UNDIFFERENTIATED PLEOMORPHIC SARCOMA OF THE PAROTID GLAND: A RARE PEDIATRIC CASE

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Abstract: Background. Undifferentiated pleomorphic sarcoma, or malignant fibrous histiocytoma (MFH) of the head and neck is an uncommon malignancy that is exceedingly rare in the pediatric population. Although MFH was once considered the most common soft tissue sarcoma in adults, recently authors have questioned its existence as a distinct pathologic entity.

Methods. In light of this debate, we present a case of MFH with giant cells involving the parotid gland, and we review its pathology.

Results. We describe a 6-year-old male with parotid gland MFH. Diagnosis was fraught with difficulty, typical of this disease. He was treated with a combination of chemotherapy and radiation therapy with a good initial response.

Conclusion. The classification of MFH has been recently debated. Nevertheless, our case is the second report of pediatric MFH involving the parotid gland. Surgical resection is the preferred treatment, but combined chemoradiation may be necessary in the head and neck region. ©2007 Wiley Periodicals, Inc. Head Neck 30: 970–973, 2008

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The entity referred to as malignant fibrous histiocytoma (MFH) has undergone a major transformation since it was first described by O’Brien and Stout1,2 in the 1960s. By the 1980s, it was recognized as the most common soft tissue sarcoma in adults.3 In recent years, however, the existence of MFH as a pathological entity has been challenged. In light of this debate, MFH of the head and neck is considered uncommon and exceedingly rare in the pediatric population. Aggressive surgical resection is the treatment of choice. We present a pediatric case of parotid gland MFH, which in today’s terminology would be best called, undifferentiated pleomorphic sarcoma with giant cells.

CASE REPORT

A 6-year-old African American boy presented with a 2-month history of a slowly enlarging but asymptomatic right-sided neck mass. Prior to being referred, he was treated with multiple courses of antibiotics without resolution. Physical examination revealed a 4-cm mass involving the
angle of the right mandible and level 2 of the neck. Otoscopic examination demonstrated extension of the tumor into the anterior and inferior aspects of the bony external auditory canal (EAC). Cranial nerve examination revealed no focal deficits. CT and MRI demonstrated a large (3 × 3 × 3.5 cm) soft tissue mass involving the superficial and deep lobes of the parotid gland with multiple hypodense regions and focal punctate calcifications (Figures 1 and 2). There was invasion of the temporal bone with destruction of the mastoid cortex, erosion into the EAC, and bilateral cervical lymphadenopathy (level 2A and retropharyngeal lymph nodes). The mass extended along the ramus of the mandible without bony or temporomandibular joint involvement.

Fine-needle aspiration of the mass revealed cellular evidence of a spindle cell neoplasm with features suggestive of sarcoma. Transcral biopsy of the EAC extension was inconclusive. Subsequently, an incisional biopsy of the neck mass was performed. Histopathology demonstrated enlarged cells with round to oval vesicular nuclei, most of which contained a small nucleolus (Figure 3). The cytoplasms were slightly eosinophilic, and the cell borders were not clearly defined. Very few mitotic figures could be identified, and there was no necrosis. The lack of necrosis is atypical of this tumor, but the biopsy was taken at the periphery, rather than at the center where more necrosis is expected. Among these cells were scattered osteoclast-like multinucleated giant cells (Figure 4). The tumor cells stained positively for CD34, CD68, INI-1, vimentin, and epithelial membrane antigen (EMA), but did not stain for CD31, CD1a, or S-100. Review of the slides by the Children’s Oncology Group (COG) Soft Tissue Sarcoma Biopathology Center suggested a diagnosis of a high-grade sarcoma with biphenotypic features. Epithelioid sarcoma, rhabdoid tumor, and synovial sarcoma were initially considered as possibilities. These diagnoses were excluded because the tumor did not show the morphology of either an epithelioid sarcoma or synovial sarcoma. Furthermore, a rhabdoid tumor was excluded by a positive stain for INI-1. The patient was also sent to the Mayo Clinic in Rochester, Minnesota, who offered a diagnosis of MFH of the soft tissue.

