Megakaryoblastic leukemia presenting as a temporal bone granulocytic sarcoma

Case report

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The unusual presentation of acute megakaryoblastic leukemia as a temporal bone granulocytic sarcoma in an infant without systemic manifestations of leukemia is reviewed. Leukemia should be considered in the differential diagnosis of skull and skull-based lesions since the appearance on neuroradiological imaging is not unique in this diagnosis. Surgical treatment, as in this case, is limited to obtaining tissue for diagnosis and draining the infection.

Key Words • granulocytic sarcoma • megakaryoblastic leukemia • temporal bone

Acute megakaryoblastic leukemia (AML) is a rare malignancy that is difficult to distinguish from other myeloid leukemias. It can present as a solid tumor (granulocytic sarcoma) and be mistaken for a metastatic tumor, such as lymphoma or neuroblastoma. Skull lesions associated with this diagnosis have been reported, but none has presented without other signs of leukemia. We report a case of aleukemic acute megakaryoblastic leukemia which presented in an infant with facial nerve paresis due to a large petrous mass. The magnetic resonance (MR) imaging characteristics and appropriate treatment of this tumor are reviewed.

Case Report

This 25-month-old boy was evaluated for right facial weakness of 10 days’ duration and 3 days of low-grade fever.

Examination. Physical examination was remarkable for a right peripheral facial nerve palsy and right posterior cervical lymphadenopathy. Organomegaly and abdominal masses were absent. Peripheral blood counts were normal (hemoglobin 11.2 gm/dl; white blood cells 16,600/cu cm, with 23% segmented neutrophils, 2% band neutrophils, 1% metamyelocytes, 63% lymphocytes, 9% monocytes, and 2% eosinophils; and platelets 337,000/cu cm). The erythrocyte sedimentation rate was slightly elevated at 42 mm/hr. Serum chemical studies, renal and hepatic function testing, and urinary catecholamine levels (homovanillic and vanillylmandelic acids) were normal. A chest radiogram was normal.

Computerized tomography (CT) of the head without contrast enhancement revealed a hyperdense mass based on the skull and lateral right petrous pyramid, involving the middle and posterior fossae. There was slight enhancement with intravenous injection of con-

FIG. 1. Left: Computerized tomography (CT) scan after intravenous administration of contrast material. The tumor extends from the middle to the posterior fossa, with minimal contrast enhancement. A hyperdense mass on the uncontrasted study is not shown. The mastoid air cells have been obliterated. Right: High-resolution CT scan via bone windows defining the extensive destruction of the lateral temporal bone, mastoid air cells, and erosion through both tables of the skull with subcutaneous extension. The denser bone of the inner-ear structures is preserved.
Megakaryoblastic leukemia presenting as a sarcoma

**Fig. 2.** T1-weighted magnetic resonance (MR) images (TR 800 msec, TE 22 msec, 5 mm thick). **Left:** Uncontrasted MR image, axial projection. The tumor gives a homogeneous signal and is slightly hypointense. The dural margin (black arrows) and erosion through the skull (open arrow) are easily appreciated. (The spotty increased signal in both temporal lobes is artifact.) **Center:** Gadolinium-enhanced MR image, coronal view. The tumor is diffusely enhanced, with its superior and inferior extent seen clearly. The extra-axial location and extension through the skull (arrow) is again easily appreciated. Cervical lymphadenopathy is also identified (asterisk). **Right:** Gadolinium-enhanced MR image, coronal view, after irradiation and chemotherapy. The tumor has involuted significantly, with only a small amount of tissue signal visible within the mastoid region (arrow).

Contrast material (Fig. 1 left). High-resolution temporal bone CT showed destruction and opacification of the mastoid air cells by the tumor (Fig. 1 right). More posteriorly, there was erosion of both tables of the skull, without significant expansion. The denser medial temporal bone and inner ear structures were preserved.

Magnetic resonance imaging defined the mass more accurately as extra-axial, with significant extension above and below the tentorium and displacement of the fourth ventricle (Fig. 2 left and center). The tumor was slightly hypointense on T1-weighted images, and isointense on T2-weighted images with some heterogeneity. The invaginated and uninvolved dura was best seen on T2-weighted images. Gadolinium administration diffusely enhanced the intracranial lesion as well as the enlarged cervical lymph nodes on MR images.

