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Myxoma of the orbit: a clinicopathologic report

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Abstract. A 27-year-old white man developed proptosis of his left eye over a period of 2 years. It was associated with vertical diplopia and displacement of the left globe down and laterally. Ultrasonography showed a cystic mass in the superior orbital region. Computed tomography (CT) demonstrated a solid, well-defined lesion behind the globe displacing the optic nerve medially. A transfrontal craniotomy revealed a nodular mass in the posterior and superior orbit, which extended anteriorly up to the globe. Histopathology, immunohistochemistry, and transmission electron microscopy proved the tumor to be a myxoma.

Introduction

Orbital myxoma is an unusual tumor composed of small cells embedded in an abundant fine granular mucinous matrix. Only a few cases have been reported in the literature [1–3, 12, 13, 19, 20]. The tumor is of mesenchymal origin and should be differentiated from benign and malignant orbital soft tissue tumors with myxomatous differentiation and from myxomatous degeneration of extraocular muscles in Graves disease. We report a case of an orbital myxoma and demonstrate the histopathologic and electron microscopic characteristics.

Case report

Clinical findings

A 27-year-old white male was seen in May 1985 for evaluation of a slowly progressive proptosis of his left eye. He had been in excellent health except for an automobile accident in 1979, where he suffered a left temporal skull fracture. This had healed completely. The patient had noticed a mild proptosis on the left eye 2 years before, however he did not seek medical attention at that time. Examination was prompted by a slow onset of intermittent vertical diplopia with an increasing left exophthalmus.

At the time of the initial ocular examination, the visual acuity was 20/20 in the right eye and 20/25 in the left. The left globe was displaced downward and laterally and exophthalmometry revealed 10 mm of axial proptosis of the left eye. There was also a decreased retropulsion noted. No bruits could be heard. There was a slight anisocoria, the left pupil being 1 mm wider than the right, however, the reaction to light and accommodation was normal and there was no afferent pupillary defect. Extraocular motility was normal in the right eye, but abduction and elevation of the left eye was impaired. The patient had binocular vertical diplopia primarily on upgaze. Slit-lamp examination of the left eye showed only mildly dilated conjunctival vessels. The remainder of the ocular examination was unremarkable.

Computerized static perimetry was performed and showed normal central and peripheral visual fields in both eyes. Visual evoked potentials (VEPs) were normal. Orbital A- and B-scan ultrasonography was performed and demonstrated a cystic tumor in the left superior orbit, which was interpreted as a cavernous hemangioma with large cystic spaces [21]. Computed tomography (CT) of the orbit revealed a large relatively sharply outlined mass of soft tissue density, behind the globe. The tumor was mainly located in the superior nasal orbit and displaced the optic nerve medially.

At the time of surgery, through a transfrontal approach, the orbital roof and the lateral orbital wall were removed, and the periorbit incised. After displacing the superior rectus muscle a nodular, large gelatinous tumor was seen, which was resected in toto. The tumor extended from the orbital apex to the globe.

Postoperatively the proptosis receded, but the motility deficit and vertical diplopia remained. Since the histologic features of the tumor, although the cells appeared benign, showed infiltrative growth, the patient was given a total of 60 Gray (Gy) external beam radiation (Co 60), fractioned in doses of 2 Gy. The radiation was performed in a wedge filter technique to minimize the dose to the lens. Follow-up CT and magnetic resonance imaging (MRI) demonstrated no evidence of local tumor recurrence and the patient is doing well now 3 years after surgery.

Results

Gross examination

The surgically excised specimen, fixed in buffered formalin, consisted of a 5 × 8 × 5 mm gray brown mass and a nodular white, partially soft gelatinous mass measuring 35 mm in diameter. Part of the tissue was embedded in paraffin and sectioned for light microscopy. The rest was processed for transmission electron microscopy.

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Light microscopy

Embedded in a fine, granular partly vacuolar matrix there were small cells with round or oval dense nuclei. The sparse cytoplasm was partly round and partly starlike distributed in the cell processes (Fig. 1). Many of the spindle- and stellate-shaped cells contained small intracytoplasmic vacuoles (Fig. 2). The cells were widely separated in some areas and densely packed in others (Fig. 3a, b). No mitotic figures were found. The content of collagen was variable and only few vessels were present. Soft tissue strands of various size were interspersed in the matrix. With Alcian-blue, the myxoid material stained strongly positive for mucopolysaccharides and the alcian blue positivity disappeared after pretreatment with hyaluronidase. In some areas aggregates of fat cells and striated muscle fibers of various size were present. Some of the muscle fibers, especially the peripheral ones, were displaced by basophilic myxoid tumor matrix, which created the impression of infiltrative growth (Fig. 4).

