
Malignant Hemangioendothelioma (Angiosarcoma) of the Skull: Plain Film, CT, and MR Appearance

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Summary: Hemangioendothelioma is a rare neoplasm of bone that uncommonly involves the skull. We present a case of grade III malignant hemangioendothelioma (also known as angiosarcoma) of the skull in a 13-year-old boy and describe the plain film, CT, and MR appearance of this neoplasm as well as its histopathology.

Index terms: Angiosarcoma; Skull, neoplasms

Primary neoplasms of the skull are rare, representing 2.6% of primary neoplasms of bone (1). Primary malignant neoplasms of the skull are even less common, accounting for only 0.8% of primary malignant neoplasms of bone (2). Hemangioendothelioma is a rare malignant neoplasm of bone that uncommonly involves the skull (3). We present a case of this rare neoplasm and describe the plain film, computed tomographic (CT), and magnetic resonance (MR) imaging findings as well as the histopathologic findings.

Case Report

A 13-year-old boy had a lump at the vertex of his skull 2 weeks after falling and hitting his head. His mother reported increasing irritability and lethargy, as well as clumsiness and falling. Plain radiographs of the skull revealed multiple, relatively well defined lytic lesions (Fig 1A). Subsequent to the hospital visit, the patient noticed several additional firm nodules, which eventually coalesced into one. CT examination showed multiple lytic lesions destroying the calvaria, with some expanding the diploic space (Fig 1B). One lesion in the left parietooccipital region was associated with a soft-tissue mass and extended intracranially. MR examination confirmed the multiple lesions in the diploic space, with some extending through the outer table and some through the inner table intracranially, compressing but not invading the underlying brain parenchyma. The lesions were isointense with gray matter on T1-weighted (608/14/2 [repetition time/

echo time/excitations]) (Fig 1C) and proton density-weighted (2500/15/1) images. On T2-weighted images (2500/90/1), the lesions were of high signal and appeared lobulated, with septa (Fig 1D). Intense and uniform enhancement of the lesions was seen after intravenous administration of contrast material (Fig 1E).

Biopsy of one of the lesions revealed variably sized, often anastomotic vascular channels lined by plump, moderately pleomorphic cells with enlarged, vesicular nuclei and abundant eosinophilic cytoplasm (Fig 1F). The lesions were subsequently surgically excised, and histopathologic findings were the same as those seen at the initial biopsy, along with solid foci of epithelioid tumor cells showing frequent mitoses. Immunostaining with antibodies to factor VIII-related antigen was positive within the tumor cells in both the vascular and solid portions of the lesions. In addition, a regional lymph node was infiltrated by similar neoplastic cells. The diagnosis of malignant hemangioendothelioma was made and confirmed by external review by the National Institutes of Health Clinical Center. Following surgery, the patient underwent three cycles of chemotherapy. The patient's family refused further treatment. At one and a half years after initial presentation, the patient was doing well, despite incomplete treatment. Skull radiographs have shown no evidence of lytic lesions.

Discussion

Hemangioendotheliomas are rare, malignant bone tumors of vascular origin. In one series of 1481 primary malignant bone tumors, only seven (0.5%) were hemangioendotheliomas (4). There is a 2:1 male predominance (5), with a median age at presentation of 32 years; 50% involve the long tubular bones (6), usually of the lower extremities (5). Of nine reported cases involving the skull, all involved males with an average age of 24 years (3). The usual presenting symptom of lesions not involving the

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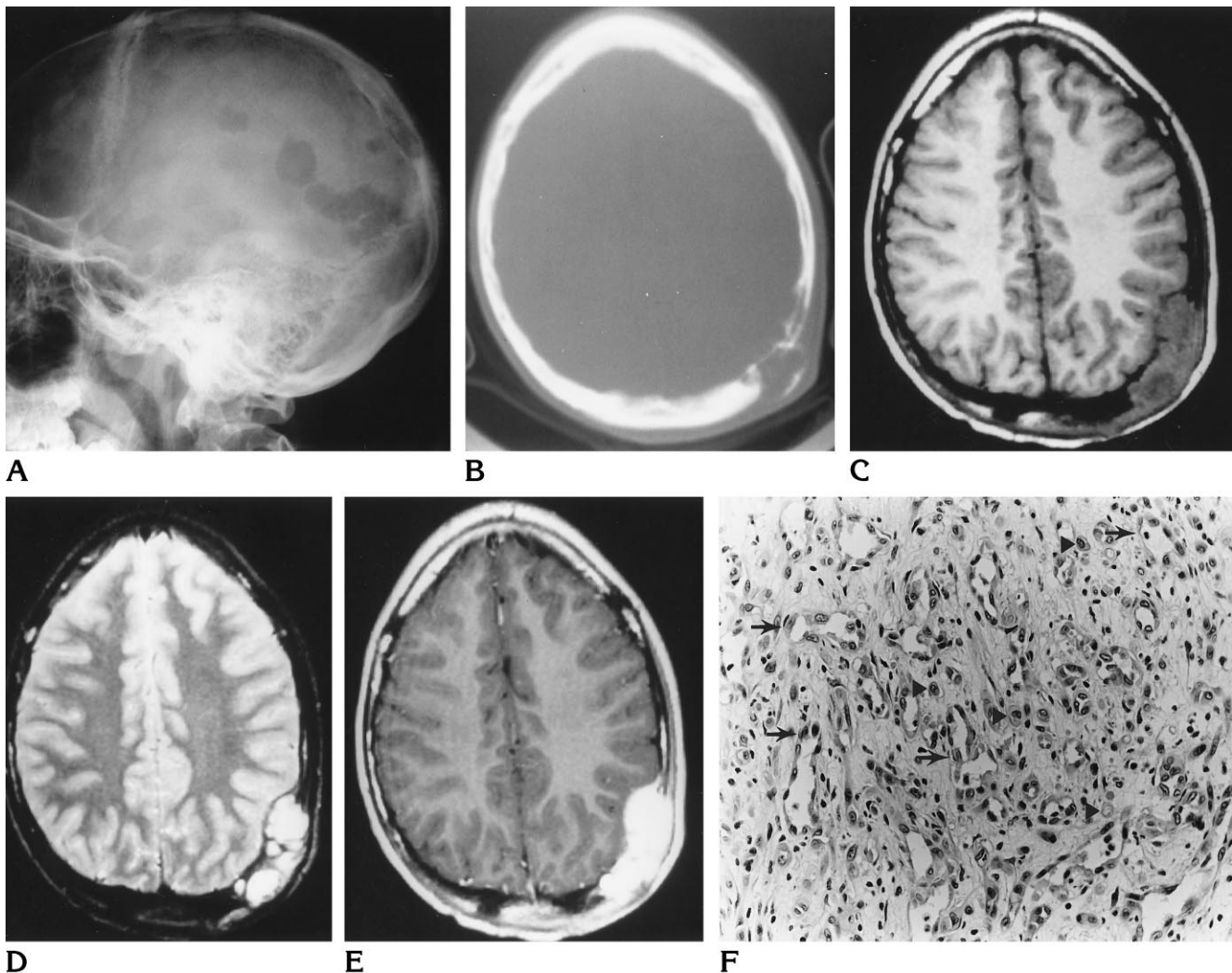


