ALK negative inflammatory myofibroblastic tumor of the orbit: A masquerading entity

Vibha Dutta, Madakshira Gopal Manoj, Ajay Malik, Poninder Kumar[1]

Inflammatory myofibroblastic tumor is a biologically distinct neoplasm of intermediate grade, which can affect every possible tissue of the human body. It is a 'masquerading tumor' as the presenting complaints vary with the affected site. Occurrence of this tumor as an orbital mass is rare and is challenging for both the clinician as well as the pathologist, due to a varied number of lesions sharing a similar picture clinically and histologically. We discuss a rare case of inflammatory myofibroblastic tumor presenting as an orbital mass and the importance of immunohistochemistry in arriving at the diagnosis, which helps dictate the treatment and prognosis of the patient.

Key words: Immunohistochemistry, myofibroblastic, neoplasm, orbit

Inflammatory myofibroblastic tumor (IMT) is a histologically unique neoplasm with a benign clinical course. However, it has been shown that these lesions may possess chromosomal aberrations with resultant monoclonality and frequently may demonstrate locally aggressive behavior.[1] It usually occurs in the soft tissue and visceral organs of the children and the young adults, but can present in infants and as late as eighth decade. However this lesion has been reported in every possible location, under many synonyms including plasma cell granuloma, plasma cell pseudotumor, inflammatory myofibrohistiocytic proliferation, omental mesenteric myxoid hamartoma, myxoid hamartoma and inflammatory pseudotumor.[1,2] It was initially thought to be a heterogenous group of reactive lesions, however it is now been established as a neoplasm with a distinct genetic basis. The lesion is composed of neoplastic proliferation of myofibroblastic cells accompanied by lymphocytes, plasma cells and eosinophils. The presence of an orbital IMT is a rare occurrence, which masquerades both clinically and histomorphologically.[3] We are describing an immunohistochemical study of a case of inflammatory myofibroblastic tumor of the orbit of a child.

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Department of Pathology, [1]Ophthalmology, Armed Forces Medical College, Pune, Maharashtra, India

Correspondence to: Dr. Ajay Malik, Department of Pathology, Armed Forces Medical College, Pune - 411 040, Maharashtra, India. E-mail: drajaymalik@gmail.com

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Case Report

An 11-year-old male patient was referred to the neurosurgery department with a three months history of progressive decreasing vision in the right eye, which was painless and gradual in onset. However, there was no associated diplopia, epiphora or fever. On examination, there was a soft tissue swelling at the superolateral angle of the right orbit measuring 3 × 3 cm. The swelling was non-tender, soft and was seen to compress the right eye ball. The ipsilateral conjunctival surface was bulging with mild chemosis. The MRI-head and neck showed a smooth lobulated intensely enhancing mass lesion along the superior and lateral aspects of the right orbit with involvement of the greater wing of the sphenoid bone and resultant mild indentation of the lateral rectus and the ocular globe [Fig. 1]. Investigations revealed a normal erythrocyte sedimentation rate (ESR), hemoglobin of 14.5 gm/dl and normocytic normochromic blood picture. An excision biopsy of the lesion was undertaken to determine the nature of the lesion. The excised tissue was

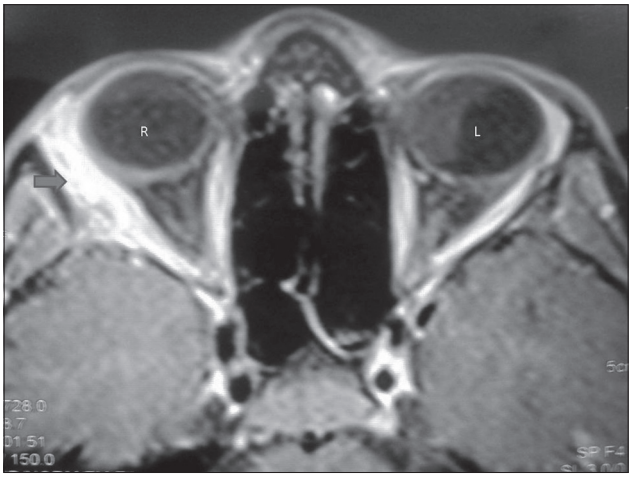

Figure 1: Magnetic resonance imaging (head and neck) showing smooth lobulated intensely enhancing mass lesion along the superior and lateral aspects of the right orbit

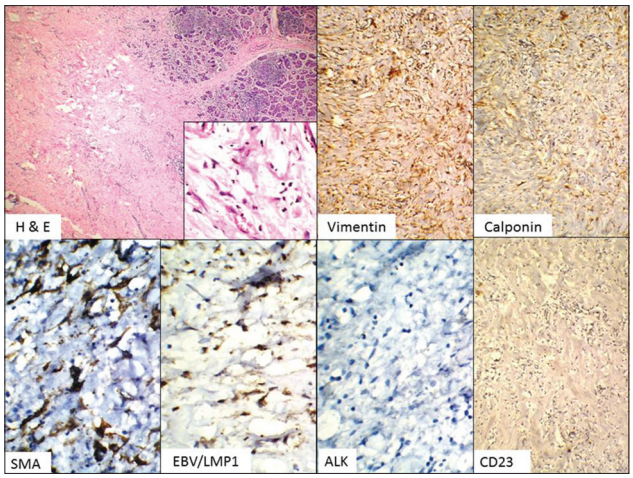

Figure 2: Composite image showing photomicrographs of (in clockwise direction) tumor stained with: Hematoxylin and Eosin (inset-higher power), vimentin, Calponin, CD23, ALK1, EBV/LMP1and SMA