The myxoma cells did not stain with immunohistochemical studies for S 100, desmin, and cytokeratin; however they were strongly positive for vimentin.

Transmission electron microscopy

Two different types of cells were encountered. Round or somewhat irregularly shaped cells were seen and they had large light nuclei with finely dispersed chromatin and light cytoplasm that contained abundant ribosomes and rough endoplasmatic reticulum (Fig. 5). The second type of cell was spindle shaped and harbored filaments arranged parallel along the long axis of these spindle cells admixed with innumerate ribosomes lying along the filaments (Fig. 6). Mitochondria appeared elongated and were also arranged along the long axis of the spindle-shaped cells and cell processes. Occasionally, an incomplete basal lamina was present around the tumor cells which were embedded in an electron-lucent matrix that also contained collagen fibrils.

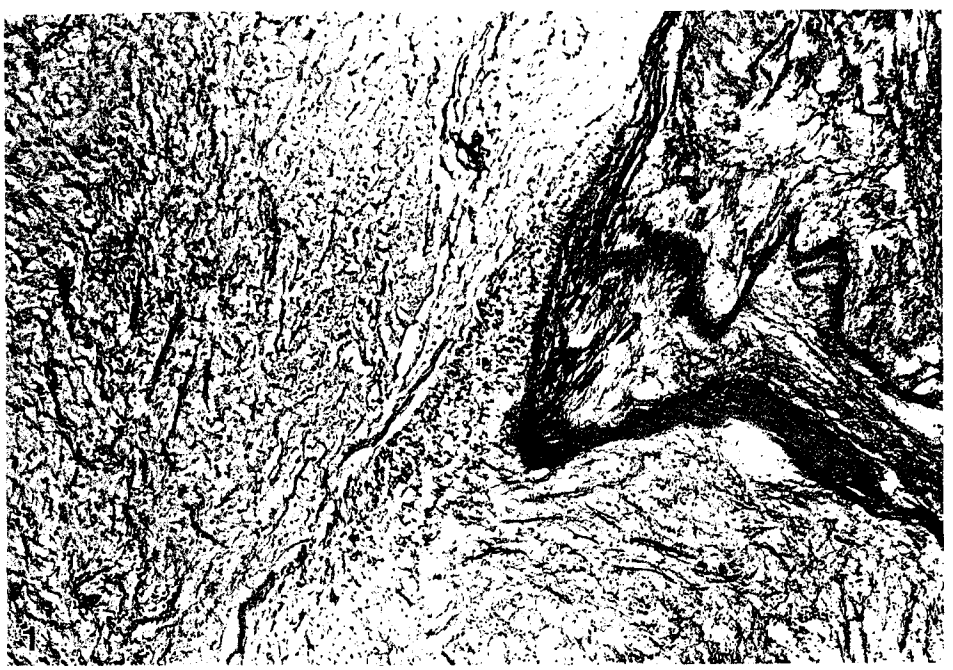

Fig. 1. Low power photomicrograph of the myxoma. Embedded in mucinous tissue are small stellate cells with little cytoplasm. On the right side of the photomicrograph fibrous tissue strands are seen. (H&E, × 4)

