Primary Orbital Ewing Sarcoma in a Middle-aged Woman

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A 43-year-old woman had unilateral exophthalmos caused by primary orbital Ewing sarcoma. Specialized immunohistochemical stains, primarily MIC-2 (CD99), aided in the diagnosis of Ewing sarcoma. Twenty-two months after radiotherapy and multiagent chemotherapy, the patient remained tumor free. To our knowledge, this is the first reported case of orbital Ewing sarcoma to present in an adult beyond the fourth decade of life.

Ewing sarcoma is a highly malignant, small round cell neoplasm that primarily involves the long bones and pelvis. It accounts for 10% of all bony tumors and 4% of tumors in the head and neck region, typically involving the mandible, maxilla, and skull. Orbital involvement is rare. This tumor typically affects white males under age 20 years. Of neuroectodermal origin, Ewing sarcoma can be confused with other small round cell tumors. Therefore, immunohistochemical studies are important for establishing an accurate diagnosis. We report a unique case of orbital Ewing sarcoma in a 43-year-old woman and the application of MIC-2 (CD99) in diagnostic analysis.

**REPORT OF A CASE**

A previously healthy 43-year-old woman developed proptosis and discomfort of her left eye over a 4-week period. Her medical history was noncontributory except for a 20 pack-year history of cigarette use. An ophthalmic examination of the right eye showed no abnormalities. The left eye, however, had a visual acuity of 20/25, mild upper-eyelid swelling, 9 mm of proptosis, 3 mm of hypogobulus, and limited supraduction (Figure 1). No mass was palpable; however, there was marked resistance to retropulsion of the eye. The remainder of the ophthalmic examination showed no abnormalities.

Axial and coronal magnetic resonance imaging of the orbits with and without gadolinium showed a large mass superonasal to the left globe, with extension of the mass into the left ethmoid sinus (Figure 2 and Figure 3). Anterior orbitotomy for incisional biopsy was performed through the left upper eyelid crease. The tumor was reddish-orange, friable, and infiltrative. Histopathologic examination of formalin-fixed tissue showed small, round cells with large nuclei, homogeneous chromatin, and scant cytoplasm (Figure 3 and Figure 4). Because of the extensive differential diagnosis for small round cell lesions, additional histochemical testing was performed. The tissue was negative for cytokeratin, desmin, CD45, and S-100 protein, but was positive for MIC-2 (CD99) (Figure 5). The specimen was submitted to the Armed Forces Institute of Pathology for further evaluation. Extensive immunohistochemical stains showed the lesion to be strongly positive for MIC-2 (CD99) and focally positive for neuron-specific enolase, but negative for leucocyte common antigen, CD3, L26, UCHL-1, cytokeratin, terminal deoxynucleotidyl transferase, CD34, myeloperoxidase, and desmin. These characteristics established the diagnosis of Ewing sarcoma.

A general medical and laboratory evaluation, including complete blood cell count, chest radiographic scan, full-body bone scan, and abdominal and chest com-
puted tomographic scan, showed no abnormalities. The patient was treated with radiation therapy (5800 cGy) to the left orbit and ethmoid sinuses and combination chemotherapy with vincristine sulfate, cyclophosphamide, mesna, ifosfamide, and etoposide. Five months after the initial diagnosis, the proptosis of the left eye had resolved. Bone scan, abdominal and chest computed tomographic scan, and brain magnetic resonance imaging showed no evidence of metastases. Follow-up coronal magnetic resonance imaging scan of the orbits demonstrated resolution of the left orbital mass 14 months after initial diagnosis (Figure 6). The patient developed keratoconjunctivitis sicca of the left eye secondary to the radiation treatment, but the condition improved substantially with punctal plugs and artificial tears.

