

Supraorbital Cutaneous Fetal Rhabdomyoma of Intermediate Type: A Case Report

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Abstract: A 7-year-old boy was presented with a long-standing slowly growing mass of the left supraorbital area. A biopsy specimen revealed a bland spindle cell proliferation with scattered polygonal cells with acidophilic cytoplasm and cross-striations. Our differential diagnosis included rhabdomyoma of fetal type, leiomyoma with trapping of regenerating skeletal muscle elements, and rhabdomyomatous mesenchymal hamartoma of the skin. Immunohistochemistry demonstrated strong positivity of myoglobin and desmin as well as negativity of caldesmon, suggesting skeletal muscle lineage. The excisional specimen confirmed our diagnosis of cutaneous fetal rhabdomyoma of intermediate type. Additional immunostaining performed on the excisional specimen showed strong Wilms Tumor 1 but only a very faint and focal p63 expression.

Key Words: cutaneous rhabdomyoma, fetal type, orbital region, p63, WT1

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INTRODUCTION

Rhabdomyoma is a rare benign tumor with striated muscle differentiation. Most rhabdomyomas arise from cardiac muscle. Extracardiac rhabdomyomas are very rare and typically occur in the head and neck region, usually in the upper aerodigestive tract.¹

Fetal rhabdomyoma was first differentiated from adult rhabdomyoma by Dehner et al² based on the presence of elongated immature rhabdomyocytes in varying stages of differentiation. Fetal type rhabdomyomas are less common than the adult type. They can be divided into 2 subgroups: the myxoid/classic type with abundant myxoid matrix and the cellular/intermediate type with thin elongated spindle cells and little stroma.^{3,4} The cellular/intermediate type demonstrates a spectrum of differentiation. Crotty et al⁵ proposed the term “juvenile rhabdomyoma” for tumors with intermediate differentiation demonstrating cross-striations in a majority of cells and a regular arrangement of cells but still containing

immature rhabdomyocytes. To our best knowledge, only 4 cases of fetal type rhabdomyoma have been previously reported in the orbital area (Table 1).^{3,4,6}

CASE REPORT

A 7-year-old otherwise healthy boy was presented with a slowly growing painless mass over his left eyebrow, which was noticed by his family since 1 year of age. Physical examination revealed a firm and non-mobile mass that extended from 2 cm above the brow to the undersurface of the superior orbital rim and from the medial brow to the zygoma and caused significant cosmetic deformity (Fig. 1). There was a mild proptosis, but no associated change of vision or limitation of eye motion. Areas of the left brow were numb and movement of the brow was diminished. The tumor was resected. Intraoperatively, the tumor was lifted off the frontal bone with a clean plane. However, the tumor did cause remodeling of the underlying bone. The supraorbital neurovascular bundle was contained within the tumor and sacrificed at the time of resection.

Representative sections of biopsy and excisional specimens were fixed in 10% formalin, embedded in paraffin, and processed routinely for the investigation under light microscopy. The tissues were stained with hematoxylin and eosin (H&E). Immunohistochemistry was performed with anti-myoglobin antibody (1:10; Dako), anti-desmin antibody (1:25; Dako), and anti-caldesmon antibody (1:50; Dako). Out of interest, we performed immunostaining on the excisional specimen to examine the expression of p63 (1:100; Dako) and Wilms Tumor 1 protein (WT1, 1:200; Dako).

Histopathologic examination of the biopsy specimen demonstrated haphazardly arranged irregularly formed bundles and fascicles of cells with spindle-shaped to oval nuclei arrayed in the subcutis (Fig. 2A). Cross-striations were visible within some of the cells at higher magnification (Figs. 2B, C). Mitotic figures were not observed. The neoplasm demonstrated positive immunostaining for myoglobin and desmin (Figs. 3A, B) and negative immunostaining for caldesmon. The excisional specimen demonstrated classic features of a fetal rhabdomyoma of intermediate type (Fig. 2D). Additional immunostaining performed on the excisional specimen showed a strong WT1 but only a very faint and focal p63 expression.

DISCUSSION

Rhabdomyomas of fetal type stain positively for desmin, muscle-specific actin, and myoglobin.^{7,8} Presentation of fetal rhabdomyoma in the skin is uncommon, but those that occur are usually located in the head and neck region, especially in the postauricular area.^{2,4,6} Walsh and Hurt described a cutaneous fetal rhabdomyoma on the chin of a 1-year-old girl.⁹ They specified that the lesion arose primarily from the reticular dermis, a point that was not specifically addressed in

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TABLE 1. Literature Summary of Fetal Rhabdomyomas in the Orbital Region

