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Myeloid Sarcoma of Both Kidneys, the Brain, and Multiple Bones in a Nonleukemic Child

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A myeloid sarcoma (MS) is an extramedullary tumor consisting of primitive granulocytic precursor cells. Although most such tumors have been reported in patients with acute myelogenous leukemia, MS is rarely recognized as an isolated tumor without any evidence of leukemia. However, in such cases, the initial diagnosis of MS can be difficult, so initial misdiagnosis rates of up to 75% have been reported. This report describes an unusual case of MS in a 3-year 5-month-old girl presenting as bilateral renal enlargements, and brain masses, with multiple bone involvements, but no hematological abnormalities.

Key Words: Myeloid sarcoma, leukemia, kidney, brain, bone, child

INTRODUCTION

A myeloid sarcoma (MS) is an extramedullary localized tumor mass composed of immature granulocytic precursor cells. It was first described by Burns in 1811.[1] This type of tumor was originally called a chloroma, by King, in 1853, who coined the term based on the green color of the tumorous mass.[2] This green color is secondary to myeloperoxidase, an enzyme found in the majority of extramedullary myeloid tumors. The granulocytic sarcoma, which was introduced by Rappaport in 1966, has been a preferred term for this tumor.[3] Recently, the World Health Organization (WHO) published the new classification of myeloid neoplasms.[4] According to the new WHO classification, the term granulocytic sarcoma has been replaced by MS.

Its association with leukemia was established by Dock in 1893.[5] Most MS cases develop during the course of leukemia or myeloproliferative disorders.[6] On rare occasions, MS occurs in a patient without the blood or bone marrow manifestations of acute leukemia.[6-12] The majority of nonleukemic patients with MS develop acute leukemia within 1 to 2 years, if the condition remains untreated.[6,12] The leukemic masses of MS are frequently found in bones, peritoneum, lymph nodes, skin, and epidural structures.[6] They are often multiple, and may involve any part of the body, either concurrently or sequentially.[13]

Nevertheless, the involvement of the kidneys has only been reported in a few autopsy studies and adult cases.[14-16] The present case represents a highly unusual presentation of the MS, showing simultaneous involvement of both kidneys, the brain, and multiple bones, in a nonleukemic child.

CASE REPORT

A 3-year 5-month-old girl was admitted to the emergency room due to abdominal distension and left leg pain. On physical examination at that time, the right cheek was swollen and the right ear canal was almost totally occluded by a mass. Huge abdominal masses were noted on both flanks extending around the umbilical level. The masses were firm and nontender. The middle of

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her left leg was also swollen.

Laboratory findings revealed a WBC count of 8,700/mm^3, with a normal differential (59% segmented neutrophils, 29% lymphocytes, and 11% monocytes), hemoglobin of 12.7 g/dl, and a platelet count of 640,000/mm^3. Serum chemical studies, liver function test, urinalysis, and chest radiogram were normal, with the exception of the lactate dehydrogenase of 753 U/L.

A computed tomography (CT) of the abdomen showed that both kidneys were markedly enlarged (Rt.: 8.5×10×7 cm, Lt.: 9×8×7 cm) (Fig. 1). The renal pelvis was symmetrically enhanced without hydronephrosis. A CT of the paranasal sinus and brain revealed complete occlusion of the entire right external auditory canal and a well marginated, homogenous enhancing mass (3×3.5×5 cm) based on the right temporal bone, involving the right sphenoid bone and middle cranial fossa (Fig. 2).

Microscopically, the kidney biopsy showed a dense interstitial infiltration of immature granulocytic cells (Fig. 3). They were positive for antilysozyme immunoperoxidase stains and negative for CAE (chloroacetate esterase). The immunohistochemical studies on the kidney frozen biopsy section demonstrated that the malignant cells expressed the LCA and CD33 antigens, but not those of the Tdt and CD20. A bone scan exhibited areas of increased uptake over both the proximal tibia and ulnar. The bone marrow aspiration and biopsy study were normal, with no leukemic cells, and the karyotype analysis of the bone marrow showed 46,XX. Examination of the cerebral spinal fluid demonstrate no leukemic cells, and normal glucose and protein levels.