COMMENT

Ewing sarcoma is a highly malignant tumor of bone, with involvement of the head and neck region and facial bones representing 4% and 2.5% of cases, respectively.1-3,6 Symptoms and signs of orbital involvement include pain, headache, decreased vision, lower eyelid swelling, palpable mass, proptosis, ophthalmoplegia, papilledema, and blindness.2,7 Fever and leukocytosis may also be associated with Ewing sarcoma.2 Computed tomographic scanning shows mottled destruction of bone but typically no soft tissue enhancement with contrast.1,6 The characteristic periosteal “onion ring” reaction seen in long bones is not usually present in orbital cases.3 Although Ewing sarcoma was previously a tumor with high mortality, the prognosis has improved greatly since the addition of multiagent chemotherapy to radiation therapy and surgical resection, with 5-year survival rates exceeding 60%.1,3 Among successfully treated patients, approximately 20% develop secondary tumors, such as osteogenic sarcoma.1

Histopathologic examination of Ewing sarcoma reveals sheets of cells with uniform round to oval nuclei, fine granular chromatin, indistinct nucleoli, and scant cytoplasm.1,3-7 These findings are consistent with other round cell tumors, such as malignant lymphoma, neuroblastoma, and rhabdomyosarcoma,6,7 but cytochemical and immunohisto-

Figure 1. Upper eyelid swelling, limitation of supraduction, and hypoglobus of the left eye.

Figure 2. An axial view magnetic resonance imaging scan of the orbits, demonstrating the lesion superior to the left globe and invading the left ethmoid sinus.

Figure 3. A coronal magnetic resonance imaging scan of the orbits, demonstrating the large superior orbital mass depressing the left globe and invading the ethmoid sinus.

Figure 4. Sheets of uniform, small, round cells with very scant cytoplasm (hematoxylin-eosin, original magnification ×400).

Figure 5. Photomicrograph demonstrating the characteristic cell membrane staining for MIC-2 gene product (CD99) by immunoperoxidase technique (original magnification ×400). Nuclei do not stain.

Figure 6. Follow-up coronal magnetic resonance imaging scan of the orbits, demonstrating resolution of the left orbital mass 14 months after initial diagnosis.
chemical studies distinguish this tumor from other small round cell tumors. Ewing sarcoma tests positive for periodic acid–Schiff stain (secondary to the abundance of glycogen), vimentin, and particularly MIC-2 (CD99), a cell-surface glycoprotein encoded by genes on chromosomes X and Y.

The MIC-2 gene product can be found in primitive neuroectodermal tumors, rhabdomyosarcoma, Ewing sarcoma, and lymphoblastic lymphoma and leukemia, but has not been found in neuroblastomas and small cell osteosarcomas.\(^4,5\) Ewing sarcoma tests negative for leukocyte common antigen, chromogranins A and B, and osteonectin, contains no neurosecretory granules, and tests weakly positive for cytokeratin.\(^4,5\) The negative terminal deoxynucleotidyl transferase and CD34 stains further support the diagnosis of Ewing sarcoma rather than lymphoblastic lymphoma in this case. A small subset of rhabdomyosarcomas can stain positive for MIC-2. Rhabdomyosarcoma, however, has a more heterogeneous MIC-2 staining pattern than Ewing sarcoma. In addition, rhabdomyosarcomas also stain for desmin and actin while Ewing sarcomas do not.\(^4,5\)

Chromosomal studies that demonstrate translocation (11;22)(q24:q12) can also confirm the diagnosis of Ewing sarcoma.

To our knowledge, this is the first reported case of orbital Ewing sarcoma in an adult beyond the fourth decade. Rare cases of Ewing sarcoma of the ethmoid sinuses have been previously reported; however, they have primarily involved children under the age of 15 years.\(^6\) Ewing sarcoma may present a diagnostic challenge to experienced ophthalmic pathologists. Special immunohistochemical stains, especially MIC-2, aid in diagnosis. Although extremely rare, this tumor should be included in the differential diagnosis of round cell orbital tumors showing bone destruction in adults.

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REFERENCES


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A look at the past . . .

AHLFELD’S experiments show that it is possible to discover the presence of foreign bodies in the eye by means of the X-rays; but that a negative result does not prove the absence of a foreign body, for this may lie in such a position as to be masked by the shadow of the orbital margin, and may be revealed only by placing the apparatus in a different position.