CASE REPORT

Giant myxofibrosarcoma of the orbit: a rare case and a review of the literature

Rachna Meel,¹ Gautam Lokdarshi,¹ Seema Kashyap,² Sanjay Sharma³¹Dr RP Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, Delhi, India²Department of Ocular Pathology, Dr RP Centre, All India Institute of Ophthalmic Sciences, New Delhi, Delhi, India³Department of Radiodiagnosis, All India Institute of Medical Sciences (AIIMS), New Delhi, Delhi, India**Correspondence to**Dr Rachna Meel,
dr.rachnameel@gmail.com

Accepted 25 May 2016

SUMMARY

A 65-year-old man presented with giant orbital myxofibrosarcoma with no extraorbital extension. Imaging was suggestive of mesenchymal malignancy with significant vascularity. Incisional biopsy was suggestive of low-grade fibromyxoid sarcoma. The clinical and imaging features did not support the pathological diagnosis. Histopathology of the exenterated sample revealed features of high-grade myxofibrosarcoma. To the best of our knowledge, this is the largest reported myxofibrosarcoma of the orbit. Adjuvant radiotherapy was advised. Correlating the case history, imaging and histopathology, this case can best be summarised as a natural history of conversion from a low to high-grade myxoid malignancy. We emphasise that the overlapping features of myxoid malignancy (fibromyxosarcoma vs myxofibrosarcoma) and regional variation in tumour morphology in biopsy specimen may mislead the clinician. Therefore, knowledge about the key differentiating features as well as incisional biopsy of each radiologically different area can increase the possibility of correct diagnosis and management of each case.

BACKGROUND

Myxofibrosarcoma is one of the most common soft tissue tumours occurring in the extremities of elderly patients. In a large series of myxofibrosarcoma (MFS) reported in the literature, only 4% of cases were located in the head and neck region.¹ We report a case of a large orbital MFS that presented us with a histological challenge and reveal some interesting imaging findings. To the best of our knowledge, this is the largest orbital MFS reported to date.

CASE PRESENTATION

A 65-year-old man, a farmer by occupation, presented with a 25-year history of a recurrent mass over his left eye. The tumour had been excised twice (22 and 12 years prior). It was a painless, slowly growing mass. However, a rapid growth was noted by the patient in the past 8 months. This was associated with gradual progressive deterioration of vision, loss of extraocular movement and inability to close the eyelid completely. No histopathology report was available. There was no history of trauma, variation in size of mass on bending/coughing or increase in size associated with upper respiratory tract infection. There were no complaints of abnormal sensations/tenderness over the mass. There was no history of sinonasal disease or

headache/vomiting to suggest a sinonasal or intracranial extension.

On examination, best corrected visual acuity in the right eye was 20/20, with no light perception in the left eye. A large multilobulated mass (size 5×7 cm) arose from the superior orbit, causing globe luxation with inferior displacement and lagophthalmos ([figure 1A](#)). The tumour extended vertically from eyebrow to middle of cheek and horizontally from bridge of nose to lateral orbital margin. The overlying skin appeared normal with signs of neither inflammation nor fixity to underlying structures. On palpation, the mass was warm, with consistency varying from soft and cystic to firm. There was no palpable pulsation and no bruit on auscultation. There was no enlargement of draining lymph nodes and systemic examination was non-contributory.

INVESTIGATIONS

Ultrasonography of the mass revealed a heterogeneous internal reflectivity, with multiple cystic areas of different sizes ([figure 1B](#)). There was no intraocular tumour extension. A contrast enhanced CT scan revealed a well-defined heterogeneous enhancing mass (7.5×4.8 cm) filling the orbit with expansion of the bony orbit. Notably, there was a well-defined area, homogeneously hyperdense and brightly enhancing with contrast, within the tumour. The globe was displaced inferomedially. There was neither bone erosion nor extension into the intracranial cavity or paranasal sinuses ([figure 1C](#)). On MRI, the mass showed a heterogeneous signal with a laminated appearance. It was isointense to muscle on T1-weighted and hyperintense to muscle on T2-weighted images. It showed a central nodule that was brightly enhancing on CT ([figure 1D](#)), an intermediate signal on T1W ([figure 1E](#)) and hypointense on T2W images ([figure 1F](#)). Multiple flow voids on MRI were suggestive of the presence of blood flow in the patent vessels within the mass ([figure 1G](#)).

