Alveolar Rhabdomyosarcoma of the Paranasal Sinuses

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History

A 14-year-old female with right cheek pain and sinus congestion presented to her family physician and was initially treated for “sinusitis.” Subsequently, proptosis developed and radiographic studies were performed.

Radiographic Features

Nuclear magnetic resonance (MR) images of the head show an expansile, infiltrating mass that is destroying the nasal and paranasal bones and is extending into the orbit and the parameningeal tissues (Fig. 1).

Diagnosis

Histological examination of hematoxylin and eosin stained slides demonstrated clusters of small round cells separated by fibrovascular septa. Focal larger cells, with eccentric nuclei and eosinophilic cytoplasm, were seen. Myxoid stroma and spindled cells were not appreciated. Immunohistochemical stains for desmin, myo-D1, myogenin, and smooth muscle actin were diffusely reactive. Focally, CD56 and keratin were noted in a dot-like pattern.

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Discussion

Rhabdomyosarcoma is a malignant neoplasm derived from mesenchymal tissues that demonstrates partial skeletal muscle differentiation. It is the most common soft tissue sarcoma of the pediatric population, accounting for up to 90% of these tumors [1] and up to 8% of all malignancies in children before adolescence [2]. Of the two histologic subtypes that occur in children, embryonal and alveolar, alveolar rhabdomyosarcomas are more common in adolescents than young children. No gender or racial predilection is reported [3]. Forty percent of rhabdomyosarcomas occur in the head and neck and usually represent the embryonal subtype, while alveolar rhabdomyosarcomas occur more frequently in the extremities. Regardless of the histologic type, lesions commonly present as rapidly growing masses whose symptoms are directly related to their anatomical location. Lesions in the paranasal sinuses frequently present with sinusitis symptoms, cranial nerve deficits, and proptosis, in contrast to lesions of the extremities that may be relatively asymptomatic.

Computed tomographic, CT, images of alveolar rhabdomyosarcoma that involve the paranasal sinuses usually show poorly defined, homogenous, soft-tissue masses that invade and destroy the adjacent bone. Hemorrhage and necrosis are generally not appreciated. Nuclear magnetic resonance imaging, MR, is generally regarded as the best modality for imaging of head and neck rhabdomyosarcomas. Lesions usually demonstrate an infiltrative, expansile, soft tissue mass with readily appreciated bony destruction [4].

Histologically, alveolar rhabdomyosarcoma has three major sub-types: those with typical features, those with a solid pattern, and those with a mixed alveolar and embryonal appearance [3]. The case presented is an example of typical alveolar rhabdomyosarcoma, possessing

Fig. 1 Nuclear magnetic resonance (MR) shows an infiltrating mass destroying the nasal and paranasal bones

Fig. 2 Tumor cells arranged in ill defined nests separated by fibrous bands

nests of tumor cells separated by fibrovascular septa (Fig. 2). The cells in these nests are more cohesive in the center and less cohesive towards the periphery. No spindled cells or solid areas are seen, ruling out solid and mixed variants. The characteristic cells of these lesions are the rhabdomyoblasts, a few of which, among the much more numerous small round cells, may be the only clue to the

Fig. 3 Left: The neoplastic cells are intermediate size with eccentrically placed brightly eosinophilic cytoplasm. Right: Myo-D1 (upper) and desmin (lower) help to confirm the myoid phenotype of the tumor cells

diagnosis of rhabdomyosarcoma. Morphologically, these cells range from small round cells to larger polygonal cells with peripherally located, small nuclei and eosinophilic cytoplasm (Figs. 2 and 3). Cross striations may be evident in the cytoplasm and are a strong clue to the diagnosis; immunohistochemical stains can highlight these cells. Alveolar rhabdomyosarcomas show strong nuclear reactivity with myogenin and myoD1. Less differentiated cells, more commonly seen in the mixed variant, may only stain with less specific muscle markers such as desmin and muscle-specific actin (Fig. 3) [3].

Alveolar rhabdomyosarcoma is associated with two specific, recurrent translocations: $t(2;13)(q35-37;q14)$ or $t(1;13)(p36;q14)$. These particular genetic alterations are present in over 70% of cases, with $t(2;13)$ being much more common than $t(1;13)$ [5]. The translocations result in chimeric genes which express PAX3/FKHR and PAX7/FKHR, respectively. PAX3 and PAX7 are DNA binding domains while FKHR is a potent transcription activator. The fusion of these two genes results in a gain of function in which genes with PAX3 or PAX7 binding sites are activated. Although these two translocations result in a similar genetic outcome, tumors with the $t(1;13)$ translocation have behaved less aggressively than those with the $t(2;13)$ translocation [1].

The treatment of alveolar rhabdomyosarcoma is a combination of surgery, radiation, and chemotherapy. Pediatric patients are staged according to the Intergroup Rhabdomyosarcoma Study (IRS) grouping system (Groups I–IV), which is based upon the presence or absence of lymph node metastasis, and the presence or absence of gross or microscopic residual tumor [6]. Prognosis is mainly based on the Group at the time of diagnosis and

histologic sub-type. Alveolar tumors are usually more aggressive than embryonal tumors, and mixed tumors generally behave as alveolar [3]. Overall survival is very good; one study found that 12% of patients with Group III or IV disease at diagnosis had adverse events more than fifteen years after adequate treatment, as opposed to 2% of patients with Group I or II disease. An ‘adverse event’ was defined as recurrent disease, a second malignant neoplasm, or death from some other cause, to include late complications of the initial therapy [7].

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