She was started on AML induction chemo-

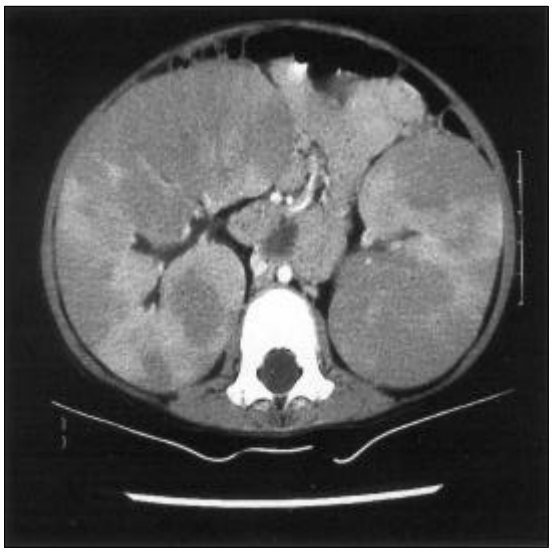

Fig. 1. The abdomen CT reveals diffuse enlargement of both kidneys, but without architectural distortion. The renal pelvis is symmetrically enhanced without hydronephrosis.

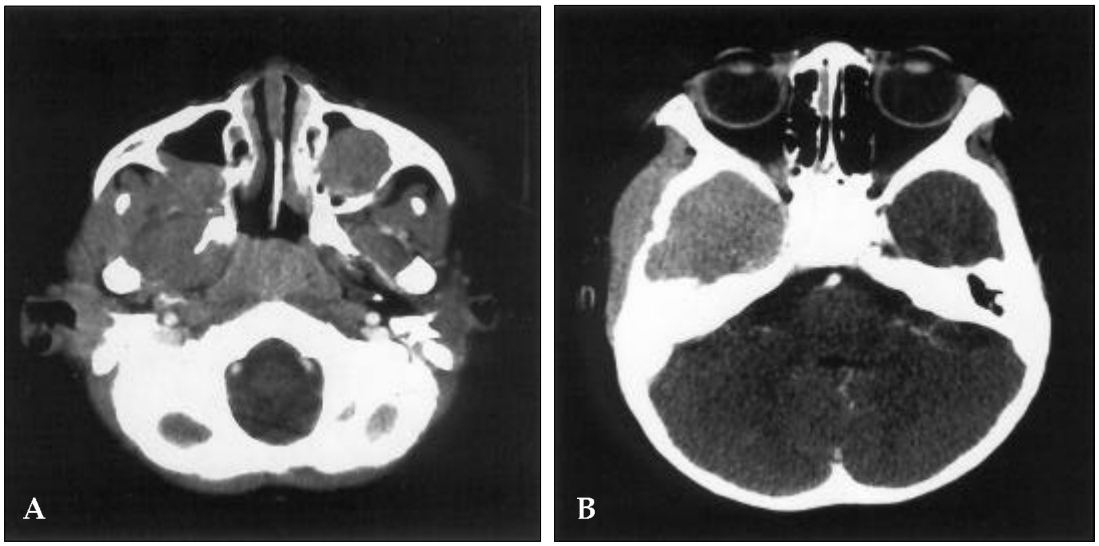

Fig. 2. PNS (A) and brain CT (B) show a well marginated homogenous enhancing lesion in the right middle cranial fossa and infratemporal fossa, with mild destruction of the adjacent bony cortex. The lesion elicits no mass effect on the brain parenchyme.