**Operation.** The patient underwent biopsy of the cranial mass where it penetrated the outer table of the skull and excisional biopsy of an enlarged posterior cervical lymph node. Concurrent evaluation of the external auditory canal revealed only a nonpurulent middle-ear effusion. Pathological examination of the cranial biopsy specimen revealed a diffuse and monotonous proliferation of small to intermediate-sized cells, with a small rim of basophilic cytoplasm, finely granular chromatin, and one to three nucleoli. The lymph-node architecture exhibited identical infiltration (Fig. 3

**Fig. 3.** **Left:** Photomicrograph of a section through the lymph node, showing metastatic tumor (asterisk) nearly obliterating the lymph tissue. H & E, × 150. **Right:** Photomicrograph of the bone marrow aspirate demonstrating atypical blasts with large nuclei and cytoplasmic projections. H & E, × 750.
The morphology was that of a small, round blue-cell neoplasm, most likely a neuroblastoma. Immunohistochemical studies for neurofilaments, synaptophysin, S-100 protein, glial fibrillary acidic protein, actin, desmin, and vimentin were initially all negative.

Postoperative Course. Lumbar puncture and bone marrow aspiration and biopsy were performed for tumor staging purposes. The cerebrospinal fluid (CSF) was acellular, with normal glucose (54 mg/dl) and protein (10 mg/dl) levels. The bone marrow obtained at biopsy was hypercellular, with partial replacement by intermediate-sized cells with round-to-oval nuclei and basophilic cytoplasm with occasional vacuoles. Small immature and abnormal megakaryocytes as well as mature megakaryocytes were abundant. Reticulin stains documented the absence of fibrosis. The aspirate demonstrated many atypical blasts with large nuclei and cytoplasmic projections (Fig. 3 right). Additional immunohistochemical studies on the bone marrow biopsy specimen demonstrated that malignant cells expressed the MB2 and M1 T antigens but failed to express leukocyte common antigen, UCHL1 (a T-cell marker) or L26 (the CD20 epitope on B cells). Repeat bone marrow aspiration for flow cytometry demonstrated reactivity for the platelet-specific glycoproteins IIb and IIIa, diagnostic of AML. Review of the peripheral blood smears failed to demonstrate peripheral blasts.

The child was entered into a pilot protocol for the treatment of acute myeloblastic leukemia (Pediatric Oncology Group protocol 9194), employing high-dose cytosine arabinoside, daunomycin, 6-thioguanine, etoposide, and intrathecal cytosine arabinoside. He also received radiation therapy (600 cGy in three daily fractions) directed to the areas of peripheral tumor. Follow-up bone marrow aspiration on Day 22 of therapy showed no excess blast cells and relative hypocellularity. Magnetic resonance images without and with gadolinium enhancement, obtained 6 weeks after initiation of therapy, showed significant resolution of the cranial tumor, with minimal tissue identified in the mastoid air cells (Fig. 2 right). The patient developed alpha hemolytic streptococcal meningitis during chemotherapy, and was effectively treated with a 6-week course of intravenous antibiotics. Participation in the Pediatric Oncology Group protocol was concluded 4 months after diagnosis, but a bone marrow relapse was discovered 3 months later. He then received an autologous bone marrow transplant (in-house protocol). Currently, 12 months after presentation, he is neurologically intact and without evidence of disease.

Discussion

Bennett, et al., categorized acute megakaryoblastic leukemia as an acute non-lymphoblastic leukemia in 1985, and added it to the French-American-British classification as stage M7. The incidence of AML has been estimated to be between 3% and 12% of myeloid leukemias, with a relatively increased frequency reported more recently because of improved cytochemical and immunohistochemical techniques. Although various karyotypic abnormalities (such as Down’s syndrome) have been associated with the diagnosis, there are no consistent chromosomal abnormalities.