TREATMENT

In view of the recent rapid growth, a provisional diagnosis of low-grade malignancy of mucoid morphology was made and an incision biopsy performed. Histopathological examination revealed a spindle cell tumour with mild to moderate pleomorphism, indistinct pale eosinophilic cytoplasm, small hyperchromatic oval nuclei, finely clumped chromatin and prominent nucleoli and no mitotic figures. Stroma was scanty with fibrous to myxoid content without necrosis. Immunohistochemistry

CrossMark

To cite: Meel R, Lokdarshi G, Kashyap S, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-214107

Figure 1 (A–I): (A) Clinical photograph showing a large multi-lobulated mass in the left orbit causing inferior displacement of the globe (arrow). (B) Ultrasonography of the orbit showing a mass filling the left orbit, with multiple cystic areas (arrows). (C) Axial non-contrast CT of the orbit showing a homogeneous hypodense nodule (arrow) within the heterogeneous orbital mass. (D) Contrast CT showing uniform and marked contrast enhancement of the nodule (arrow). (E) Axial T1W-MRI showing a uniformly hypointense nodule. (F) Axial and (G) sagittal T2W-MRI showing the nodule uniformly hypointense. (G) T2W-sagittal MRI showing the mass in relation to the globe, with areas of curvilinear flow voids (arrows) suggestive of patent blood vessels. (H) Microphotograph shows spindle cells with eosinophilic cytoplasm in an abundant myxoid stroma (arrow) and multiple mitotic figures (H&E stain, 40 $\times$). (I) Microphotograph showing a hypercellular area corresponding to the nodule, with pleomorphic cells with vesicular to hyperchromatic prominent nuclei, multinucleated tumour giant cells (arrow), bizarre cells and a large number of mitotic figures (H&E stain, 100 $\times$).

was positive for vimentin. Therefore, a diagnosis of low-grade fibromyxoid sarcoma (LGFMS) was made. A metastatic work up including liver function tests, kidney function test, CT of the chest and ultrasound of the abdomen, was negative for metastasis. Total orbital exenteration, including of the lids and periorbital, was performed under general anaesthesia.

On gross pathological examination, the exenterated specimen (measuring 10 $\times$ 8 $\times$ 7 cm) showed several gelatinous areas and multiple cystic spaces (size—0.2 to 1 cm) on the cut section. A focal grey-white area was seen with necrotic and haemorrhagic areas. On fine microscopic examination, abundant myxoid stroma with vacuoles and multiple thin walled arborising blood vessels were present (figure 1H). Within the focal grey-white nodule, highly pleomorphic cells with vesicular to hyperchromatic prominent nuclei, multinucleated tumour giant cells, bizarre cells and a large number of mitotic figures (both typical and atypical) were seen (figure 1I). Based on the findings described above, the diagnosis was revised to high-grade MFS. Excision margins were involved by the tumour. Therefore, adjuvant external beam radiotherapy (EBRT) was advised in a dose of 45 Grays fractionated over 15 sessions.

OUTCOME AND FOLLOW-UP

The patient was lost to follow-up.

DISCUSSION

Myxoid soft tissue tumours are characterised by an abundant mucoid extracellular matrix, resulting in a strikingly similar gross and imaging picture. Many tumours fall into this broad category. Despite their similar clinical and imaging picture, these

tumours may display highly variable biological behaviour ranging from a harmless longstanding mass to a highly malignant neoplasm.² Thus, it is important to accurately diagnose these histopathologically in order to prognosticate and manage the tumour.

In the current case, the patient presented with an orbital tumour of mucoid morphology, as suggested by imaging, of long-standing duration, with a recurrent nature and a recent rapid increase in size, which was likely due to tumour grade progression. Interestingly, imaging showed an area within the tumour that had conspicuously different imaging characteristics as compared to the rest of the tumour. This was likely to be the area of suspected tumour progression.