Fig 1. Thirteen-year-old boy with hemangioendothelioma of the skull.

A, Lateral skull radiograph shows multiple, relatively well circumscribed lytic lesions.

B, CT scan of the head obtained with bone windows shows a lytic lesion with apparent expansion of the diploic space, indicating that the tumor arises in the diploic space rather than within cortical bone.

C-E, MR images of the head show multiple lesions of the diploic space, with involvement of the inner and outer tables of the skull. Some of the lesions extend intracranially and appear to compress the underlying brain, but without intraparenchymal extension. The lesions are isointense with gray matter on the T1-weighted image (608/14/2) (C) and of high signal on the T2-weighted image (2500/90/1) (D), with a lobulated and septated appearance. After administration of contrast material, intense and relatively uniform enhancement is seen (E).

F, Photomicrograph shows variably sized anastomosing vascular channels lined by pleomorphic endothelial cells (arrows). Individual tumor cells can be seen within the intervening stroma (arrowheads) (hematoxylin-eosin, original magnification $\times 350$).

skull is pain (5, 6), whereas in the skull it is that of a local mass or swelling (3).

The lesions are characterized by a rich network of anastomosing vessels lined by atypical endothelial cells. Immunohistochemistry is helpful in confirming the diagnosis by identifying factor VIII-related antigen, which is a marker for vascular endothelial cells. Three histologic grades can be identified, in part on the basis of

the degree of tumor cell differentiation (5). Tumor differentiation is more pronounced and diffuse in grade I lesions and decreases with increasing malignancy. Grade I lesions have a uniformly good prognosis. They may remain stable over many years even without treatment. Treatment usually involves curettage or radiation alone. Grade II hemangioendotheliomas often have a good prognosis and are usually

treated by resection and radiation (5). Multicentricity, which is common, usually indicates grade I or II lesions. However, there are frequently concurrent areas of both grade II and III within the same lesion, which accounts for the variable malignant potential and unpredictable clinical behavior of grade II lesions. Some researchers have questioned whether low-grade lesions may, in fact, progress to high-grade tumors, thus accounting for their variable malignant potential (5). Grade III lesions demonstrate undifferentiated pleomorphic cells with atypical mitotic figures (5). Epithelioid sarcomas are the main differential consideration pathologically. Although the malignant cells are epithelioid, they do not line vascular spaces and are not positive with factor VIII-related antigen immunostaining. Grade III lesions are usually solitary and carry a very poor prognosis. They are treated as osteosarcomas, with ablative surgery, adjuvant chemotherapy, and radiation (5).

Our case was thought to be grade III, and as such was treated as an osteosarcoma, with excision, chemotherapy, and radiation. It has been suggested that hemangioendotheliomas of the skull have a worse prognosis than those elsewhere because of secondary involvement of the brain (3). Metastases to bone and lung are common with grade III lesions (7). This would suggest that follow-up should include MR imaging of the region of surgery for evaluation of recurrence, as well as bone scans and chest radiography for evaluation of metastatic disease.

Controversy exists as to the appropriate name of this entity. Many different names have been used (3), but the two most accepted terms are *hemangioendothelioma* and *angiosarcoma*. *Hemangioendothelioma* is the preferred name because *angiosarcoma* implies a high-grade

malignancy (6) and, as noted above, not all these lesions are of high grade.

Plain radiographs reveal lytic lesions, usually multiple, with no surrounding sclerosis. In the skull, the frontal region is most commonly involved (3). CT scans show similar findings and may demonstrate expansion of bone because of involvement of the diploic space and enhancement (3). As expected, a nuclear bone scan will show areas of increased activity (8). MR images reveal multiple lesions of the diploic space, with extension through the inner and outer tables. The lesions are isointense with gray matter on T1-weighted and proton density-weighted images and of increased signal on T2-weighted images. On T2-weighted images, the lesions may have a lobulated and septated appearance, which may relate to the coalescence of multiple lesions. After administration of contrast material, intense and relatively uniform enhancement is seen.

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