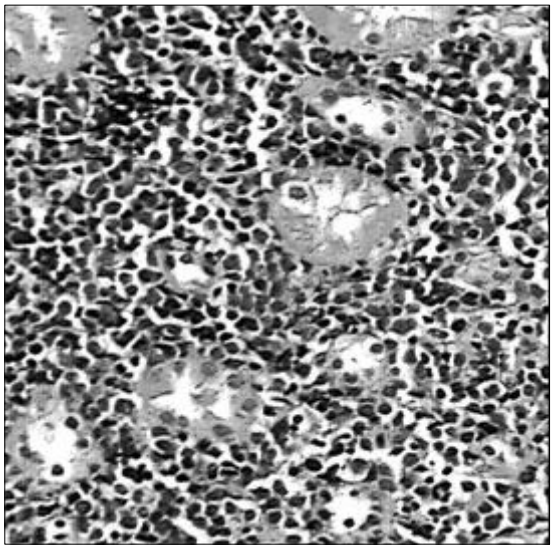

Fig. 3. The infiltrating cells were ovoid or polygonal in shape. The nuclei were hyperchromatic, with occasional prominent nucleoli. The cytoplasm was generally scanty (Hematoxylin-Eosin stain, × 400).

therapy, consisting of N4-behenoyl-1-beta-D-arabinofuranosylcytosine (BHAC), 300 mg/m^2/day, intravenously (IV), for seven days (Day 0-6), 6-thioguanine, 100 mg/m^2, orally, every 12 hours, for seven days (Day 0-6), idarubicin 12mg/m^2/day, IV, for 3 days (Day 0-2), and cytosine arabinoside, 70 mg, intrathecally (Day 0). The renal masses and multiple bone lesions, including the brain occupying mass, responded rapidly to the chemotherapy. The size of her kidneys was normalized, and the brain occupying masses and multiple bone lesions disappeared after three cycles of chemotherapy.

DISCUSSION

MS describes a rare extramedullary tumorous aggregate of malignant myeloid precursor cells. They are frequently misdiagnosed, especially when the diagnosis is not clinically suspected due to lack of evidence of leukemia elsewhere. The diagnosis is further complicated by the inconsistent morphologic features of MS. Up to 75% of isolated MS may initially be misdiagnosed, usually as a malignant lymphoma.[7] The most commonly confused tumors are high grade lymphomas and other small round cell tumors, including Ewing's sarcoma. The correct diagnosis is made when the lesion recurs or after leukemia develops.[6-8]

Traditionally, the presence of eosinophilic myelocytes, in hematoxylin and eosin stained paraffin embedded tumor biopsy sections, has been an important clue to the diagnosis of MS, even in the absence of a known diagnosis of leukemia, but it may not be present in 50-70% of cases.[6,7,17,18] So, when eosinophilic myelocytes are absent, some special stains must be used. The histochemical staining of biopsy imprints, with naphthol ASD-chloro-acetate esterase (CAE), or immunochemical staining, with antilysozyme, by the immunoperoxidase technique, are special stains for confirming the diagnosis of MS.[6,7] Both tests should be performed, as cases are frequently esterase-negative, but lysozyme-positive. However, with the diagnostic limitations of both of these special stains, immunohistochemical - phenotyping of paraffin sections, with a panel of monoclonal antibodies, have to be performed.[17,18] Traweek, et al. suggest that an immunohistochemical panel, including CD20, CD43, CD68, and MPO, can successfully identify the vast majority (96%) of MS cases in paraffin sections, and there is an association between the morphology and phenotype in these lesions.18

Additionally, the immunochemical - staining of frozen sections, or biopsy imprints, flow cytometric analysis of disaggregated cells from biopsy samples, with myeloid antigen specific monoclonal antibodies, and electron microscopy can be also helpful.[13,17-19] The present case was successfully diagnosed by CD 33 staining of the frozen tissue.