Additional workup revealed multiple rightsided pulmonary nodules (up to 5 mm in greatest dimension) that were suspicious for metastatic disease. Given this significant finding, and the morbidity associated with complete extirpation of a parotid tumor, the patient was treated with a combination of chemotherapy and radiation therapy. After neoadjuvant chemotherapy, which consisted of doxorubicin and ifosfamide, there was complete resolution of the pulmonary nodules, but minimal response at the primary site. Concurrent chemotherapy (vincristine and ifosfamide) and radiation
therapy (5940 cGy) was then administered with a complete clinical response at the primary site. He finished treatment with a chemotherapy regimen of vincristine, actinomycin D, and cyclophosphamide. Sixteen months after diagnosis, the patient was well. CT demonstrated residual changes at the primary site, no cervical lymphadenopathy, and no lung nodules. Total body technetium-99 scintigraphy showed no evidence of metastasis.

**DISCUSSION**

Until recently, MFH was considered the most common soft tissue sarcoma in adults, accounting for up to 40% of soft tissue tumors. It is an aggressive sarcoma that is infrequently described in the pediatric population. Although no etiological factors have been recognized, MFH has been reported secondarily following radiation therapy and traumatic burn injuries. Others have suggested an association with Paget’s disease and fibrous dysplasia. MFH most commonly occurs in the extremities, trunk, and retroperitoneum, but primary lesions of the viscera, trachea, and genitals have also been reported. Head and neck involvement has been described in up to 10% of cases with the majority occurring in the sinonasal tract. A review of the English-language literature revealed 21 cases of parotid gland MFH; only one of these involved a pediatric patient. Thus, our patient represents a rare pediatric case of MFH, and only the second reported pediatric case to involve the parotid gland.

Recently, the existence of MFH as a distinct clinical and pathological entity has been called into question, partly because the histopathological diagnosis of MFH is difficult and requires examining multiple microscopic sections of the tumor. Using ancillary techniques, including electron microscopy, immunohistochemistry, and molecular genetics, some authors have proposed that MFH may simply represent a morphological pattern that is often present in a variety of poorly differentiated sarcomas. Further complicating the issue, the immunohistochemistry profile of MFH varies. Most tumors are positive for vimentin, actin, CD-68, α1-antitrypsin, and α1-antichymotrypsin. They are variably positive for smooth muscle actin, desmin, keratin, EMA, S-100, and neurofilament.

In the most recent World Health Organization classification, MFH is considered a diagnosis of exclusion and is under consideration to be renamed as, undifferentiated high-grade pleomorphic sarcoma. In this case, the most appropriate name for the tumor would be undifferentiated pleomorphic sarcoma with giant cells. Although the consultants, the Mayo Clinic and COG Soft Tissue Sarcoma Biopathology Center, diagnosed the tumor as MFH and high-grade sarcoma with biphenotypic features, respectively, these are the different terms for the same entity. MFH is a high-grade sarcoma, and it is composed of malignant cells with round and spindle appearance (biphenotypic). The current lesion has osteoclast-like giant cells, which is seen in a variety of malignancies, including MFH.
A tumor should only receive the diagnosis of undifferentiated high-grade pleomorphic sarcoma or MFH after it has been adequately sampled, and ancillary techniques, such as immunohistochemistry, fail to reveal a line of differentiation. Using this new approach, it is believed that MFH or undifferentiated high-grade pleomorphic sarcoma represents no more than 5% of adult soft tissue sarcomas. In addition, pathological review of tumors previously diagnosed as MFH have shown that only 13% to 16% of cases can be potentially classified as MFH.

Currently, the treatment of choice for the primary site is surgical resection with cervical lymphadenectomy for advanced tumors and in cases with obvious lymph node involvement. Postoperative radiation therapy is reported to improve local control, and in view of the high rate of local recurrence, it is recommended. The incidence of metastasis is reported to be as high as 44%, and metastasis most commonly involves the lung, regional lymph nodes, liver, and bone. The use of chemotherapy and/or radiation therapy as a primary treatment modality has been less successful. Chemoresistance is not uncommon, and these treatments are still under investigation. Overall survival rates for MFH range from 30% to 74%. Male sex, advanced age, tumors arising from bone, and increased depth of invasion are poor prognostic indicators.

In conclusion, there is significant controversy regarding the existence and classification of MFH. Undifferentiated high-grade pleomorphic sarcoma is a better term for this entity. Nevertheless, our case represents only the second report of pediatric MFH or undifferentiated high-grade pleomorphic sarcoma involving the parotid gland. Aggressive surgical resection is the treatment of choice. Our patient, who had pulmonary metastasis at presentation, received a combination of neo-adjuvant and adjuvant chemotherapy with concurrent chemotheraphy and radiation therapy. Although still early in the course of the disease, he has had a good initial response.

REFERENCES