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CASE REPORT

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Isolated meningeal chloroma (granulocytic sarcoma) in a child with acute lymphoblastic leukemia mimicking a falx meningioma

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Abstract *Background*: Isolated chloromas (granulocytic sarcomas) are rare tumors. Chloromas are masses composed of immature granulocytic cells. Granulocytic sarcoma occurs primarily in patients with acute myelogenous leukemia, but can also arise in patients with other myeloproliferative disorders, though rarely in patients with acute lymphoblastic leukemia (ALL). When dural-based, granulocytic sarcoma may be indistinguishable from meningioma radiologically. *Case history*: We now describe one patient affected by ALL with isolated granulocytic sarcoma mimicking meningioma as initial CNS relapses. A 12-year-old girl who had been diagnosed with ALL and undergone chemotherapy presented with generalized tonic-clonic seizure while in complete remission. Computed tomographic scan and magnetic resonance imaging showed a small mass mimicking a meningioma at the anterior falx. The patient was developed speech disturbance 6 days later. Follow-up magnetic resonance imaging demonstrated a rapidly growing mass with intralesional hemorrhage. Bone marrow biopsy and cerebrospinal fluid study were negative for leukemia. The patient underwent open surgery. The pathological diagnosis was acute lymphoblastic leukemia. *Conclusions*: These unusual clinical manifestations and radiological findings in acute lymphoblastic leukemia should be regarded as a recurrence of leukemia. Early detection and antileukemic treatment of granulocytic sarcoma are necessary and important for a favorable prognosis.

Keywords Acute lymphoblastic leukemia · Chloroma · Granulocytic sarcoma · Meningioma

Introduction

The leukemias are a heterogeneous group of hematological malignancies resulting from a neoplastic proliferation of hematopoietic cells in an undifferentiated or partially differentiated stage of maturation. In their disease course, approximately 25–50% of leukemic patients will suffer a CNS complication. Prior to the advent of CNS prophylaxis, CNS relapses occurred in as many as 75% of patients with ALL [4]. This rate has been dramatically reduced by CNS prophylaxis, but relapses still occur. CNS leukemia is believed to develop as a result of leukemic metastases resulting either from hematogenous spread or from direct extension from involved cranial bone marrow. CNS involvement may be either meningeal or parenchymal, although in the overwhelming majority of cases it is meningeal. Infiltration of the meninges by leukemic cells can affect the dura, the leptomeninges, or both [1] and can be diffuse or focal. In rare cases, leptomeningeal tumor may be focal rather than diffuse, and differentiation from parenchymal lesions may be difficult. Intracranial masses called chloromas or granulocytic sarcomas can occur in leukemia, albeit rarely. For this reason, we now describe one patient affected by ALL who had an isolated granulocytic sarcoma mimicking meningioma as an initial CNS relapse. Our aim is

to emphasize the diagnostic difficulties of CNS relapse of acute lymphoblastic leukemia and to add new findings determined by magnetic resonance imaging. These unusual radiological and pathological findings in ALL should be seen as a recurrence of ALL.