Given such a high rate of initial misdiagnosis of isolated MS, with no evidence of leukemia, it is not surprising to see a great variety of reported managements for MS.[8] Systemic, as well as site directed, therapy has also been advocated for patients who present with MS without a known bone marrow disorder. Several reports have shown that the best results were seen in those patients receiving acute myelogenous leukemia induction chemotherapy, and neither local radiotherapy nor surgery had an effect on survival.[8,19,20] A few patients with isolated MS also underwent allogeneic or autologous bone marrow transplan-

tation.[20] However, the efficacy of allogeneic or autologous bone marrow transplantation in the treatment of MS remains to be determined.[9,20]

To date, the administration of antileukemic chemotherapy, on diagnosis of MS, has been associated with a significantly lower probability of developing acute myelogenous leukemia and longer survival.[20] Therefore, with a high index of suspicion, MS should be included in the differential diagnosis of the intermediate-sized, or large cell hematopoietic tumors occurring at unusual sites outside of the lymphoid organs.[18]

REFERENCES

1. Burns A. Observations of surgical anatomy. In Head and Neck. Edinburgh, Scotland: Thomas Royce; 1811. p.364-6.
2. King A. Case of chloroma. Monthly J Med Soc 1853; 17:97.
3. Rappaport H. Tumors of the hematopoietic system. In Atlas of Tumor Pathology, Section 3, Fascicle 8. Washington DC: Armed Forces Institute of Pathology; 1966. p.241-3.
4. Vardiman JW, Harris NL, Brunning RD. The World Health Organization (WHO) classification of the myeloid neoplasms. Blood 2002;100:2292-302.
5. Dock G. Chloroma and its relation to leukemia. Am J Med Sci 1893;106:152-7.
6. Neiman RS, Barcos M, Berald C, Bonner H, Mann R, Rydell RE, et al. Granulocytic sarcoma: a clinicopathologic study of 61 biopsied cases. Cancer 1981;48:1426-37.
7. Meis JM, Butler JJ, Osborne BM, Manning JT. Granulocytic sarcoma in nonleukemia patients. Cancer 1986;58:2697-709.
8. Eshghabadi M, Shojania AM, Carr I. Isolated granulocytic sarcoma: report of a case and review of the literature. J Clin Oncol 1986;4:912-7.
9. Sisack MJ, Dunsmore K, Sidhu-Malik N. Granulocytic sarcoma in the absence of myeloid leukemia. J Am Acad Dermatol 1997;37:308-11.
10. Wright DH, Hise JH, Bauserman SC, Naul LG. Intracranial granulocytic sarcoma: CT, MR, and angiography. J Comput Assist Tomogr 1992;16:487-9.
11. Hurwitz BS, Sutherland JC, Walker MD. Central nervous system chloromas preceding acute leukemia by one year. Neurology 1970;20:771-5.
12. Kause JR. Granulocytic sarcoma preceding acute leukemia. A report of six cases. Cancer 1979;44:1017-21.
13. Pui MH, Fletcher BD, Langston JW. Granulocytic sarcoma in childhood leukemia: imaging features. Radiology 1994;190:698-702.
14. Lin PI, Ishimani T, McGregor DH, Hiromu O, Steer A. Autopsy study of granulocytic sarcoma (chloroma) in patients with myelogenous leukemia. Hiroshima-Nagasaki 1949-1969. Cancer 1973;31:948-55.
15. Bagg MD, Wettlaufer JN, Willadsen DS, Ho V, Lane D, Thrasher JB. Granulocytic sarcoma presenting as a diffuse renal mass before hematological manifestations of acute myelogenous leukemia. J Urol 1994;152:2092-3.
16. Chan YF. Granulocytic sarcoma (chloroma) of kidney and prostate. Br J Urol 1990;65:655-6.
17. Davey FR, Olson S, Kurec AS, Eastman-Abara R, Gottlieb AJ, Mason DY. The immunophenotyping of extramedullary myeloid cell tumors in paraffin-embedded tissue sections. Am J Surg Pathol 1988;12:699-707.
18. Traweek ST, Arber DA, Rappaport H, Brynes RK. Extramedullary myeloid cell tumors: an immunohistochemical and morphologic study of 28 cases. Am J Surg Pathol 1993;17:1011-9.
19. Baer MR. Management of unusual presentation of acute leukemia. Hematol Oncol Clin North Am 1993;7:275-92.
20. Imrie KR, Kovacs MJ, Selby D, Lipton J, Patterson BJ, Pantalony D, et al. Isolated chloroma: the effect of early antileukemic therapy. Ann Intern Med 1995;123:351-3.