Histopathological examination of the incision biopsy specimen was suggestive of LGFMS. LGFMS usually presents at around 35 years of age. It is known to have an indolent course with multiple recurrences and eventual metastasis in 50% of cases. The primary site of metastasis is usually the lung. Histologically, it is characterised by a mixture of fibrous and myxoid areas with bland spindle shaped tumour cells arranged in whorled patterns. The cells have scant eosinophilic cytoplasm and small, uniform, hyperchromatic, oval nuclei. Mitoses are rare. Recurrences have been reported to show increased cellularity but progression to a more pleomorphic tumour type has not been reported in the literature.² The current patient had a much older age at presentation and, despite multiple recurrences, there was no metastasis even after 25 years of having the disease. On the contrary, there was clinical and imaging evidence of likely tumour dedifferentiation, which is uncharacteristic of this tumour.

Table 1 Clinical findings of previously reported MFS of the orbit in the literature

	Age (years)	Clinical presentation	Duration of symptoms	Size (cm)	Location and extent	Management				
						Surgery	Adjuvant radiotherapy	Adjuvant chemotherapy	Histopathology	Follow-up
Wang <i>et al</i> ⁹	63	Proptosis, DV, weight loss	10 days	–	Inferomedial orbit	Mass excision	NA	NA	Low-grade MFS	Died of metastasis; 2 months
Zhang <i>et al</i> ⁶	27	Upper eyelid lump	6 weeks	3×3	Superolateral orbit, with erosion of frontal bone	Fronto-orbital craniotomy	+	Adriamycin, Doxorubicin, Ifosfamide	High-grade MFS	No recurrence; 6 months
Gire <i>et al</i> ⁷	17	Idiopathic orbital inflammation	6 months	2	Inferomedial orbit	Mass excision†	NA*	–	Low-grade MFS	No recurrence; 2 years
Current case	65	Proptosis, DV	25 years	7×5	Whole orbit was involved	Exenteration	+	–	High-grade MFS	No recurrence; 6 months

*Patient refused radiotherapy.

†Patient refused exenteration.

DV, diminution of vision; MFS, myxofibrosarcoma; NA, not available.

The histopathological examination of the main tumour mass, however, revealed features of a high-grade MFS. MFS is a tumour of older age and presents at around 65 years of age. Histologically, it may show a wide range of cellularity and cytological atypia resulting in various histological grades.^{3–4} It is characterised by hypocellular areas of small fusiform or stellate cells with small, pleomorphic, hyperchromatic and indistinct nuclei and scant eosinophilic cytoplasm in an abundant myxoid matrix. Mitoses are seen even in low-grade lesions, unlike in LGFMS, and, with increasing tumour grade, the number of mitosis and tumour cellularity increases. Solid cellular lesions may be seen in high-grade lesions. MFSs also have a characteristic thin walled curvilinear vasculature, which increases with tumour grade.^{3–4}

Many of these histological features were reflected in imaging findings in the current case. On CT scan, a well-defined homogeneously hyperdense area was present within the heterogeneous tumour mass, which had a remarkably higher and uniform contrast uptake compared with the rest of the tumour. This suggested that this area perhaps had increased cellularity and vascularity likely due to tumour grade progression. On MRI, in T1W images this area was uniformly hyperintense as compared with the rest of the tumour, and on T2W images it was uniformly hypointense, suggesting an increased cellularity in this area. Also, there were multiple small curvilinear flow void areas throughout the tumour, reflecting the typical curvilinear blood vessels characteristic of this tumour.

Clinically, low-grade MFS does not have metastatic potential, but a high-grade tumour is reported to have a 5-year survival rate of only 60–77%.^{1–4–5} Lungs, regional lymph nodes, pleura and bone are common sites for its metastasis.⁶ Low-grade lesions are typically characterised by high local recurrence and an increased risk of progression to a higher grade in the recurrent lesions, as was seen in the current case.

MFS in the orbit is extremely rare and only three cases have been reported to date, of which one was probably metastatic and not a primary orbital tumour.^{7–9} The salient clinical features of these cases are described in table 1.

