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Clinical pathologic reviews

Malignant rhabdoid transformation of a longstanding, aggressive, and recurrent orbital angiomyxoma

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ARTICLE INFO

Article history:
Received 3 July 2014
Received in revised form
4 December 2014
Accepted 9 December 2014
Available online 17 December 2014
Stefan Seregard and **Hans Grossniklaus**, Editors

Keywords:
orbit
angiomyxoma
rhabdoid tumor
vimentin
cytokeratin
INI1

ABSTRACT

A 47-year-old woman presented with a medial orbital tumor initially diagnosed as either a myxoid neurofibroma or myoepithelioma. Over 30 years the tumor recurred seven times and was serially debulked. Careful histopathologic analysis coupled with immunohistochemical studies performed on the last two biopsies established the rare diagnosis of a locally aggressive angiomyxoma (because of its local infiltrative growth) with myofibroblastic features (smooth muscle actin and calponin positivity and desmin negativity). The last recurrence manifested at a shorter interval than the earlier ones, suggesting an accelerating clinical course. By this late stage there was complete blindness, a frozen globe, and extreme, unmeasurable proptosis accompanied by massive chemosis and eyelid fullness. An exenteration was performed, and the orbital contents contained a persistent angiomyxoma, but additionally, another cellular population had emerged—mitotically active cells with a malignant rhabdoid phenotype (round shape, cytoplasmic hyaline/globoid inclusions composed of whorls of compact vimentin filaments as well as epithelial membrane antigen and focal cytokeratin positivity). This is the first orbital case of a rhabdoid transformation of a benign orbital mesenchymal tumor. Shortly after the exenteration, multifocal metastases, notably to the lungs, were found, leading to the introduction of chemotherapy, which was discontinued because of nonresponsiveness of the tumor and patient intolerance. After 1 year of follow up, the patient is still alive, but has persistent active disease with widespread metastases and a guarded prognosis.

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0039-6257/$ – see front matter
http://dx.doi.org/10.1016/j.survophthal.2014.12.002

1. Introduction

A clinically and pathologically challenging orbital myxoid tumor that was debulked seven times over more than 30 years ultimately transformed into a rhabdoid malignancy. The myxoid lesion was finally diagnosed microscopically as a rare neoplastic entity, namely, a locally aggressive, but non-metastasizing, deep angiomyxoma.[3,14,28,64] This type of angiomyxoma must be distinguished from superficial cutaneous examples, which produce much less morbidity.[2,8] The focal malignant transformation of the present orbital tumor in an adult into a rhabdoid tumor, which classically affects children,[4,24,46] is an event in orbital pathology that has not been previously reported and is referred to as a *composite tumor*.[20,69] The immunohistochemical identification of various biomarkers led to the accurate diagnosis of both the antecedent angiomyxoma and the emergent rhabdoid tumor cellular clone.[10,28,53,58]

2. Case report

2.1. Clinical findings

A 47-year-old woman presented in 1981 with a 1-year history of painless left upper and lower eyelid swelling. After partial excision of the superonasal portion it was diagnosed as a "neurofibroma." Histologic slides are no longer available for our review. In 2000, examination for a recurrence revealed visual acuities of 20/20 in the right eye and 20/30 in the left eye. There were 6 mm of left-sided proptosis, diplopia on right gaze, and a palpable mass below the left medial canthus (Fig. 1A). Computed axial tomography demonstrated a multiloculated mass with internal septa in the left medial orbit (Fig. 1B). Although there was no relative afferent pupillary defect, the optic nerve was radiographically bowed outward by the tumor. The medial wall of the orbit was bowed toward the ethmoid sinus, suggesting chronicity. Surgical exploration of the left medial orbit revealed a poorly defined, nonencapsulated tumor with a gelatinous texture. The loose, jelly-like composition of the mass rendered it nearly impossible to grasp with forceps or dissect with a scalpel. Complete excision was thus precluded. The excised tissue from this procedure was initially interpreted histopathologically as a myxoid myoepithelioma.

The patient was subsequently followed for over a decade during which time five recurrences developed at 1- to 2-year intervals. Although remaining pathologically benign, the tumor continued to expand locally, necessitating a medial wall bony orbital decompression and dacryocystorhinostomy. In 2012, the tumor began behaving in a more locally aggressive manner, growing with increasing rapidity. Because of concomitant medical issues, including a possible cryoglobulinemia stemming from a chronic systemic inflammatory process of unclear etiology, she deferred surgery at that time. She returned with further progression. Her vision had declined to no light perception in the left eye, and the globe was frozen. Proptosis exceeded the limits of Hertel exophthalmometry (>35 mm) with severe lagophthalmos and bullous interpalepbral chemosis (Fig. 1C). Computed tomography scanning disclosed a massive retro-orbital and medial orbital mass extending outwards through the medial orbital wall where a previous decompression with bone removal had facilitated spread of lesional tissue into the ethmoid sinus (Fig. 1D). The patient elected to undergo surgery. Because of absence of muscle and visual function, an aggressive removal of the myxoid tissue was performed with a microdebrider.[17] She still wished to preserve the globe and therefore refused exenteration at that time.

Despite an aggressive surgical debulking, the tumor recurred within months. She agreed to exenteration and a planned prosthetic reconstruction. Histopathologic evaluation disclosed a persistent benign myxoid tumor with a new population of epithelioid malignant cells. Shortly after surgery, lung and other metastases were discovered. After two courses chemotherapy was stopped because of nonresponsiveness of the metastases, patient intolerance, and poor prognosis. She was still alive 1 year later.

2.2. Histopathologic and immunohistochemical findings

Slides of biopsies from five tumor recurrences dating back to June of 2000 were available for review. Only the last disclosed a malignant transformation. The overall architecture and cytologic features were otherwise preserved throughout the clinical course. The three most recent specimens obtained in April 2013, September 2012, and September 2011 were extensively analyzed, including with immunohistochemical probes. The dominant histopathologic picture throughout all but the last recurrence was that of a myxoid, hypocellular lesion with lakes or pools of extracellular mucin (mucopolysaccharides) subdivided into lobules by fibrous septa (Fig. 2A). The tumor was characterized by infiltrative borders extending into the orbital fat and between striated extraocular muscle fibers. Lymphoid aggregates (Fig. 2B) sometimes exhibiting germinal centers (Fig. 2C) were scattered within the substance of the myxoid tumor and in the septa in all biopsies. Chronic inflammatory cells and mast cells were randomly and widely scattered within myxoid stroma. All biopsies revealed many variably sized blood vessels with moderately prominent fibrous or myoid walls (Fig. 2B–2D) and frequently displayed a loose cuff of surrounding chronic inflammatory cells. The individual tumor cells were typically spindle-shaped (Fig. 2E), but also adopted multipolar appearance (Fig. 2F, and upper right inset). Their nuclei were small with punctate nucleoli when discernible. Cytologic atypia, nuclear hyperchromasia or pleomorphism, mitoses, or foci of necrosis were not observed. There were solitary cytoplasmic vacuoles of signet ring–type cells and intranuclear sequestrations of cytoplasm. Rounded multivacuolated cells interpreted as muciphages (Fig. 2F, inset bottom left) were widely dispersed. Plasmacytoid or hyaline cells (Fig. 3A) were focally observed in the last two biopsies.

The Alcian blue stain was intensely positive (Fig. 3B) and enclosed each individual tumor cell in a pseudolacuna (Fig. 3C) created by retraction of the tumor cells' cytoplasm during fixation from the enveloping myxoid matrix. The Masson trichrome stain disclosed that the tumor cells'