

Nodular fasciitis of the periorbital soft tissue in an adolescent confirmed by USP6 gene rearrangement

Douglas P. Dworak, M.D., FACS^{a,*}, Amanda C. Maltry, M.D.^b, W. Robert Bell, M.D.^b

^a St. Paul Eye Clinic P.A., Woodbury, MN, USA

^b University of Minnesota Medical Center, Department of Ophthalmology and Visual Neurosciences, Department of Laboratory Medicine and Pathology, Minneapolis, MN, USA

ABSTRACT

Nodular fasciitis is a benign, idiopathic condition that can simulate both benign and malignant neoplasms. In adults, it generally occurs in the subcutaneous or superficial fascia of the trunk or upper extremities; occurrence in the periorbital region is far less common. We describe a case of a 16-year-old male with a 4-month history of a nodular, non-tender, progressively enlarging mass of the superotemporal periorbital region. Histopathologic analysis of the excisional biopsy demonstrated nodular fasciitis, confirmed by molecular cytogenetic analysis that showed rearrangement of USP6.

1. Introduction

Nodular fasciitis is a self-limiting soft tissue lesion that can simulate benign and malignant neoplasms. It typically develops in the superficial fascia and extends into the subcutis of the trunk or upper extremities.¹⁻⁴ Periorbital involvement is far less common, with only 33 such cases reported.^{1,3,5-16} Lesions in the periorbital and orbital tissues often can be confused with malignancy and need to be ruled out. Herein, the authors report a case of nodular fasciitis involving the periorbital soft tissue confirmed by molecular cytogenetic analysis. The collection and evaluation of protected patient health information were in compliance with the Health Insurance Portability and Accountability Act of 1996 and adhered to the ethical principles outlined in the Declaration of Helsinki as amended in 2013.

2. Case report

A 16-year-old male presented with a 4-month history of a progressively enlarging mass in the anterior aspect of the superotemporal left orbit. There was no history of prior trauma, surgery, or periorbital disease. Past medical history was unremarkable.

External examination revealed a subtle enlargement over the left superotemporal orbital rim (Fig. 1). The mass was firm, non-tender, and adherent to the underlying bone. The skin over the lesion was mobile. Computerized tomography (CT) of the orbits with and without contrast demonstrated a nodular lesion of the superotemporal periorbital region measuring 15 mm in greatest dimension abutting the lateral rim of the

left orbit (Fig. 2A and B). The mass was hyperdense without osseous erosive changes or extension into the orbit. Given the location, a dermoid cyst was considered first; however, the lumen of a dermoid cyst is typically hypodense, with low signal attenuation similar to fat. An epidermoid inclusion cyst was less likely given there was no fluid attenuation. In order to rule out other benign and malignant mesenchymal tumors, an orbitotomy with excisional biopsy was performed.

Gross examination of the specimen showed a well circumscribed, 1.5 x 1.2 x 1.1 cm gray-tan nodule with no hemorrhage or necrosis, and microscopic examination showed a variably cellular spindle cell lesion with surrounding pseudocapsule. Spindle cells were haphazardly arranged in a myxoid background in the setting of extravasated red blood cells. A few multinucleated giant cells and scattered mitoses were evident (Fig. 3A and B). By immunohistochemistry, the spindle cells were negative for S100; with the exception of background small blood vessels, CD34 was negative. Molecular cytogenetic analysis with fluorescence in situ hybridization (FISH) with a break apart probe to the USP6 locus (17p1.2) showed a signal pattern indicative of USP6 rearrangement (Fig. 4), supporting a diagnosis of nodular fasciitis. The patient demonstrated no evidence of recurrence of subsequent postoperative examinations.

3. Discussion

Nodular fasciitis was first described as pseudosarcomatous fibromatosis by Konwaler et al. in 1955.¹⁷ The authors described the lesion as a benign inflammatory lesion, distinguishing it from fibrosarcoma.

* Corresponding author. St. Paul Eye Clinic P.A., 2080 Woodwinds Drive, Woodbury, MN, 55125, USA.

E-mail address: dougp22@gmail.com (D.P. Dworak).

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Fig. 1. External examination revealed a subtle enlargement over the left superotemporal orbital rim.

Although nodular fasciitis was initially believed to be a reactive growth at the site of previous trauma, the absence of such a history in many cases suggests that it may likely be a self-limiting, benign tumor of mesenchymal cells usually occurring in subcutaneous or superficial fascia.⁴

This soft tissue lesion typically presents in young adults but may occur in all age groups, although it is rare in children. It most often arises on the upper extremities, trunk, and head and neck, but can occur in almost any anatomic location and at varying depths including intramuscular, intravascular, intradermal or periosteal (parosteal fasciitis).^{5,7,18} In children, the head and neck region, including the orbit and

periorbital region, is the most common site of origin.^{6,19} Periorbital cases in this age group may mimic a dermoid cyst, as in our case.^{1,3,7,12}

Nodular fasciitis typically presents as a rapidly enlarging mass that may be tender, with a differential diagnosis ranging from a dermoid cyst to a soft tissue sarcoma.¹ On magnetic resonance imaging, it appears as a discrete soft tissue mass with enhancement.²⁰ Histologically the lesion is composed of plump, regular spindle cells (fibroblasts or myoblasts) with a “tissue culture-like” pattern.⁴ Mitotic figures may be plentiful but are not atypical, and extravasated red blood cells and inflammatory cells are often present.⁴ Immunohistochemical staining is usually strongly positive for smooth muscle actin and muscle specific actin and negative for S100 protein and keratin.⁴