The typical adult patient suffering from AML presents with anemia and/or leukopenia, normal platelet counts, and few if any peripheral blood blasts. Lymphadenopathy and organomegaly are usually absent. Bone marrow analysis shows hypoplastic granulopoiesis and dysplastic megakaryocytes. Children with AML have a different clinical presentation and course. A review of 20 such children, ranging in age from 5 months to 14 years, revealed that 50% were under 2 years of age. Low to normal peripheral white blood cell counts were found in 12 of 19 patients. Organomegaly was usually prominent in the children. In patients undergoing bone marrow biopsy, reticulin fibrosis was a consistent finding. Clumping of blast cells in the marrow, simulating metastatic disease, is rare.

Although adults respond uniformly poorly to therapy, children have variable responses to treatment, with better outcomes in younger children.

The presentation of extramedullary collections of immature granulocytic series cells was first reported involving the orbit by Burns1 in 1811. The common name “chloroma” was used by King in 1853, based on the greenish color of the gross tumor, which is secondary to the enzyme myeloperoxidase present in the tumor. Since these tumors are composed of immature granulocytes, resemble sarcomas, and are not always green, Rappaport18 proposed the now preferred term “granulocytic sarcoma.” They may represent extramedullary foci of malignant granulopoiesis.

Granulocytic sarcomas are reported in 3% to 9% of patients with acute or chronic myelogenous leukemia, and 60% of patients with granulocytic sarcomas are less than 15 years of age. Although the diagnosis of acute myelogenous leukemia and granulocytic sarcoma is frequently concurrent (in 5% to 13% of cases), the extramedullary tumor may precede the systemic disease by up to 2 years. Up to 35% of adult patients present with a granulocytic sarcoma and no diagnosis of a myeloproliferative disorder.

The most common sites of involvement by granulocytic sarcomas are the lymph nodes, skin, vertebral column, sternum, and cranium (including the orbit). In children, orbital involvement with unilateral exophthalmos is the most common presentation. Granulocytic sarcomas of bone occur in the subperiosteal region and multiple lesions are frequent.

In their thorough review, Sowers, et al., describe cranial granulocytic sarcomas as diffusely hyperdense on unenhanced CT scans, usually based in the dura, and able to extend through the calvaria. These tumors exhibit homogeneous enhancement on administration of contrast material. In the adult their appearance is very suggestive of a meningioma, while in the child the differential diagnosis would include rhabdomyosarcoma, neuroblastoma, primitive neuroectodermal tumor, and Ewing’s sarcoma.

When granulocytic sarcomas involve the temporal bone, the clinical symptoms will generally correlate with the degree of bone involvement. There have been several reports of granulocytic sarcomas involving the...
Megakaryoblastic leukemia presenting as a sarcoma

temporal bone, but all of the patients had concurrent clinically apparent leukemia. Levy, et al., reported a 3-year-old child who presented with facial nerve paresis and decreased hearing; however, the CT scan was normal. Their patient subsequently developed additional cranial nerve deficits as the tumor enlarged into the cerebellopontine angle.

Because granulocytic sarcomas are very sensitive to radiation therapy, the role of surgery is limited to obtaining a tissue diagnosis and drainage of infection. In cases with facial nerve palsy, operative decompression is not necessary, as the tumor regresses with standard irradiation and chemotherapy.

Our patient represents the first case of granulocytic sarcoma reported with extensive MR imaging evaluation before and after therapy. A broad differential diagnosis must be maintained due to the lack of unique signal characteristics. Our findings parallel those reported by Sowers, et al., and reconfirm the utility of MR imaging in defining the extent of neoplasms. The physician’s ability to accurately define the degree of temporal bone involvement and assess for loculations suggesting infection directly affects treatment decisions.

There have only been two previous reports of AML presenting as granulocytic sarcoma involving the skull. Both were in children less than 18 months of age who had extensive or multiple cranial tumors, as well as other manifestations of leukemia (peripheral or CSF blasts). Our patient had the unusual presentation of AML with a large temporal bone granulocytic sarcoma and no peripheral abnormalities.

Conclusions

Solid tumor manifestations of leukemia should be included in the differential diagnosis of skull masses in infants and children. Since up to 35% of patients with granulocytic sarcoma may present without a prior diagnosis of leukemia, this diagnosis must also be considered in adult skull lesions initially diagnosed as lymphoma. The surgical treatment of temporal bone granulocytic sarcoma can be limited to establishing a tissue diagnosis and the effective drainage of infection, with subsequent medical and radiation therapy of this systemic disease.

References


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