Rhabdomyosarcoma of the middle ear and mastoid: A case report and review of the literature

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Abstract
We report a case of rhabdomyosarcoma of the middle ear and mastoid in a 3-year-old boy. The patient was treated according to Intergroup Rhabdomyosarcoma Study IV protocol (chemo- and radiotherapy), and he experienced a complete remission. However, 7 months after the completion of treatment, he experienced a recurrence at the primary site that spread to the brain. Despite treatment, the patient died of progressive metastasis to the lung 4 months later.

Introduction
Weber first described rhabdomyosarcoma in 1854. Nearly 80 years later, Soderberg described the first case of rhabdomyosarcoma of the middle ear and mastoid. Rhabdomyosarcomas are the most common soft-tissue tumors in children. Rhabdomyosarcomas of the head and neck account for approximately 41% of all pediatric rhabdomyosarcomas, and rhabdomyosarcomas of the temporal bone account for approximately 8% of all such tumors in the head and neck. Rhabdomyosarcomas of the middle ear and mastoid are rare.

Prior to the introduction of the first Intergroup Rhabdomyosarcoma Study (IRS) protocol in 1972, surgical resection was considered to be the mainstay of treatment; second-line treatment was radiation therapy at the primary site, although this often resulted in major morbidity and was associated with a poor prognosis. The authors of the original IRS protocol recommended multiagent chemotherapy along with radiotherapy as the mainstay of treatment; they advised that surgical resection should be performed only if major morbidity can be avoided. The original protocol was revised in 1978 (IRS II), in 1984 (IRS III), and in 1991 (IRS IV). The chemotherapeutic element of the IRS IV protocol is significantly different from its predecessors in that the newer agents etoposide, ifosfamide, and melphalan have been added to the standard treatment with vincristine, actinomycin D, and cyclophosphamide. With respect to the radiotherapeutic component of treatment, the amount of radiation delivered to the head and neck is usually limited to 4,000 to 4,500 Gy. Salvage therapy for patients with recurrent rhabdomyosarcoma remains problematic.

Pediatric rhabdomyosarcomas that arise in the temporal bone are generally considered to be aggressive neoplasms by virtue of their proximity to vital structures, their tendency to spread intracranially, and their potential for meningeal involvement. In this article, we describe a case of pediatric rhabdomyosarcoma of the middle ear and mastoid that ultimately proved to be fatal.

Case report
A 3-year-old boy was referred to our clinic with 2-month history of right-sided otalgia and bleeding from the external auditory canal. Physical examination revealed that a fleshy polypoid mass had occupied the entire external auditory canal. No cranial nerve involvement was noted, and there was no evidence of cervical lymphadenopathy. The ear was examined under general anesthesia, and a biopsy sample was obtained. The size of the mass prevented visualization of anatomic landmarks and middle ear structures. The histopathologic features of the biopsy specimen were consistent with an embryonal rhabdomyosarcoma (figure 1). Cell staining was positive for desmin and negative for alpha-smooth-muscle actin.

Computed tomography (CT) of the temporal bone and the brain confirmed that the mass had occupied the middle ear and mastoid; some bone destruction was evident (figure 2). The tumor also involved the squama of the temporal bone, the zygomatic process, and the greater wing of the sphenoid bone. Only minimal intracranial extension just anterior to the petrous temporal bone was seen. The chest x-ray was clear. A bone scan revealed isotope uptake in the right temporal bone but no evidence of metastatic disease. The disease was classified as IRS stage III-A.

The patient was started on radiotherapy (4,500 Gy)
and chemotherapy with vincristine, actinomycin D, cyclophosphamide, etoposide, ifosfamide, and melphalan, in accordance with the IRS IV protocol. Four weeks after the completion of radio- and chemotherapy, magnetic resonance imaging (MRI) of the brain detected no evidence of residual disease. CT of the temporal bone and brain confirmed the complete resolution of the tumor. A repeat chest x-ray was clear.

Seven months later, the child returned with right-sided facial palsy and headache. MRI of the brain detected a recurrence of the tumor in the right cerebellopontine angle (figure 3) and in the lung. The parents refused further chemotherapy, and the child died 4 months later.

