CASE REPORT

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EWING SARCOMA OF THE MANDIBULAR CONDYLE: MULTIDISCIPLINARY MANAGEMENT OPTIMIZES OUTCOME

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Abstract: Background. Ewing sarcoma (ES) is a rare, primary malignancy of bone that occurs in childhood and early adolescence. Improved methods of diagnosis and treatment have dramatically increased survival over the last 20 years. Treatment mainstays are chemotherapy and surgical tumor resection. ES usually occurs in long bones of the axial skeleton; however, it may rarely arise in facial structures, particularly the mandible. In these cases, resection presents a challenging postsurgical reconstruction.

Methods and Results. We present the clinical findings and management of a case of ES that developed in the left mandibular condyle of a 15-year-old female. Chemotherapy and segmental mandibulectomy were used to achieve local control. An innovative temporomandibular joint reconstruction was successfully accomplished using a microvascular fibular free flap and conchal cartilage graft.


Keywords: Ewing sarcoma; TMJ reconstruction; conchal cartilage graft; temporoparietal fascial flap; fibular free flap

Malignant primary bone tumors in the jaws are rare, and the small round blue cell tumors of childhood, such as Ewing sarcoma (ES), are challenging cases for diagnosis, treatment, and reconstruction. The serious nature of ES requires definitive treatment; in addition to chemotherapy, surgical resection with generous, tumor-free margins is the standard of care. Because of the complicated anatomy of the jaws, treatment can result in significant disfigurement, loss of function, and psychosocial morbidity. We describe the clinical findings and management in a case of ES that developed in the left mandibular condyle of a 15-year-old female. Treatment included preoperative and postoperative chemotherapy and segmental mandibulectomy, including total condylectomy. A novel approach to successfully reconstruct the surgical defect was utilized. The man-
The mandibular ramus was replaced with a fibular microvascular free flap, and the temporomandibular joint (TMJ) was recreated with a temporoparietal fascial rotation flap and autologous conchal cartilage graft.

**CASE REPORT**

A 15-year-old girl had a 1-year history of left facial edema and pain that was treated by third molar extractions. Subsequently, she experienced increasing pain and swelling. CT imaging revealed an expansile bony lesion of the left condylar process. The patient was then referred to the Head and Neck Center at Roswell Park Cancer Institute (RPCI) for further care.

In June 2004, the patient presented slight trismus and a conspicuous left preauricular mass, which was not painful on palpation. A panoramic radiograph showed enlargement of the left condylar head and neck (Figure 1). The previous CT imaging was reviewed, and a representative axial view was illustrated (Figure 2). The expansion of the left condyle, with spiculated periosteal new bone formation, was suggestive of a malignant process. Three-dimensional volumetric rendering allowed visualization of the extent of the neoplasm (Figure 3). The clinical differential diagnosis was osteosarcoma, chondrosarcoma, or benign fibrousseous lesion. An open incisional biopsy of the left condyle was taken through a small preauricular incision.

Histopathology showed a highly cellular infiltrate arranged in sheets that infiltrated bony trabeculae, with little stroma (Figure 4A). The infiltrate consisted of a dense, monotonous population of small, round, hyperchromatic cells with scant cytoplasm and indistinct cell borders. Nuclei were small and uniform, with fine nuclear chromatin and inconspicuous nucleoli. Periodic acid-Schiff (PAS) staining showed that tumor cells were positive for cytoplasmic glycogen, removable with diastase. Immunohistochemical studies included positive and negative controls for each assay. Tumor cells were positive for the protein products of the Friend Leukemia Virus 1 (flI1) and the Monoclonal Imperial Cancer [Research Fund] 2 (mic2) genes, FLI1 and CD99 (Figures 4B and 4C). Antibodies to leukocyte common antigen (LCA) were not reactive with tumoral tissue. The diagnosis was ES/primitive neuroectodermal tumor (ES/PNET).

A radionuclide bone scan with technetium 99m-labeled phosphate compounds, revealed increased uptake in the left mandible. The patient received 5 courses of induction chemotherapy with vincristine, cyclophosphamide, mesna, and doxorubicin. She was assigned to the Children’s Oncology Group Protocol AEWS 00-31 and received ifosfamide, and etoposide, administered according to protocol-recommended dosages and schedules. A nearly complete clinical response was noted after induction chemotherapy.

A surgical procedure was performed to resect the malignant tissue with generous surgical margins and to reconstruct the resulting defect.
tomy, including the ramus, coronoid, and condylar processes (Figure 5). The bony defect of the ramus was reconstructed using a microvascular fibular free flap. The TMJ was reconstructed utilizing a temporoparietal fascial rotational flap and an autologous conchal cartilage graft, anchored to the proximal fibular graft. This not only restored nor-

![Figure 3](image3.jpg) **FIGURE 3.** Posterior, anterior, and lateral views of a 3D volumetric rendering of the left mandibular ramus, condylar, and coronoid processes created from the CT scan shows the tumor expansion of these structures. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

![Figure 4](image4.jpg) **FIGURE 4.** (A) Hematoxylin-eosin–stained sections show dense sheets of a highly cellular monotonous population of densely packed, small, round cells with small, uniform, hyperchromatic round nuclei. Immunohistochemical studies with antibodies to FLI1 (B), and CD99 (C), show tumor cells staining positive for these Ewings sarcoma markers. Original magnification of all photomicrographs is x20. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
mal anatomy, but also replaced resected tissues with similar tissues. The postoperative panoramic radiograph (Figure 6) revealed a well-aligned reconstruction with intact plating.