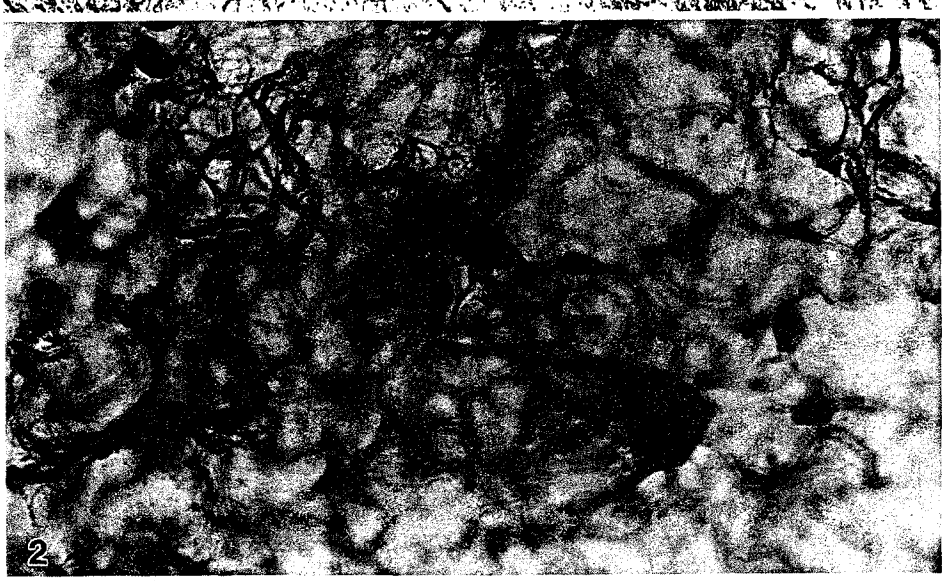

Fig. 2. Stellate myxoma cells with small intracytoplasmic inclusions. (H&E, × 188)

On transmission electron microscopy no osmophilic oil droplets as seen in spindle cell lipoma or a liposarcoma could be demonstrated.

Discussion

Myxomas are most commonly found in the cardiac atria [11] and in skeletal muscle tissue of the extremities. However, they have been reported to occur in the jaw, skin, gastrointestinal tract, and genitourinary system [10]. In the ocular tissues they have also been encountered in the conjunctiva [8, 24, 25, 26, 27, 29], cornea [5, 23], and the eyelids [6]. Conjunctival myxomas occur predominantly in the 4th to 6th decades of life and present as painless growing white gelatinous lesions in the bulbar conjunctiva. Many of these tumors have been clinically misdiagnosed as conjunctival cysts or lymphangiomas. They are usually cured by local excision. In the orbit, myxomas are extremely rare and only a few cases have been reported [1–4, 7, 12, 13, 15, 16, 19, 20].

The myxoma originates presumably from a fibroblastic stem cell, which produces large amounts of glycosaminoglycans that inhibit the polymerization of normal collagen fibrils; therefore, the myxoma is also referred to as fibromyxoma. Another now abandoned theory suggested that the myxoma arises from remnants of primitive mesenchyme as is present in the mucoid tissue of the umbilical cord [11].

Usually myxomas are poorly vascularized. The starlike and spindle-shaped cells are separated by a mucinous matrix that mainly consists of hyaluronic acid and chondroitin