Discussion
Numerous clinical studies of rhabdomyosarcomas have been completed as a result of the efforts of large numbers of cooperating groups, including the IRS investigators, who have pooled their patient data and resources. Rhabdomyosarcomas exhibit a bimodal pattern of age distribution; their incidence peaks between the ages of 2 and 5 years and spikes again in late adolescence.9 Overall, 63% of all cases occur in patients younger than 10 years.9

Horn and Enterline devised a system of classifying rhabdomyosarcomas according to their histologic features; the four types are embryonal (the most common rhabdomyosarcoma of the head and neck), pleomorphic, alveolar, and botryoid.10 Affected patients often exhibit more than one type. The alveolar type has consistently been marked by a translocation of chromosomes (2; 13) (q35q14); in the embryonal type, the maternal allele is lost.9

The clinical presentation of rhabdomyosarcoma of the middle ear and mastoid is similar to that of chronic suppurative otitis media; presenting signs include purulent and occasionally blood-stained discharge, aural polyps, and granulation tissue. As a result, the consequences of misdiagnosis can be serious if a patient with rhabdomyosarcoma is being treated with antibiotics. The most common neurologic feature of rhabdomyosarcoma is facial nerve involvement. Tissue biopsy analysis is the key to diagnosis, and it should be performed as soon as possible. Immunohistochemical analysis with desmin is specific and sensitive for rhabdomyosarcoma. Recently, the demonstration of fetal hemoglobin in tumor tissue by immunoperoxidase staining has been shown to be reliably accurate in identifying rhabdomyosarcoma.9

Figure 1. Histopathology demonstrates sheets of rounded tumor cells with scant cytoplasm and inconspicuous nucleoli (H&E, original magnification ×20).

Figure 2. At the initial presentation, CT through the temporal bone shows the tumor involvement of the right middle ear and mastoid and the erosion of the petrous bone and mastoid.

Figure 3. Seven months following the completion of initial therapy, axial postcontrast T2-weighted MRI shows the welld-defined 1.25 × 1 × 1 cm lesion in right cerebellopontine angle.
The development of the IRS protocol has led to a better understanding of the disease process and better use of radiotherapy and new chemotherapeutic agents. As a result, the prognosis for patients with some types of rhabdomyosarcoma has steadily improved. For example, patients with orbital tumors generally have a better prognosis than do patients with tumors in parameningeal sites (the nasopharynx, middle ear, mastoid area, parapharyngeal fossa, and parapharyngeal space). In a study of 103 children who had been treated under the IRS I protocol, the 3-year relapse-free survival rate was 46% for patients with parameningeal tumors, compared with 91% for patients with rhabdomyosarcomas of the eye and orbit and 75% for those with other head and neck rhabdomyosarcomas. Moreover, according to the second report of the IRS investigators, patients with rhabdomyosarcomas at nonmeningeal sites experienced a higher tumor-free survival rate at 3 years (81%) than did patients with meningeal involvement (51%). Finally, another review of the IRS I protocol revealed that children who develop a recurrence after having achieved a complete response to treatment have a 95% probability of dying of the recurrence, regardless of further treatment. Tumors in the parameningeal sites usually behave more aggressively than do tumors at other sites in the head and neck, primarily because of their proximity to the meninges and brain. Patients with rhabdomyosarcoma of the middle ear and mastoid have a particularly poor prognosis. The difference in survival is directly related to the higher incidence of intracranial extension in patients with middle ear or mastoid tumors. The final results of the IRS IV trial, which has been in progress since 1991, have yet to be compiled.

The basic goal of therapy for rhabdomyosarcoma (as it is for most solid tumors) is locoregional control, and prevention or treatment of systemic metastasis. Therefore, all patients are treated systemically with chemotherapy and locally and regionally with radiotherapy, surgery, or both. Occult nodal metastasis is uncommon, and prophylactic neck dissection is not warranted. Surgical excision is not always possible, especially in difficult-to-reach anatomic areas or when the tumor involves intracranial structures.

The role of bone marrow transplant in patients with unfavorable tumor characteristics has been the subject of recent interest. The concept of using bone marrow rescue in this patient population is based on the fact that the very high doses of chemotherapy used in bone marrow transplantations may be able to eradicate residual disease. By infusing patients with their own stem cells before rescuing their bone marrow, we may be able to prevent the bone marrow toxicity that has traditionally limited the dosage of chemotherapeutic agents. Studies are under way.

References