The patient completed postoperative chemotherapy in compliance with the protocol. Surgical pathology showed no evidence of residual tumor within the specimen, indicating a complete response consistent with a favorable long-term prognosis. An oral-examination was performed on a follow-up visit 2 years and 6 months postsurgery. On mandibular opening, the patient showed slight deviation to the surgical side, although her occlusion was nearly perfect (Figure 7A). There was no facial asymmetry (Figure 7B). The patient reported normal mastication without trismus, and she is able to eat a regular diet. MRI and CT imaging of the maxillofacial and neck region show no evidence of locoregional recurrence.

**DISCUSSION**

Ewing initially described Ewing sarcoma in 1921 as a primary malignant bone neoplasm of unknown origin. ES accounts for 1% of all childhood malignancies and is most often found in the pelvis or long bones of the axial skeleton. There is a 1% to 2% incidence of ES in the facial skeleton.

![FIGURE 5. Gross appearance of mandibular resection specimen shows the enlargement of the misshapen mandibular condyle and the temporomandibular joint soft tissues. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

![FIGURE 6. Postoperative panoramic radiograph shows the reconstruction of the ramus and temporomandibular joint with all plating intact.]

![FIGURE 7. Postoperative clinical photographs, 2 years and 6 months postsurgery. The patient has good occlusion (A) and facial symmetry (B). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
The mandibular ramus is the most frequent site of occurrence in the jaws, often necessitating TMJ reconstruction after surgical treatment.

**Diagnosis.** As in our case, the most common clinical presentation of ES is local bone pain and a mass.\(^1\) While imaging studies are useful to delineate the character and extent of the lesions, ES is diagnosed on histopathologic criteria. ES is a poorly differentiated mesenchymal neoplasm and histologically similar to several other small, round, blue cell tumors of childhood (eg, neuroblastoma, rhabdomyosarcoma, and lymphoma).\(^6\)

Recent immunohistochemical, molecular and genetic studies have characterized the ES lineage as a primitive neuroectodermal tumor (PNET).\(^7\) PNETs represent a spectrum of differentiation and may occur within the central nervous system or peripherally. A chart illustrates the traditional nomenclature (Figure 8) of PNETs. The peripheral primitive neuroectodermal tumor (pPNET) exhibits neural differentiation, while ES is a less differentiated tumor. PNETs share many common pathologic features, thus most contemporary authors refer to these neoplasms as ES/PNET.\(^6\)

More than 90% of ES/PNET share a chromosomal translocation (t:11;22) (q:24:12) which leads to production of an EWS and FLI1 fusion transcript.\(^7\) This transcript codes for a chimeric protein that functions as an aberrant oncogenic transcription factor.\(^8\) Additionally, ES/PNET expresses elevated levels of a 32-kDa cell surface glycoprotein p30-32, known as cluster differentiation 99 (CD99), a mic2 gene product. As in the present case, positive immunohistochemical reactivity using antibodies to FLI1 and CD99 confirms the diagnosis of ES.\(^9,10\)

**Treatment.** Over the previous 2 decades, advances in chemotherapeutic drugs and surgical techniques increased the 5 year survival rate of ES patients from 10% to 50%–70%.\(^11,12\) Wide surgical resection in conjunction with chemotherapy is the cornerstone of ES treatment\(^1\) while radiation therapy is avoided for 2 reasons. First, therapeutic radiation carries a high risk for future development of a secondary malignant neoplasm, usually a sarcoma, in the radiation site.\(^13\) Second, radiation treatment may interfere with facial growth and should be avoided in cases in which there is potential disruption. Since most cases of gnathic ES occur in children and adolescents, radiotherapy is rarely used.

In this case, an innovative, single-stage approach consisting of wide surgical resection, and reconstruction of the mandible and TMJ was performed. The resected ramus was replaced with a fibular microvascular free flap, the utility of which has been well documented.\(^14,15\) This flap provides an ample length of vascularized bone, making it possible to reconstruct most extensive bony defects. In addition, donor site morbidity is low.

TMJ disc removal and replacement previously has been performed using various autologous, allogeneic, and alloplastic materials\(^16–18\) with widely varying rates of success. In the present case, the TMJ was recreated using a temporoparietal fascial rotation flap to recreate the joint capsule and an autogenous conchal cartilage graft to recreate the articular disc as previously described.\(^16,18,19\) Conchal cartilage offers several advantages as an interpositional disc following TMJ disectomy. It is easily harvested from the posterior auricle adjacent to the surgical site and an adequate size graft can be harvested with no donor site morbidity. In addition, the natural cartilage concavity corresponds to the morphology of the resected disc.

Although both of these reconstructive modalities have been reported separately, the case presented combines these reconstructive techniques synchronously, achieving excellent cosmesis and function. A single-stage reconstruction, as illustrated by this case, provides superior results for the rehabilitation of this patient population. Close communication between pathology, head and neck surgery, diagnostic imaging, pediatric and dental oncology was essential to diagnose, treat, and reconstruct this case of ES of the mandibular condyle. Management by a multidisciplinary oncology team produces an optimal result that eliminates disease and restores function, aesthetics and quality of life.

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**FIGURE 8.** This chart illustrates the traditional nomenclature of tumors in the primitive neuroectodermal tumor group. Recently, the recognition of many common pathological features shared by these tumors, have led most contemporary authors refer to these neoplasms as Ewing sarcoma/primitive neuroectodermal tumor (ES/PNET).

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<tr>
<th>Tumor Type</th>
<th>Abbreviation</th>
<th>Nomenclature</th>
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<tbody>
<tr>
<td>Peripheral PNET</td>
<td>pPNET</td>
<td>Peripherally differentiated</td>
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<tr>
<td>Neural differentiation</td>
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<td>Bone: Ewing sarcoma (ES)</td>
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<tr>
<td>Poorly differentiated</td>
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<td>Soft tissue: pPNET</td>
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Ewing Sarcoma of the Mandibular Condyle
REFERENCES