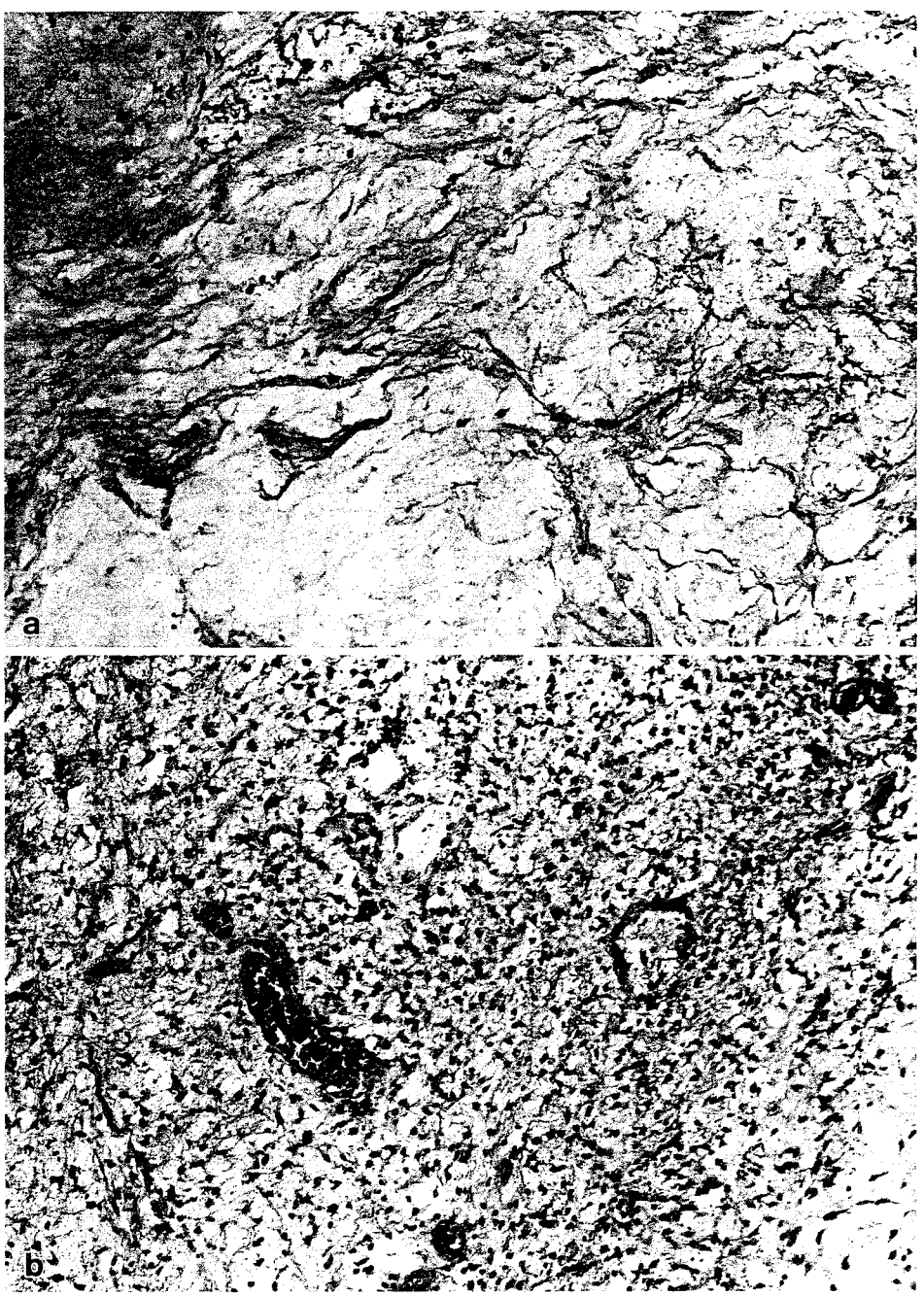

Fig. 3a, b. Low power photomicrograph of the myxomatous area of the tumor. Here the cells are widely separated by abundant mucinous matrix produced by mature myxoma cells (**a**). In other parts of the tumor the cells are more densely packed and have a smaller round nucleus and less cytoplasm (**b**). (H&E, ×37)

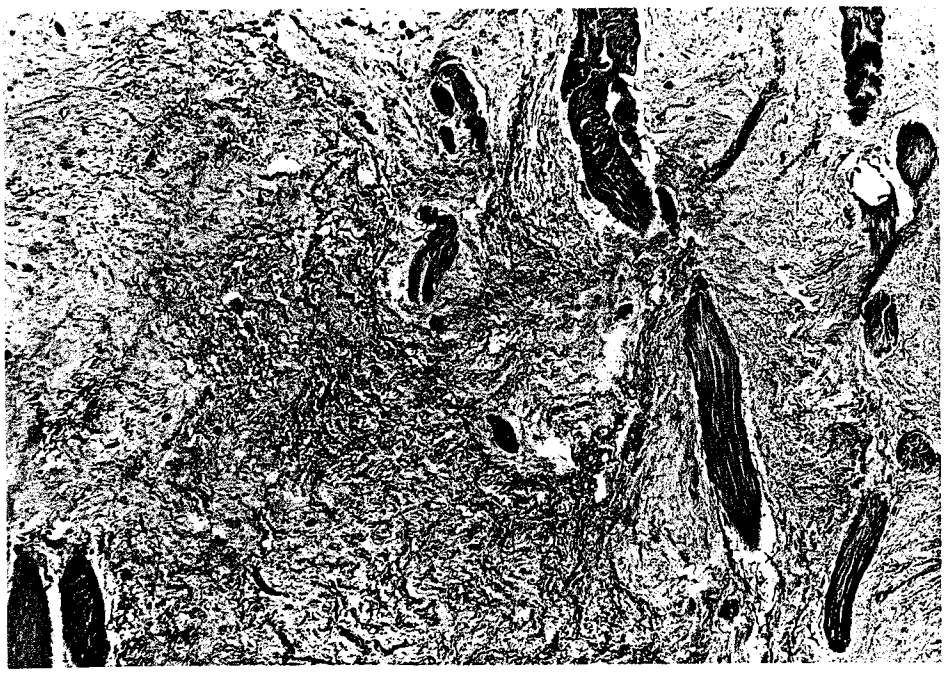

Fig. 4. Bundles of striated muscle cells are separated by the myxoma cells and their abundant mucinous matrix. (Alcian-blue, × 100)

