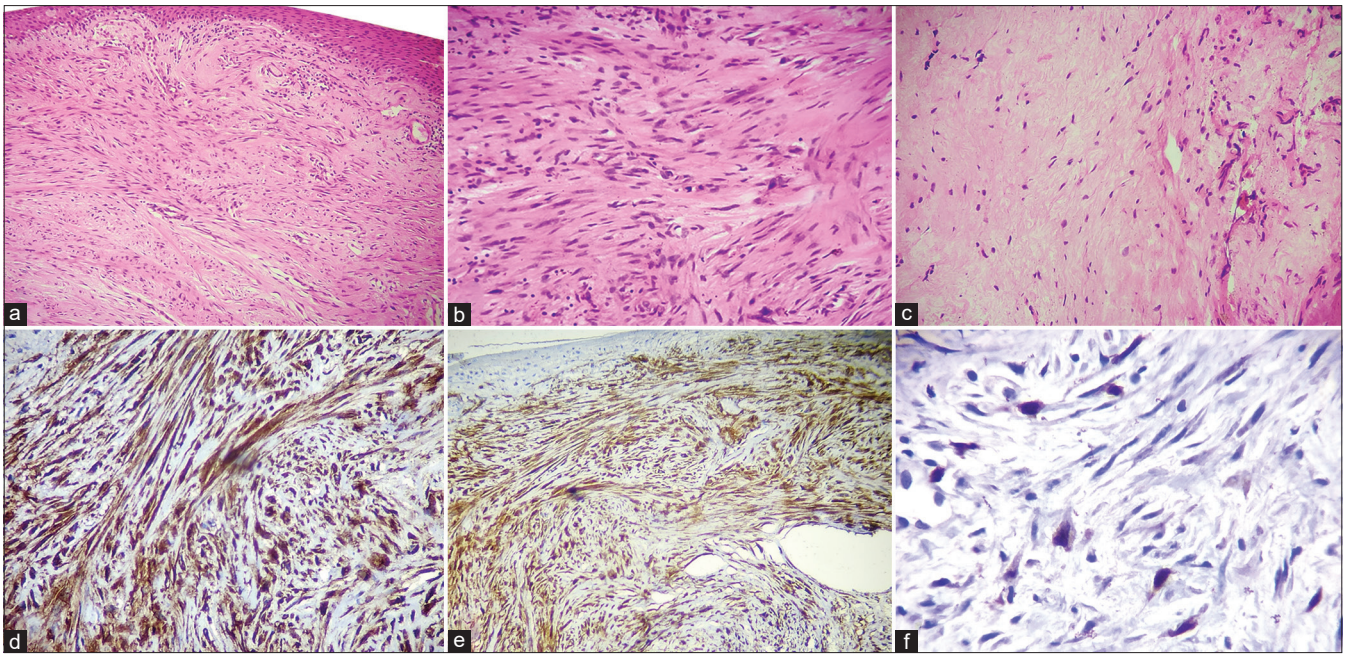

Figure 2: Histopathological features of LGMS. (a) Poorly circumscribed mass in the substantia propria composed of spindle-shaped cells in a sheet-like and fascicular pattern. (Hematoxylin and eosin, ×40). (b) Fascicular and vague storiform arrangement of spindle-shaped cells having indistinct borders, eosinophilic cytoplasm and fusiform nuclei. (Hematoxylin and eosin, ×100) (c) Loose areas with abundant fibromyxoid stroma. (Hematoxylin and eosin, ×40). (d) Diffuse and strong positivity of tumor cells for smooth muscle actin (SMA, ×200). (e) Diffuse and strong, vimentin positivity in tumor cells (Vimentin, ×100). (f) Atypical nuclei showing Ki-67 positivity (Ki-67, ×400)

Discussion

Myofibroblasts, initially described as modified fibroblasts by Gabbiani *et al*.[3] are present in some normal and granulation tissues. They have morphological and functional features of fibroblasts and smooth muscle cells. Given the overlapping light microscopic and immunohistochemical features, their identification is often challenging. LGMS is a malignant tumor of myofibroblastic origin occurring at submucosal and subcutaneous locations. Myofibroblastic sarcoma was first described in 1978 by Vasudev *et al*.[4] and confirmed by Mentzel *et al*.[5] in 1998. The morphological diagnosis standard was further clarified by Montgomery *et al*.[6] in 2001 subsequent to which, WHO included LGMS as a distinct entity in 2002.[1]

