Prenatal Presentation of Fronto-orbital Congenital Infantile Fibrosarcoma: A Clinicopathologic Report

Congenital infantile fibrosarcoma (CIFS) is a mesenchymal tumor that occurs in the first year of life and rarely involves the orbit. We describe a patient with a prenatal presentation of orbital and forehead CIFS.

Report of a Case | A prenatal ultrasonographic scan at 37 weeks’ gestation showed a large right frontal mass with orbital involvement (Figure 1A), prompting early cesarean delivery. At birth, the mass was 9 × 7 × 4 cm, firm, nonpulsatile, and opaque, with dark and vascular discoloration inferiorly (Figure 1B). Postnatal ultrasonography, computed tomography, and magnetic resonance imaging showed a variegated soft-tissue mass at the glabella extending into the right superomedial orbit and displacing the right globe downward (Figure 1C and D). The anterior tables of both frontal bones were thinned, including a 5-mm-diameter bony defect with associated periosteal thickening. On day 8, the lesion was surgically excised, with preservation of pseudocapsule integrity except in the deep orbit, where the tumor tail was excised piecemeal. The frontal defect was reconstructed with local flaps.

Morphological, immunohistochemical, and molecular features were consistent with a diagnosis of CIFS. Fluorescence in situ hybridization confirmed translocation involving ETV6

Figure 1. Ultrasonographic, Clinical, Computed Tomographic, and Magnetic Resonance Images

A, The 4.5 × 4.2 × 3.0-cm mass on a prenatal ultrasonographic scan at 37 weeks’ gestation. B, Clinical image from day 1 of life. C, Sagittal computed tomographic image showing globe displacement and compression by the mass. D, Postnatal sagittal magnetic resonance image showing a large variegated lesion with patchy intrallesional hyperattenuations consistent with hemorrhage.
on chromosome 12 and NTRK3 on chromosome 15, supporting this diagnosis (Figure 2A-C). One year postoperatively, there has been no clinicoradiological evidence of CIFS recurrence (Figure 2D). Visual acuities are equal and ocular movements are full without strabismus. The cranial defect closed spontaneously. The cosmetic appearance is excellent.

**Comment** | Congenital infantile fibrous sarcoma is a mesenchymal spindle cell tumor found in infants. Forty percent of cases are diagnosed at birth or in utero, mainly affecting the extremities.1,2 Rarely it can be identified on prenatal ultrasonographic scans.3 Prenatal death has been reported from intrauterine CIFS rupture.4 It is a rare cause of orbital mass in infancy. Treatment is usually total surgical excision. Fortunately, fewer than 10% metastasize.7 Neoadjuvant chemotherapy is sometimes used to minimize mutilating effects of surgery.2 Postresection adjuvant chemotherapy is occasionally required. The local recurrence rate is 40% to 50%.5

Large orbital masses rarely present at birth. Differential causes include teratoma, rhabdomyosarcoma, neuroblastoma, and granulocytic sarcoma, a manifestation of leukemia.7 Rarer causes include malignant rhabdoid tumor, infantile solitary myofibroma, and congenital fibromatosis or myofibromatosis. Hemangioma, dermoid cyst, and venous-lymphatic malformation are other differential diagnoses of orbital mass in infancy.

Sarcomas and fibrous tumors of infancy have similar histological findings and are differentiated by immunohistochemistry and molecular tests. The presence of chromosomal translocation t(12;15)(p13;q25) for an ETV6-NTRK3 fusion gene is specific for CIFS.5,6 This translocation is not present in other spindle cell tumors of infancy or childhood, including spindle cell or embryonal rhabdomyosarcoma, malignant fibrous histiocytoma, infant fibromatosis, aggressive fibromatosis, or myofibromatosis.6 In our patient, the morphological and immunohistochemical characteristics suggested granulocytic sarcoma (chloroma) because a reactive inflammatory component composed mostly of histiocytes and lymphocytes, uncommon in CIFS, was evident. However, the ETV6-NTRK3 translocation was diagnostic. This case illustrates the importance of looking for the ETV6-NTRK3 translocation, as treatment with intensive chemotherapy for granulocytic sarcoma would have resulted in significant unnecessary morbidity and possibly mortality for this infant.

To our knowledge, this is the first report of a prenatally identified orbital CIFS treated by vision-sparing surgical excision. Although the early result is excellent, long-term surveillance is planned owing to the risk of recurrence.

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**Figure 2. Histopathologic Findings and Clinical Image**

A, The tumor is cellular and composed of plump and spindle-shaped fibroblast-type stromal cells with a moderate amount of slightly eosinophilic cytoplasm (hematoxylin-eosin, original magnification ×400). B, The fibroblast-type cells stained for vimentin only. Fluorescence in situ hybridization confirmed the ETV6-NTRK3 translocation specific for congenital infantile fibrosarcoma. Other markers, including CD99, actin, desmin, myogenin, anaplastic lymphoma kinase 1, myeloperoxidase, CD117, S-100 protein, and BAF47, were negative or nonsupportive of other mesenchymal tumors (vimentin, original magnification ×400). C, Immunohistochemical staining for CD163 highlights a prominent reactive inflammatory component, mostly histiocytes (CD163, original magnification ×400). D, Clinical image at age 10 months.

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Letters

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This case demonstrates that CIFS is a differential diagnosis of prenatal orbital mass. The ETV6-NTRK3 translocation is present in orbital CIFS. Early cesarean delivery and prompt surgical excision can provide excellent functional and cosmetic results.

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Conflict of Interest Disclosures: None reported.


OBSERVATION

Growth of Type 1 Neovascularization Following Cessation of Anti–Vascular Endothelial Growth Factor Therapy as a Possible Explanation for Treatment Resistance

Intravitreal anti–vascular endothelial growth factor (anti–VEGF) therapy is currently the standard of care for the treatment of neovascular age-related macular degeneration. Herein, we describe a mechanism by which some patients who initially show a robust response to treatment may later in their course become refractory to this therapy.

Report of Cases | Case 1. An 86-year-old woman received intravitreal ranibizumab in her left eye for type 1 (subretinal pigment epithelium) neovascularization associated with neovascular age-related macular degeneration (Figure 1A and B). Over the course of 4 monthly injections, there was complete resolution of subretinal pigment epithelium hemorrhage. Consolidation of the type 1 neovascular tissue and resolution of all fluid was noted with spectral-domain optical coherence tomography (SD-OCT) (Figure 1C). The patient was then switched to optical coherence tomography–guided therapy with pro re nata dosing. For the next 10 months, the type 1 vessels were noted to gradually increase in size, but because there was no visible hemorrhage and there was no fluid present on SD-OCT, injec...