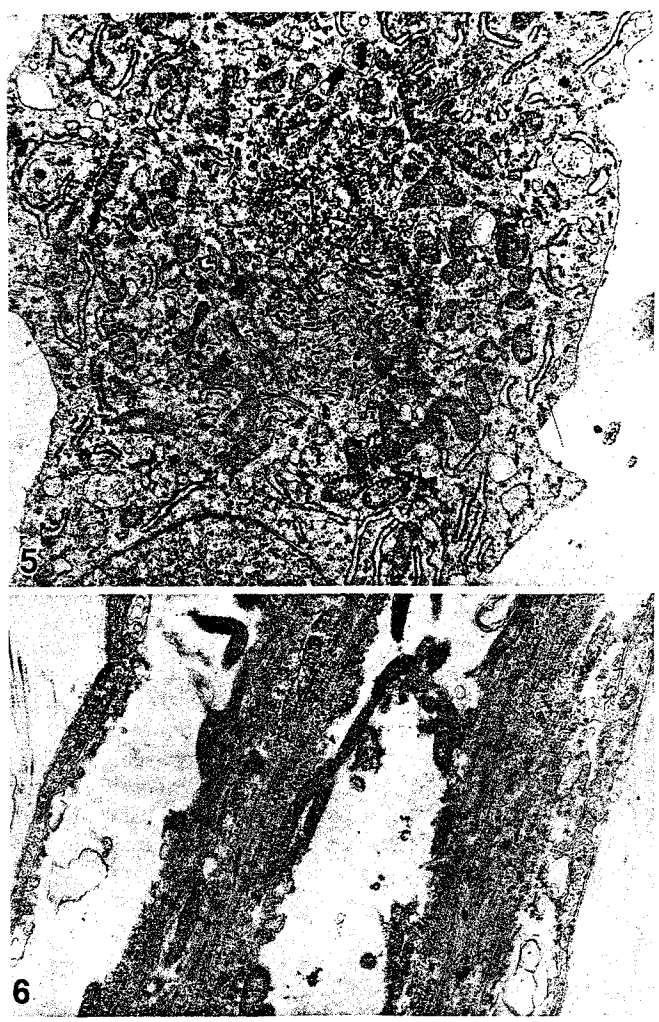

Fig. 5. Ultrastructural view shows a light cell rich in rough endoplasmic reticulum and haphazardly arranged mitochondria (× 12,700)

sulfate. The mucoid tissue largely consists of acid mucopolysaccharides and stains red with mucicarmine, faint purple with hemalaum, and blue with Alcian blue. The loss of staining with Alcian blue after hyaluronidase treatment, which indicates a high content of hyaluronic acid in the mucoid material, is not diagnostic; the sulfated mucopolysaccharides, as produced by myxoid chondromatous tumors, are also susceptible to hyaluronidase. As Kindblom et al. [17, 18] and later others [24, 25] have shown, myxomas stain positive with Alcian-blue at pH levels of 2.5–0.5. In myxomas the positive staining is eliminated with hyaluronidase digestion. At the same pH levels Alcian-blue stains sulphated mucosubstances and keratan sulfates that are found in chondromas and chondrosarcomas. This reaction is in contrast not inhibited by enzymatic pretreatment with hyaluronidase. The histochemical investigation of the heteroglycan content in the mucoid-producing soft tissue tumors may be a valuable diagnostic aid in the differential diagnosis of these tumors.

In our patient, the tumor seems to have grown partly among muscle fibers, which has been reported mainly in myxomas in limb skeletal muscles and only rarely in the head and neck region [9, 10, 14, 22]. The reported orbital myxomas grew extremely slowly and therefore caused adaptation of the adjacent tissues. The superior orbit was affected most frequently. Differentiation of a benign myxoma from sarcomas, especially liposarcomas, botryoid type rhabdomyosarcomas, or, rarely, myxoid variants of malignant fibrous histiocytomas, which may entail mucinous areas as well, can be difficult [7, 16, 28]. Also benign orbital tumors such as neurofibromas often undergo extensive myxomatous degeneration. Usually the myxomatous variants of sarcomas are more cellular and have a more prominent vasculature. They also show signs of malignancy such

Fig. 6. Transmission electron microscopic picture of a dark cell with elongated processes that harbor filaments in parallel and ribosomes along the filaments. (× 15,200)

as mitotic activity and nuclear pleomorphism. In our case we could not find specific cellular elements of these malignant tumors, like lipoblasts, rhabdomyoblasts, histiocytes, and chondroblasts.

Metastases have not been described for orbital myxomas so far, however, local recurrence after incomplete removal may take place in this locally infiltrative growing tumor. Miettinen et al. [22] have reported an increased association of intramuscular myxomas with minor radiologic bone abnormalities such as fibrous dysplasia. In our patient it remains unclear whether the preceding trauma may have played a role in the development of the tumor. In one previously reported series of 18 intramuscular myxomas in two instances preceding trauma to the area of tumor involvement had been documented [17].

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