LGMS generally affects middle-aged patients (average age, 40 years), but can affect any age-group and has a male predominance.[7,8] Although LGMS has been described at several anatomical locations of the human body, the head and neck region is frequently affected.[5-9] Ophthalmic involvement is extremely rare. Patients usually present with a slow-growing, painless mass.[2,7] Given the rarity of this tumor and the sparsity of imaging studies, radiological features are yet to be clearly understood.[7-9] Histopathology is essential for diagnosis. Microscopically, these are poorly circumscribed, infiltrative and invade the adjacent tissues. They comprise of relatively uniform, spindle-shaped cells arranged in fascicular, sheet-like or storiform patterns. The intervening stroma varies in cellularity and is fibrocollagenous to fibromyxoid. Individual cells have eosinophilic cytoplasm and slender fusiform nuclei. Nuclear atypia is minimal to moderate, and mitotic rate is low.[2,7,8] Foci of necrosis have been documented.[7] Tumor cells express muscle-specific actin, α-smooth muscle actin, fibronectin, desmin, calponin and vimentin but not S100, CK, CD34, EMA and laminin.[2,7,8] Ki67-labeling index ranges from 8-45%.[7] The clinicopathological features in our patient were similar to those published in literature. Fibromatosis, leiomyosarcoma, fibrosarcoma and inflammatory myofibroblastic tumor are common differential diagnoses. Leiomyosarcoma is positive for h-caldesmon, negative for fibronectin and has scattered, pan-cytoplasmic presence of myofilaments in smooth-muscle cells as opposed to sub-plasmalemmal localisation in myofibroblasts. Characteristic herring-bone fascicular architecture of the spindle cells and presence of tapering nuclei helps distinction from fibrosarcoma. IMT displays inflammatory cells and lacks nuclear atypia. Although ALK1-negativity does not exclude a IMT, positive staining is helpful in excluding a LGMS.[8]

LGMS is locally aggressive, may recur, sometimes metastasize or may even progress to higher grade sarcomas.[9] Though not included in the WHO classification, intermediate- and high-grade counterparts are described and associated with higher frequency of relapse and metastases.[9,10] No validated treatment protocols exist for this tumor. In general, complete surgical excision with clear margins is the treatment of choice. Role of chemotherapy and radiotherapy is uncertain and needs investigations.[2] Post complete excision with clear margins and plaque brachytherapy, our patient continues to be on remission.

Conclusion

To conclude, we describe a rare case of a limbal, low-grade myofibroblastic sarcoma. These are rare, locally aggressive tumorous proliferations of myofibroblasts, usually affecting middle-aged adults and have a predilection for head-neck region. LGMS pose a diagnostic dilemma, not only in differentiating low-grade ones from intermediate- and high-grade lesions but also in distinguishing it from local morphological mimics. Thorough light microscopic evaluation with immunostaining is the gold standard for diagnosis. Complete surgical excision with

clear margins is the treatment of choice. Given its propensity to recur, and sometimes metastasize, a long-term follow-up of affected patients is essential.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Mentzel T, Fletcher JA. Low grade myofibroblastic sarcoma. In: Fletcher CDM, Unni K, Mertens F, editors. Pathology and Genetics. WHO Classification of Tumors of the Soft Tissue and Bone. Lyon, France: IARC Press; 2002: p. 94-5.
2. Zhang S, Ma T, Wang Z. Low-grade myofibroblastic sarcoma of the orbit: A case report and literature review. Medicine (Baltimore) 2017;96:e9172.
3. Gabbiani G, Ryan GB, Gajn O. Presence of modified fibroblasts in granulation tissue and their possible role in wounded on traction. Experientia 1971;27:549-50.
4. Vasudev KS, Harris M. A sarcoma of myofibroblasts: An ultrastructural study. Arch Pathol Lab Med 1978;102:185-8.
5. Mentzel T, Dyr S, Kaethknma PD, Fletcher CDM. Low grade myofibroblastic sarcoma: Analysis of 18 cases in the spectrum of myofibroblastic tumors. Am J Surg Pathol 1998;22:1228-38.
6. Montgomery E, Goldlum J, Fisher C. Myofibrosarcoma: A clinicopathologic study. Am J Surg Pathol 2001;25:219-28.
7. Cai ZG, Pan CC, Yu DH, Feng ZZ, Ma L, Zhao Y, *et al*. Myofibroblastic sarcoma: A clinicopathologic analysis of 15 cases and review of literature. Int J Clin Pathol 2016;9:1568-77.
8. Peng L, Tu Y, Li Y, Xiao W. Low-grade myofibroblastic sarcoma of the pancreas: A case report and literature review. J Can Res Ther 2018;14:S796-9.
9. Wang L, Li L-X, Chen D-Q, Yang L, Li S-K, Cheng C. Low-grade myofibroblastic sarcoma: Clinical and imaging findings. BMC Med Imaging 2019;19:36.
10. Koga S, Ikeda S, Urata J, Chijiwa R, Abe K, Hayashi T, *et al*. Primary high-grade myofibroblastic sarcoma arising from the pericardium. Circ J 2008;72:337-9.