Case	Age (yr)	Sex	Site	Presentation	Histologic Subtype	Mitotic Figures	Reference
1	20	F	Orbit	Proptosis	Intermediate	N/A	Di Sant' Agnese and Knowles, 1980
2	9	M	Eyebrow	Asymptomatic mass, recurrence 7 months after excision	N/A	None	Konrad et al, 1982; Konrad and Hübner, 1983
3	18	M	Orbit	Proptosis, decreased vision	Intermediate	None	Kapadia et al, 1993
4	30	M	Eyebrow	Asymptomatic mass	Intermediate	None	Kapadia et al, 1993
5	7	M	Eyebrow	Mild proptosis, mild ptosis	Intermediate	None	The presented case



FIGURE 1. Clinical image: The 7-year-old boy was presented for evaluation of a slow-growing painless mass over his left eyebrow. There is mild proptosis and ptosis of the left eyelid and brow droop.

the previous case reports. In our case, the neoplasm was located predominantly in the subcutis.

It has been recently reported that p63 expression can be detected in the cytoplasm of cells delineated from skeletal muscles.¹⁰ Out of curiosity, we also performed p63 immunostaining on the excisional specimen of the presented case. As shown in Figure 3D, there was only faint and focal expression

of p63. Our result suggested that p63 might not be a reliable marker for skeletal muscle differentiation.

Intriguingly, staining with anti-WT1 antibody showed prominent positivity in the presented case. It also defined the cross-striations beautifully (Fig. 3C). WT1 is not yet a common marker used to determine the lineage of muscle cells. We examined WT1 expression in this particular case because we have repeatedly observed unusually strong expression of WT1 in skeletal muscle. The study of Parenti et al published in 2013 showed 100% cytoplasmic WT1 expression in the developing skeletal and cardiac muscle cells of human embryos and fetuses.¹¹ Although WT1 is potentially useful to identify developing skeletal muscle cells, it may not be helpful for differentiating rhabdomyomas from rhabdomyosarcomas because strong positive staining was also observed in the latter entity.¹² The role of WT1 in the pathogenesis of skeletal muscle tumors is certainly worthy of further investigation.

Our histopathologic differential for the initial biopsy included rhabdomyoma of fetal type, leiomyoma with trapping of skeletal muscle fibers, and rhabdomyomatous mesenchymal hamartoma.

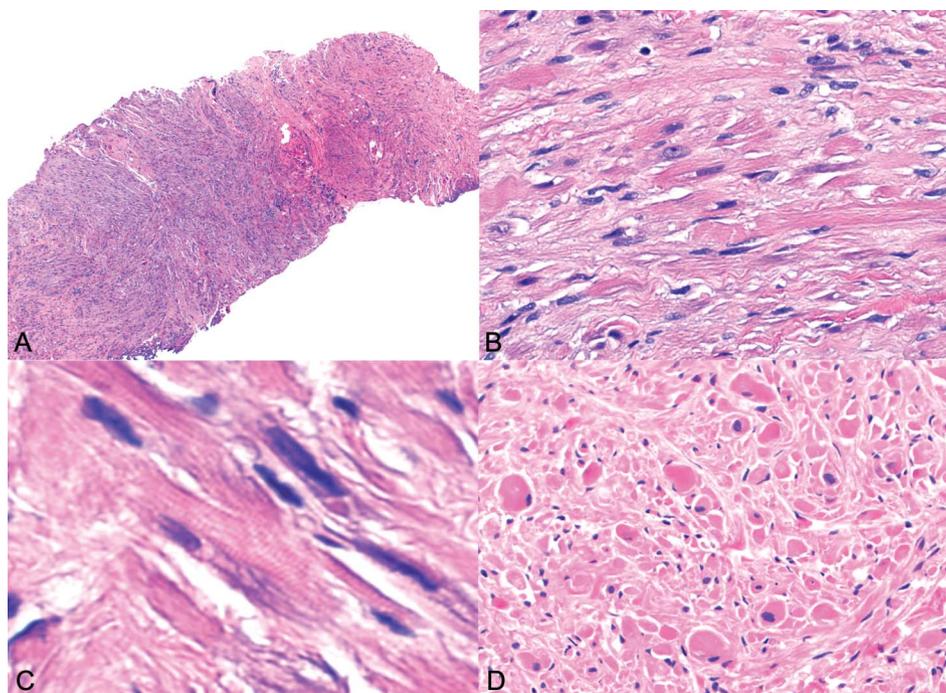
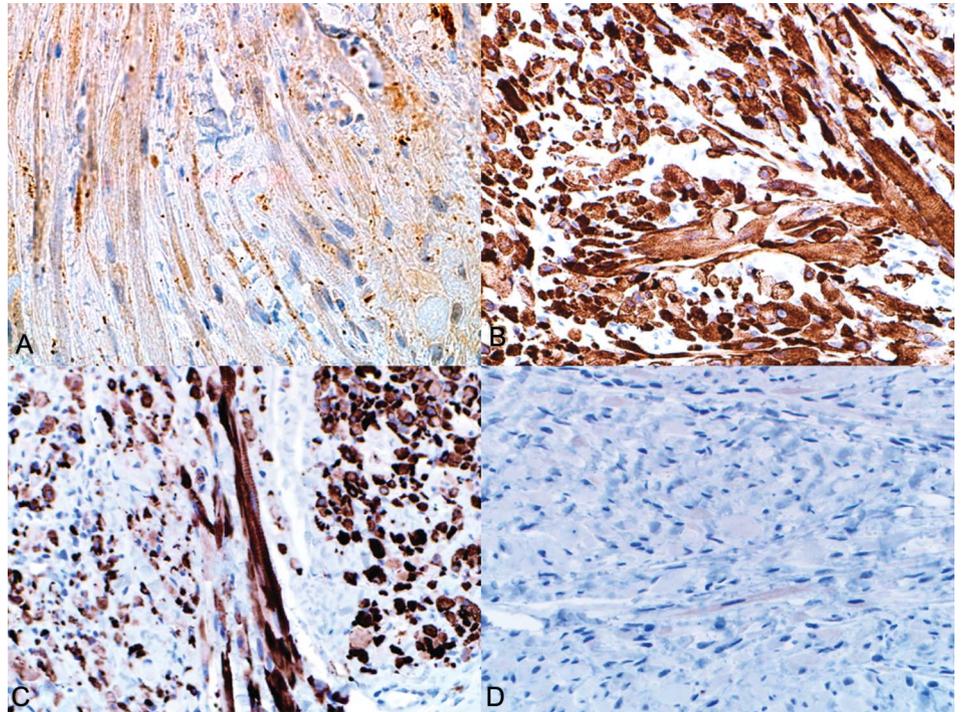