Erickson-Johnson et al. described a USP6-MYH9 fusion resulting from a t(17; 22)(p13; q1.1) in 92% of 48 cases of nodular fasciitis.²¹ Molecular testing showed that the coding region of USP6 was fused to the promoter region of MYH9, resulting in increased USP6 expression.²¹ This gene fusion is not, however, essential for nodular fasciitis, as there are reported cases that lack this rearrangement.¹⁹ Additionally, 7 fusion partners other than MYH9 have been identified in nodular fasciitis, suggesting that nodular fasciitis is a neoplastic rather than reactive process, albeit transient with a tendency to resolve spontaneously.^{18,22} Analogously, as the majority of cases of primary aneurysmal bone cysts are characterized by USP6 rearrangement, these lesions, also once thought to be reactive, are now recognized as neoplastic.^{4,18}

Nodular fasciitis is a rare lesion of mesenchymal origin that should be included in the differential diagnosis of orbital and periorbital masses, especially in children. The rapidly progressive growth of these tumors may be concerning for more aggressive behavior; thus, surgical excision with histopathologic diagnosis is the preferred treatment for nodular fasciitis, especially for periorbital lesions that include malignant

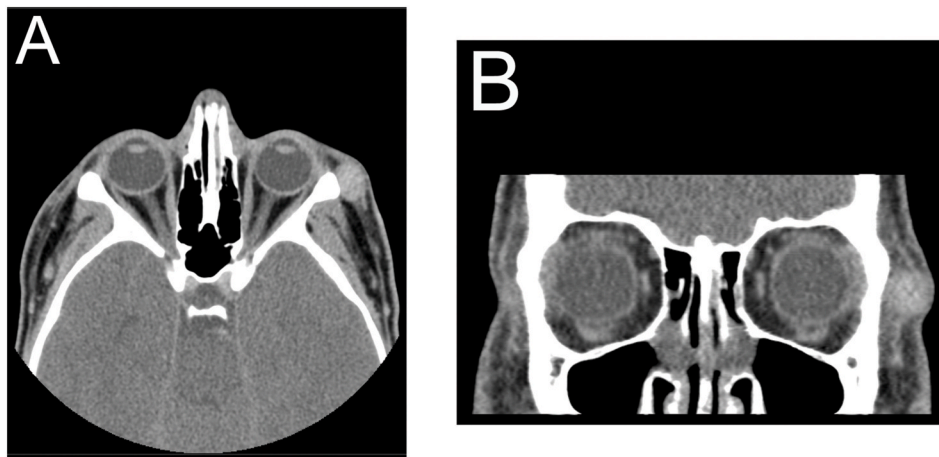


Fig. 2. Orbital CT imaging of nodular fasciitis. A: Axial view shows a contrast-enhancing hyperdense mass in the left superotemporal peri-orbital soft tissue. B: Coronal view shows the mass abutting the lateral rim of the left orbit without osseous erosive changes.

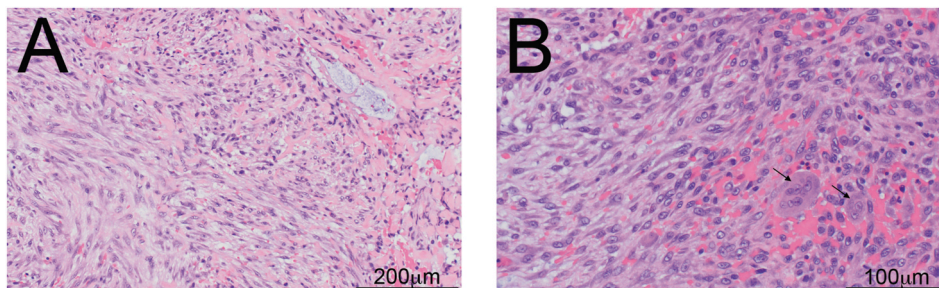


Fig. 3. A: Hematoxylin and Eosin stain showing spindle myofibroblastic cells in a myxoid background intermixed with dense collagenous bundles within the mass 200x B: In some regions, extravasated blood and occasional giant cells (arrows), 400x are identified (B).

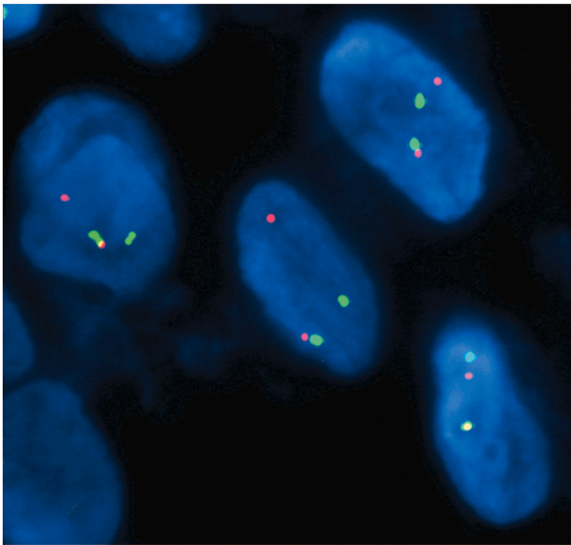


Fig. 4. Florescent in-situ hybridization analysis of USP6 (17p13) dual-color break-apart probe shows multiple nuclei with separation of red and green signals. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

or vision-threatening tumors in the differential diagnosis.¹ We recommend the use of Fluorescence in situ hybridization (FISH) or other molecular testing to evaluate for USP6 rearrangement to aid diagnosis when encountered in small biopsies. MYH9-USP6 is the most common fusion recognized in nodular fasciitis, but a variety of other promoter swapping gene fusions have been identified. The more we study USP6 rearrangements, the better we understand it as a potential oncogene and view nodular fasciitis as a transient neoplasm.

Patient consent

Consent to publish this case report has been obtained from the patient(s) in writing.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

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