received in fragmented bits, with the largest bit measuring 2.5 × 1.5 × 0.5 cm.[3] The tissue was subjected to routine fixation and processing. Multiple step sections (hematoxylin and eosin) of the tissue showed a relatively preserved lacrimal gland with an adjacent lesion composed of haphazardly arranged spindle to stellate cells in a loose fibrocollagenous matrix with prominent vascularity [Fig. 2]. The matrix was infiltrated by numerous plasma cells, lymphocytes and few eosinophils. The immunohistochemical (IHC) study [Fig. 2] showed the spindle/stellate cells to be positive for vimentin, smooth muscle actin (SMA) and calponin, confirming the myofibroblastic nature of the cells. These cells were negative for desmin, S100, CD34, CD99, Bcl2, Alk, Pancytokeratin (CK), CD23, p53 and CD117. These spindle/stellate cells also showed positivity for EBV/LMP-1 antigen thereby establishing the presence of EBV infection. Co-relating histomorphology and IHC, a final diagnosis of inflammatory myofibroblastic tumor was offered. The patient was administered oral low dose prednisone and is currently under regular monthly review in ophthalmology OPD to look for an early recurrence.

Discussion

Inflammatory myofibroblastic tumor (IMT) is defined as a tumor composed of cytologically bland spindled myofibroblasts with admixed inflammatory cells, predominantly occurs in infants and children but can also be seen in elderly.[1-6] This tumor has historically been reported by many synonyms; such as inflammatory fibrosarcoma, inflammatory myofibrohistiocytic proliferation, inflammatory pseudotumor, omental-mesenteric myxoid hamartoma, plasma cell granuloma and plasma cell pseudotumor. The affected individuals are all under 30 years with majority of them being under 14 years of age. One third of the cases have associated fever, growth failure, malaise, weight loss, anemia, thrombocytosis, polyclonal hyperglobulinemia and elevated ESR.[1] It has been seen that the symptoms disappear after excision of mass. Grossly, the tumor is circumscribed and may be firm, fleshy or gelatinous with a tan-white cut surface. Histologically, IMT is usually infiltrative and composed of stellate/spindle shaped myofibroblasts and inflammatory cells. The spindle or stellate cells are cytologically bland, have variable amounts of pale eosinophilic cytoplasm, central vesicular oval nuclei with small nucleoli. These cells do not show hyperchromasia as a rule. Mitotic Figures are low, about 1-2/10 high power fields and atypical mitosis are rare. Few cases show the presence of scattered large 'Ganglion-like' cells, which have abundant eosinophilic to amphophilic cytoplasm and prominent large nucleoli. The stroma shows prominent inflammatory cells, composed chiefly of lymphocytes and plasma cells and occasional neutrophils and eosinophils. Few foci of germinal centers may also be seen. Occasional presence of foamy histiocytes has also been reported. Three histological patterns have been described in IMT: loose or myxoid stroma with prominent vascularity; compact spindle cells and densely collagenous with fewer spindle cells and inflammatory cells.[2] Histology of our case showed the first pattern of loose stroma with prominent vascularity. Ultrastructure of spindle cell show filamentous bundles, pinocytotic vesicles and basal lamina consistent with that of myofibroblast. All cases of IMT show strong positivity for vimentin, smooth muscle actin (SMA) and calponin.[2] ALK1 is positive in only 50% of all IMT cases, with one series showing ALK1 negativity in all cases of orbital IMT.[4,5] Thirty percent of cases show focal positivity for keratin and desmin. However, IMT is consistently negative for S100, CD117, CD23 and CD34.[2] Immunohistochemistry is helpful to differentiate the tumor from histologically similar lesions such as Follicular dendritic cell tumor (Positive for CD23, Negative for SMA), Solitary fibrous tumor (positive for CD34) and GIST (Positive for CD117).[1] Few reports have shown an association of EBV virus with IMT, which was analyzed in our case by subjecting the tumor to EBV/LMP1 immunohistochemistry, which revealed a strong positivity in the spindle/stellate cells.[1] The treatment of choice is surgical excision, though 25-35% of cases recur with anecdotal cases of metastases. Few studies have proposed few predictors of malignant behavior: frequent 'Ganglion like' cells, atypical mitosis, p53 positivity by immunohistochemistry and DNA aneuploidy by flow cytometry.[1,6] The index case has a low probability of malignant transformation, as it did not show any 'ganglion-like' cells and was negative for p53 by immunohistochemistry. Although the parents declined postoperative orbital irradiation, no recurrence has been noted and the child continues to be on a close clinical follow-up.

To conclude, IMT is a distinct neoplasm of intermediate biological potential with a predilection for developing in the children and the young adults. Histological features in are varied, which do not correlate well with clinical behavior. Chromosomal translocations leading to activation of the ALK tyrosine kinase (and overexpression of the ALK protein) can be detected in approximately 50% of IMTs, with most orbital IMTs being negative. Inflammatory myofibroblastic tumor is a diagnosis of exclusion in middle-aged or older adults, and in somatic soft tissues. The presence of more than mild nuclear atypia argues against the diagnosis. Immunohistochemistry is very useful to establish diagnosis and differentiate it from close histologic mimickers.

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