Case report

A 12-year-old girl was originally examined in April 1998 because of fever and back pain and was diagnosed with ALL with hyperdiploidy and collapse of vertebral bodies T-5 to L-3. Laboratory findings were abnormal: hemoglobin concentration, 3.9 g/dl; white blood cell count, 900 cells/mm^3; and platelet count, 21,000 cells/mm^3. The differential counts of white blood cells were as follows: segmented neutrophils, 10%; lymphocytes, 70%; monocytes, 7%; band form of neutrophils, 1%; and blasts, 12%. Bone marrow biopsy confirmed ALL, subtype L1. The girl underwent induction chemotherapy with vincristine, L-asparaginase, doxorubicin, dexamethasone, and intrathecal administration of cytosine arabinoside (Ara-C). Consolidation chemotherapy was achieved with cyclophosphamide, 6-thioguanine, cytosine arabinoside, and intrathecal administration of Ara-C. Complete remission was confirmed by the absence of any hematological malignancy on bone marrow study. She presented with a sudden attack of generalized tonic-clonic seizure and was admitted in April 2001. She underwent computed tomographic (CT) brain scan, magnetic resonance imaging (MRI) examination of the brain, cerebrospinal fluid (CSF) study, and bone marrow aspiration study. The CT scan showed a mass at the anterior falx with strong contrast enhancement (Fig. 1A). MRI demonstrated a round mass measuring 1.5 cm. The lesion showed low signal intensity on precontrast T1-weighted images and isosignal intensity on T2-weighted images. Contrast enhancement of the lesion was similar to that of meningiomas (Fig. 1B). CSF study disclosed a negative white blood cell count. Bone marrow aspiration demonstrated normocellular marrow. There was no maturation arrest in granulocytic and erythroid cells. Megakaryocytes were adequate in number. The girl was discharged 4 days after admission for follow-up in the outpatient clinic. The patient was admitted again with a recent onset of speech disturbance in March 2001. The physical examination demonstrated motor aphasia and disturbance of high-cortical functions, including calculation, and memory. Mentally the patient was lethargic and confused. Complex partial seizures lasting 2 min were identified. The complete blood count (CBC) checked in the laboratory test and the differential counts were within normal limits. MRI was performed as a matter of urgency. T2-weighted axial and coronal MRI images showed a 3-cm mass in the interhemispheric fissure, which was much larger than before (Fig. 2A). This lesion revealed heterogeneous signal intensity, which consisted of high and low signal intensities on T2-weighted images (Fig. 2B). The low signal intensity suggested intratumoral hemorrhage. Gadolinium enhancement was not so prominent as on previous MRI films (Fig. 2C). Four-vessel angiography demonstrated a mass effect only, causing displacement of both pericallosal arteries. The patient underwent open surgery through an interhemispheric approach. The dura and cerebral cortex were grossly normal. A well-demarcated mass was attached to the anterior falx and was located extra-axially. The mass was pinkish in color because of the intralesional bleeding, and it was friable in consistency. Removal of the tumor was subtotal because of massive bleeding resulting from hypervascularity of the lesion. Histological examination revealed that the mass was composed of diffuse proliferation of lymphoblasts (Fig. 3A). Immunohistochemical staining for differentiation of ALL from acute myeloblastic leukemia (AML) demonstrated positivity of the tumor cells to terminal deoxynucleotidyltransferase (Fig. 3B), CD 10, and CD20, while myeloperoxidase and CD3 were negative. The results of histological examination were con-

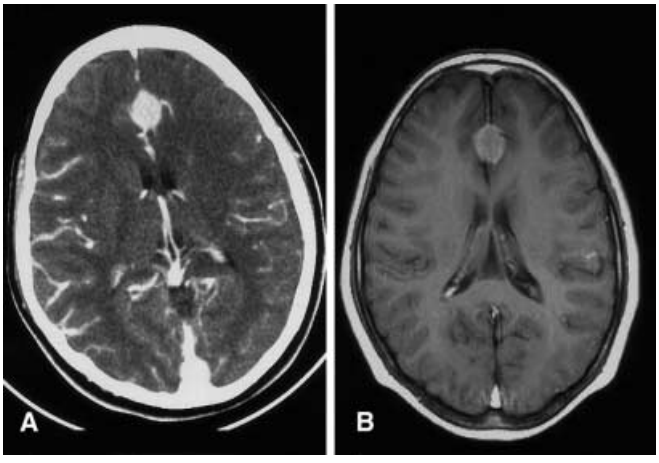

Fig. 1 **A** Computed tomographic scan showing a mass at the anterior falx with strong contrast enhancement. **B** Initial T1-weighted magnetic resonance imaging scan with Gadolinium enhancement demonstrates well-contrast enhancement of the lesion similar to those of meningiomas

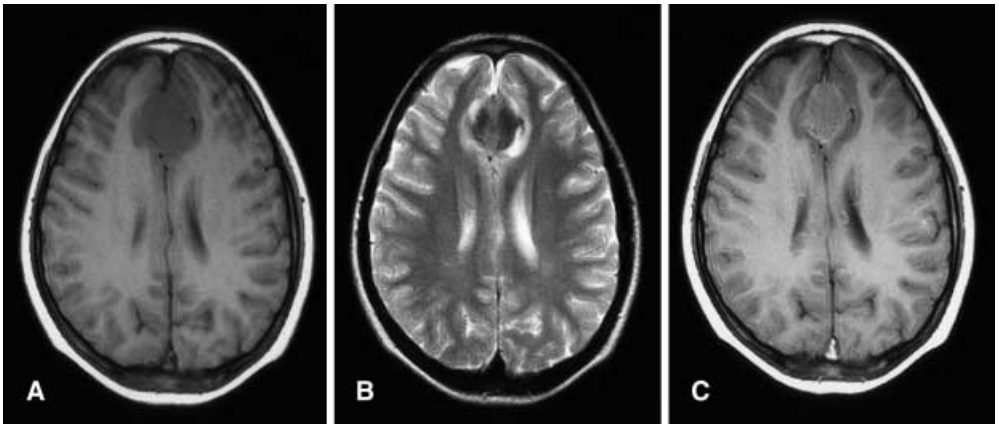

Fig. 2 **A** Preoperative T1-weighted magnetic resonance imaging scans revealing 3-cm-sized mass in the interhemispheric fissure, which was much increased than in Fig. 1. **B** This lesion reveals heterogeneous signal intensity, which consisted of high and low signal intensities on T2-weighted images. **C** Gadolinium enhancement was not so prominent as Fig. 1

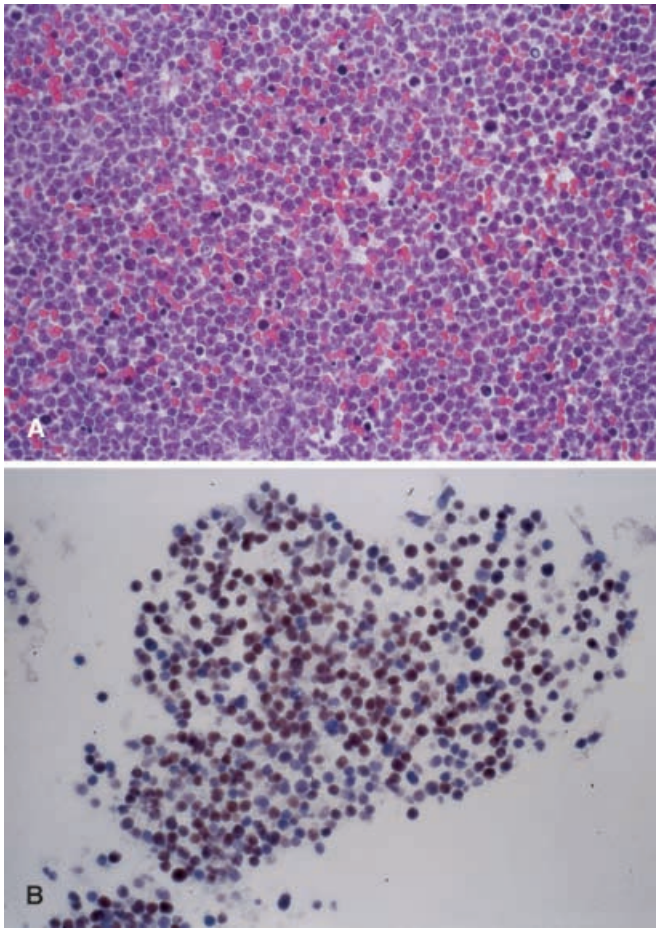

Fig. 3 **A** Diffuse proliferation of lymphoblasts showing finely dispersed chromatin pattern and small nucleoli. (Hematoxylin and eosin staining, ×400.) **B** Immunohistochemical staining demonstrate positivity of the tumor cells to terminal deoxynucleotidyltransferase. (×400)

sistent with a relapse of ALL. Postoperatively, the patient's mental status and speech disturbance were improved. Routine laboratory examinations including CBC were normal for 5 days after biopsy, but the patient presented with spiking fever 6 days after biopsy. Blasts had suddenly appeared in the peripheral blood. She was transferred to a bone marrow transplantation center for active antileukemic therapy, where she underwent chemotherapy with intrathecal therapy and cranial irradiation. Six months after the radiotherapy her neurological status remains stable, with no radiographic evidence of disease progression on MR imaging.

Discussion

Chloromas (granulocytic sarcoma) are masses composed of immature granulocytic cells. The term 'chloroma' is derived from the Greek word *chloros* (green) and describes the lesion's typical greenish appearance. The color is due to high expression of myeloperoxidase and is not always seen because it fades rapidly after exposure to oxygen [15]. Granulocytic sarcoma (the preferred term, as not all lesions have the greenish tint) occurs primarily in patients with AML, but can also arise in patients with myeloproliferative and myelodysplastic syndromes [5, 11, 14]. As in the present case, granulocytic sarcoma can also occur in patients with ALL. However, we found differentiation in the case of this intracranial extra-axial mass highly problematic, because we knew that most granulocytic sarcomas have occurred in the presence of AML. Recent evidence suggests that granulocytic sarcomas are increasing in frequency because of improved antileukemic therapy and longer remission in patients with AML [18]. Extracranial sites, such as skin, bone, and soft tissue, are far more commonly affected than the CNS [11, 13]. Symptoms are related to the location of the lesion. A retrospective analysis of 90 patients with isolated chloromas suggests an altered predilection pattern in these cases, with more visceral manifestations and very rare involvement of the CNS [8]. Signs of neurological compression are the most characteristic indications of CNS involvement [6, 12, 15]. As might be expected, intracranial granulocytic sarcomas present as signs of increased intracranial pressure or as a mass effect. Granulocytic sarcoma can arise within the parenchyma or start in the dura [2, 9, 16]. On CT scan, these lesions are typically isodense or hyperdense on precontrast scans and enhance brightly [2]. Leukemic masses are isointense or hyperintense relative to the brain on T1-weighted images, and they enhance prominently with gadopentetate dimeglumine [16]. Neither cysts nor necrosis are typically observed. Multiple lesions have been reported [19]. In our case, the atypical MRI findings, with the mass strongly enhanced in the initial films but not in preoperative films, confused us. We were able to differentiate it from cerebrovascular or infectious disease because of its rapid growth, the atypical MRI findings, and the negative results of bone marrow biopsy and CSF study. In addition, the patient underwent four-vessel angiography, which was negative except for the mass effect. The poor contrast enhancement can be attributed to the intratumoral hemorrhage.

Granulocytic sarcomas are more common in younger patients [17]. With a median survival of 22 months, they are associated with a poor prognosis. Granulocytic sarcoma can be the first sign of relapse after bone marrow transplantation [3] or precede the onset of systemic disease [2, 11]. Most, but not all [5, 10], localized cases finally progress to overt leukemia, as in our case. Imrie et al. demonstrated that surgical resection and/or irradiation, although highly effective in local control, do not influence survival [8]. The best results have been achieved with antileukemic chemotherapy containing Ara-C in quite high doses. An equally favorable outcome in the few reported patients with autologous and allogeneic bone marrow transplantation after induction therapy suggests that intensified consolidation is useful [7, 8].

In conclusion, we present a case of granulocytic sarcoma in acute lymphoblastic leukemia mimicking meningioma. These unusual radiological and pathological findings in ALL should be regarded as a recurrence of ALL. Even if complete remission confirmed by the absence of any hematological malignancy in bone marrow study is obtained, the leukemic patient with neurological symptoms and signs must be examined, with a radiological evaluation, as soon as possible. Early detection and active antileukemic treatment of granulocytic sarcoma are necessary and important for a favorable prognosis.

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