FIGURE 2. A, Overview of the initial biopsy demonstrates an area of high cellular density. B, At higher power, well-differentiated muscle fibers are interspersed among collagen, showing the characteristic arrangement of myofibrils. C, High power view of cross-striations, a feature of skeletal muscle cells. D, The excisional specimen showed plump muscle cells with abundant eosinophilic cytoplasm. There is almost no myxoid stroma, which is typically seen in classic (myxoid) fetal type rhabdomyoma.

FIGURE 3. A, Positive immunostaining for myoglobin and negative staining for caldesmon (not shown here) spoke for skeletal muscle differentiation. B, Positive immunostaining for desmin can be found both in smooth and skeletal muscles. C, Prominent cytoplasmic WT1 expression was detected in the haphazardly arranged muscle cells of the excisional specimen. Cross-striations could be easily identified. D, At low power, the specimen seemed to be negative of p63 expression (not shown here). At higher magnification, focal positivity with very faint staining could be seen.



In the scenario of leiomyoma with trapped skeletal muscle elements and skeletal muscle regeneration, the spindled cells without evident cross-striations would represent cells of the primary smooth muscle neoplasm. The scattered polygonal cells with cross-striations would represent entrapped skeletal muscle elements, and spindled cells with cross-striations would represent reactive myoblasts. However, in this situation, a portion of the spindled cells should stain with caldesmon, a sensitive marker for smooth muscle differentiation. The lack of immunostaining for caldesmon in this case supported a primary skeletal muscle neoplasm. Skeletal muscle regeneration can often be seen in biopsies of facial skin because of the presence of superficial skeletal muscle in this anatomic area and can be mistaken for neoplastic processes.^{13,14}

We also considered rhabdomyomatous mesenchymal hamartoma in our differential diagnosis. Rhabdomyomatous mesenchymal hamartoma is a relatively rare entity that consists of mature skeletal muscle elements admixed with adipose tissue, with increased neural and adnexal elements, and increased collagen fibers¹⁵ that may present in the orbital area in infancy.¹⁶ However, S-100 staining demonstrated a normal number of associated neural elements, and adipocytes were not appreciated within the neoplasm.

Although rhabdomyoma is a benign tumor, surgical intervention has been advocated because of the potential difficulty in distinguishing fetal rhabdomyoma from well-differentiated rhabdomyosarcoma. Although embryonal rhabdomyosarcoma is characterized by alternating cellular and myxoid areas with undifferentiated cells and rhabdomyoblasts of various degrees of differentiation, fetal rhabdomyoma tends to be more circumscribed and located more superficially in the subcutis. The presence of mitotic figures, cellular atypia

and/or pleomorphism, as well as necrotic areas suggests a malignant process and favors the diagnosis of rhabdomyosarcoma.

In cases involving the orbit, cosmetic and functional consequences provide an additional rationale for surgical excision. In the presented case, continued growth was observed over 6 years with increasing deformity likely resulting in a more complicated surgical removal, arguing for early excision when possible. Incomplete excision is thought to be associated with rare cases of recurrence.^{7,17}

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