The management of LGMFS is aimed at taking care of high recurrence rates and therefore wide local excision with adjuvant radiotherapy is standard protocol for peripheral LGMFS.¹⁰ Reported recurrence is as high as 60%, irrespective of

histopathological grade.¹ Wide local excision may not be possible in the orbit, so adjuvant therapy assumes greater relevance. High-grade tumours are refractory to current nonsurgical treatment options.^{1–4–5} In a study reported by Huang *et al*,¹ it was found that risk of metastasis and disease-specific mortality increases significantly for tumour size of over 5 cm, presence of necrosis and decrease in myxoid proportion (<75% of stroma). Tumour necrosis ≥10% and high mitotic index ≥20/10 high power field (HPF) are also reported as independent adverse prognostic factors.¹¹ In orbital MFS, exenteration followed by EBRT appears to be the most logical and safe approach.

To conclude, the current report describes a rare case of orbital LGMFS and documents the natural history and typical relentless recurrence associated with progression of this condition to a higher grade. To the best of our knowledge, this is the largest orbital MFS reported to date. It further illustrates that incision biopsy may not be representative of the whole tumour in terms of final diagnosis and tumour grade. Careful radiological assessment and clinical correlation may help identify suspicious areas of tumour progression and guide in accurate histopathological evaluation.

Learning points

- ▶ In cases of large myxoid tumour, preoperative radiological imaging should be carefully analysed to determine appropriate areas for biopsy.
- ▶ We suggest obtaining biopsy samples from more than one area of tumour if there is significant regional difference on MRI (eg, based on MRI signal and contrast enhancement).
- ▶ Exenteration followed by external beam radiotherapy is the logical and safe approach for orbital myxofibrosarcoma.

Contributors RM and GL were involved in the preparation and editing of the manuscript. RM and GL were involved in the literature search. RM, GL, SK and SS were involved in the review or approval of the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Huang HY, Lal P, Qin J, *et al.* Low-grade myxofibrosarcoma: a clinicopathologic analysis of 49 cases treated at a single institution with simultaneous assessment of the efficacy of 3-tier and 4-tier grading systems. *Hum Pathol* 2004;35:612–21.
- 2 Graadt van Roggen JF, Hogendoorn PC, Fletcher CD. Myxoid tumors of soft tissue. *Histopathology* 1999;35:291–312.
- 3 Weiss SW, Enzinger FM. Myxoid variant of malignant fibrous histiocytoma. *Cancer* 1977;39:1672–85.
- 4 Mentzel T, Calonje E, Wadden C, *et al.* Myxofibrosarcoma. Clinicopathologic analysis of 75 cases with emphasis on the low grade variant. *Am J Surg Pathol* 1996;20:391–405.
- 5 Sanfilippo R, Miceli R, Grosso F, *et al.* Myxofibrosarcoma: prognostic factors and survival in a series of patients treated at a single institution. *Ann Surg Oncol* 2011;18:720–5.
- 6 Waters B, Panicek DM, Lefkowitz RA, *et al.* Low-grade myxofibrosarcoma: CT and MRI patterns in recurrent disease. *Am J Roentgenol* 2007;188:W193–198.
- 7 Gire J, Weinbreck N, Labrousse F, *et al.* Myxofibrosarcoma of the orbit: case report and review of literature. *Ophthalm Plast Reconstr Surg* 2012;28:e9–e11.
- 8 Zhang Q, Wojno TH, Yaffe BM, *et al.* Myxofibrosarcoma of the orbit: a clinicopathologic case report. *Ophthalm Plast Reconstr Surg* 2010;26:129–31.
- 9 Wang M, Khurana RN, Parikh JG, *et al.* Myxofibrosarcoma of the orbit: an underrecognized entity? Case report and review of the literature. *Ophthalmology* 2008;115:1237–40.
- 10 Dewan V, Darbyshire A, Sumathi V, *et al.* Prognostic and survival factors in myxofibrosarcoma. *Sarcoma* 2012;2012:830879.
- 11 Lin CN, Chou SC, Li CF, *et al.* Prognostic factors of myxosarcomas: Implication of margin status, tumor necrosis and mitotic rate on survival. *J Surg Oncol* 2006;93:294–303.

Copyright 2016 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow