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CORRESPONDENCE

Isolated Intracranial Myeloid Sarcoma at Age 6 Months with Metastases

Case Report and Review of the Literature

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Introduction

Myeloid sarcoma (MS) is a neoplasm formed by the infiltration of protogranulocytes or immature myeloid cells into organs and tissues other than bone marrow [1]. It can be associated with acute myeloid leukemia (AML) or chronic myeloid leukemia (CML) and other myeloproliferative disorders at the same time or before or after [2]. Isolated MS is defined as the disease without evidence of AML in bone marrow biopsy and failure to develop into AML within 30 days after the diagnosis of MS, which has an incidence of approximately 2 out of 1 million adults and 0.7 out of 1 million children; however, in infants it is even rarer [3, 4]. An MS can invade any anatomical site [1], the occurrence of MS in the central nervous system (CNS) is rare [5] and isolated primary intracranial MS should be carefully considered. This article presents a unique case of isolated intracranial MS at in a 6-month-old patient with extensive brain metastases to highlight the unusual clinical and imaging presentation of this entity.

Case Report

In February 2016 a 6-month-old male patient was admitted to hospital on an emergency basis because of occasional fever accompanied by vomiting for 1 day and convulsions on 3 occasions. The infant was full-term with vaginal delivery without a history of leukemia. The examination was unremarkable apart from severe anemia and no tumor cells were found in the first bone marrow biopsy. Computed tomography (CT) of the head revealed a hyperdense space-occupying lesion beside the left frontotemporal area, which mostly involved the cerebral cortex and gray matter. Magnetic resonance imaging (MRI) examination revealed a large irregular mass with cystic and solid appearance in the left frontotemporal region, with obscure margins and absence of peritumoral edema. The solid portion of the mass was mildly hypointense on T1-weighted imaging (T1WI) and isointense/mildly hyperintense on T2WI, with obvious inhomogeneous enhancement. Diffusely thickened meninges were present in the right temporal region and the left cerebral hemisphere and the left cerebral gyrus was enlarged (Fig. 1a–e). The patient underwent a craniotomy for resection of the brain tumor in March 2016. The tumor mass was dark red in color, pliable and located in the frontal, parietal and temporal lobes. The mass exhibited clear borders and a rich blood supply and adhered slightly to the surrounding brain tissues and falx cerebri. The histopathological examination showed brain tissue infiltrated by atypical round cells with little cytoplasm and prominent nucleoli. Immunohistochemistry (IHC) was positive for cluster of differentiation (CD) 68, CD43, CD117, CD138, vimentin (Vim), leukocyte common antigen (LCA) and myeloperoxidase (MPO) and the proliferation fraction (Ki-67) was 90% (Fig. 2a–c). The pathological diagnosis was intracranial MS and the second bone marrow biopsy showed no tumor cells.

The MRI images 15 days after the operation showed meningeal multiple enhanced nodules in the right temporal lobe, bilateral cerebral hemisphere, cerebellar hemisphere vermis and interpeduncular cistern (Fig. 3a–c). The patient was in a very poor state of health after surgery and not administered chemotherapy because of the parent's refusal and ultimately died.

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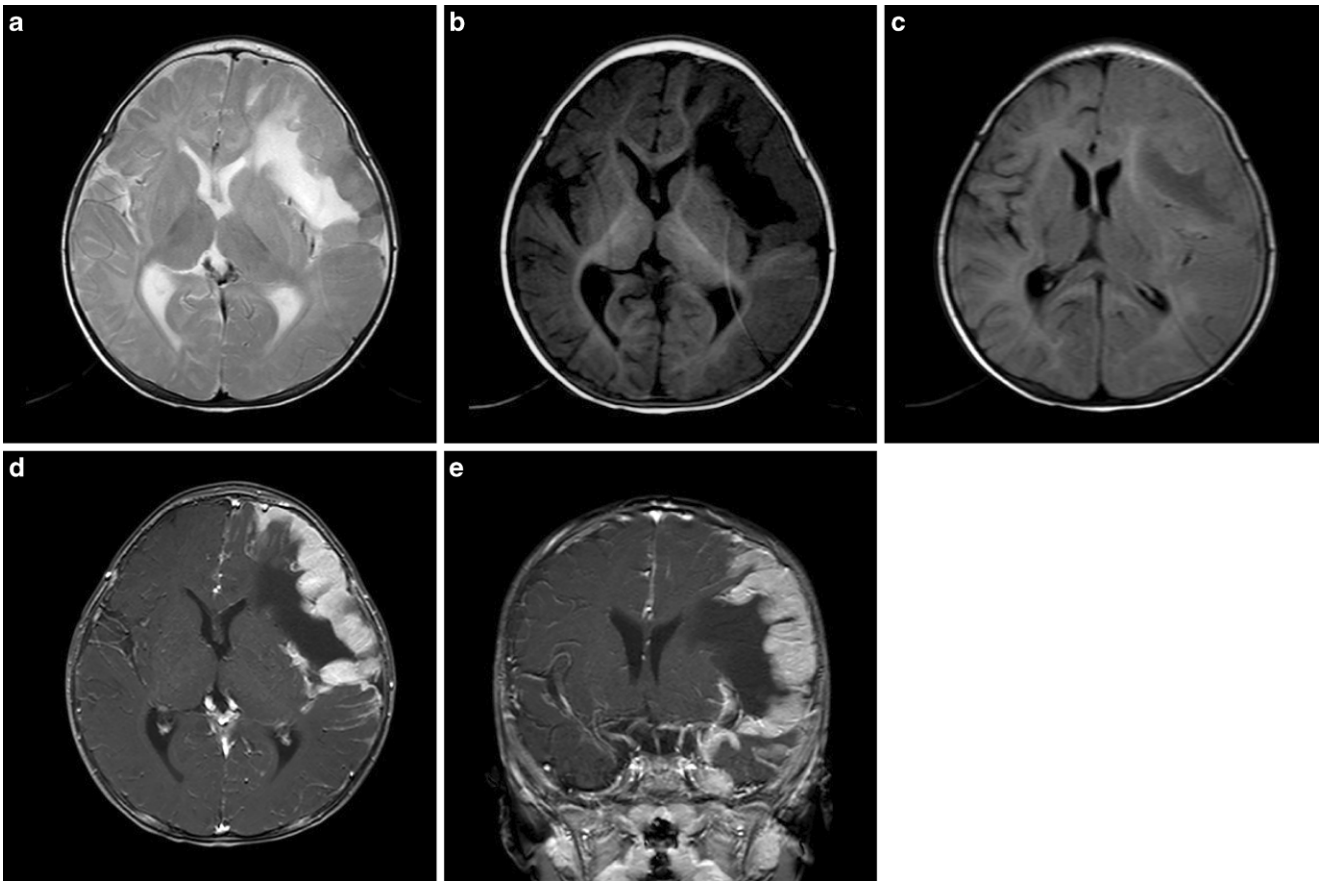

Fig. 1 An irregular mass in the left frontotemporal. Cross-sectional (**a**–**d**) and longitudinal (**e**) MR images of the brain showing: the solid portion of the tumor appears isointense/mildly hyperintense with brain parenchyma on T2-weighted images (**a**), while it is mildly hypointense on T1-weighted images (**b**) and isointense on fluid-attenuated inversion recovery (FLAIR) images (**c**) with surrounding cystic portion and inhomogeneous enhancement on contrast (**d**, **e**). The diffusely thickened meninges occur in the left cerebral hemisphere and right temporal region (**e**). Both lesions are based in the cerebral cortex and meninges

Discussion

Myeloid sarcoma, which was previously known as granulocytic sarcoma or chloroma, is an uncommon malignant tumor characterized by extramedullary blast proliferation of myeloid lineages that subsequently destroy the normal architecture of adjacent tissue [6]. Tumors can appear prior to, during or after systemic leukemia and isolated MS is a rare condition. Patients with MS without preference for gender have a wide age range (0–81 years old) with a distribution biased towards children and young adults [7]. It is a particularly rare occurrence in infancy. To our knowledge, only three cases of intracranial MS been described in infants ([8, 9]; Table 1). All of those cases were associated with AML and without any CNS metastasis and Olar et al. described two cases diagnosed with CNS MS following tissue examination [9]. The patient in this study was a 6-month-old male in which MS was an isolated diagnosis. Bain et al. reported a case of isolated MS in a 4-month-old female who presented with cutaneous lesions without evidence of leukemia [10]. Symptoms depend on the location of the lesion and tumor size in the CNS [5, 11].

Radiologically, intracranial MS is usually connected with the meninges or the ependyma and may invade the brain parenchyma; thus, it may appear as a meningeal infiltration or intravascular tumor or masses in parenchymal form [7, 12]; however, most are in the form of focal masses without adjacent bone destruction [7, 13, 14]. Typically, the lesion appears as a hyperdense mass on a noncontrast CT scan and isointense or slightly hypointense in T1WI and T2WI and generally shows homogeneous contrast enhancement [7, 15, 16]. In this case the MRI findings (Fig. 1) met the criteria of these studies. More importantly particular attention should be paid to neuromeningeal infiltration and implantation metastasis because leukemia cells can infiltrate dural and subarachnoidal spaces through the arachnoidal veins as well as the risk of surgery. Qian et al. reported a 27-year-old patient with isolated primary intracranial MS and neuromeningeal infiltration, which showed a mass involving both the inside and outside of the lumbar spinal canal

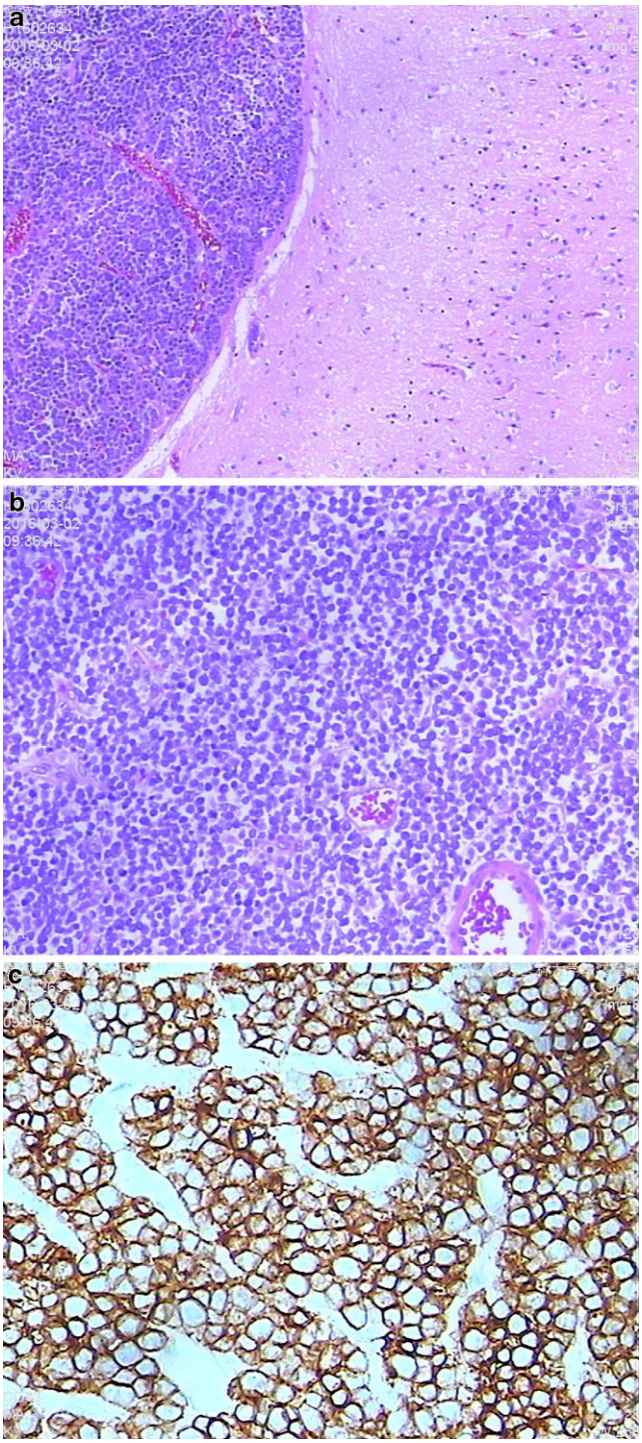

Fig. 2 **a** Tissue diffusely infiltrated by tumor cells with clear demarcation from normal brain tissue (H&E ×40). **b** Round-shaped malignant lymphoid cells with less cytoplasm, hyperchromatic nuclei and obvious nuclear mitosis (H&E, ×200). **c** Representative image of tumor cells stained for CD43 (IHC, ×200)

[6]. In this case, MRI scan revealed scattered multiple enhanced nodules in the brain and meningeal metastases after surgery, which indicated the possibility of metastasis and malignant progression after clinical treatment. It is noteworthy that the performances of functional MRI for intracranial MS had limited value for the differential diagnosis. Hakyemez et al. observed that diffusion-weighted imaging, perfusion-weighted MRI and MR spectroscopy findings were not helpful in differentiating the lesion from other extra-axial tumors, such as lymphoma and meningioma [15].

An MS may present with variable morphological and phenotypic features, which always creates a challenge in the pathological diagnostics. The pathogenesis is believed to be an aberrant expression of homing signals for the leukemic blasts on extramedullary sites [17]. Histologically, the cells are predominantly arranged diffusely and there is a mixture of myeloblasts, neutrophils and eosinophilic granulocytes [18]. Obvious small nucleoli and predominantly round or oval nuclei were seen in most cases. The diagnosis of MS is validated by the results of immunophenotypic analyses. The use of IHC and special staining methods showed positive results for CD68/KP1, MPO, CD43, CD117, CD99, CD68/PGM1, lysozyme, CD34, terminal deoxynucleotidyl transferase (TdT), CD56, CD30, glycophorin and CD4 and the specificity and sensitivity of MPO in the diagnosis of MS were higher [12, 18]. The histology and IHC in this case accorded with the relevant literature very well. The combined application of morphology, IHC and special staining methods help in the diagnosis of this tumor.

Most patients with isolated MS progress to AML within months of diagnosis and seldomly survive more than 1 year [19]. Pileri et al. concluded that the treatment response of MS patients was not related to the status of MS (isolation or leukemia correlation), age, sex and location [20]. Systemic chemotherapy is recommended for primary MS as it significantly reduces the probability of development to leukemia [21, 22]; however, the most appropriate treatment of MS without bone marrow involvement in children remain unclear but pediatric MS patients responded favorably to treatment [23]. Surgical excision may involve certain risks that cause leukemic cell metastasis to the brain tissues via the cerebrospinal fluid and an appropriate chemotherapy regimen for treatment of isolated MS should be used before or after operation [22]. In this study the intracranial metastasis occurred in a short time period perhaps due to the omission of chemotherapy for this infant. Thus, surgery plus chemotherapy remains the most commonly used treatment for MS.

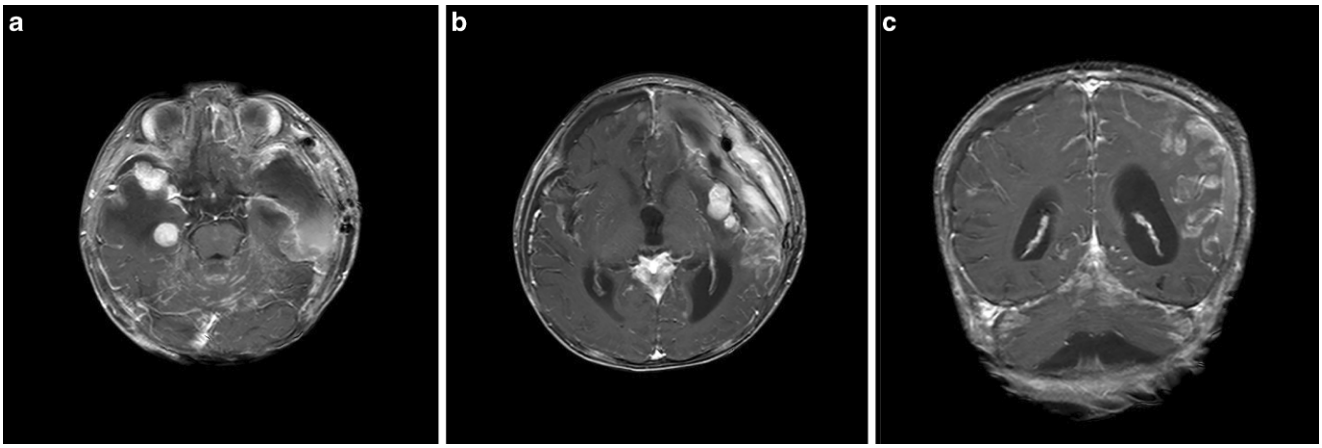

Fig. 3 Postcontrast cross-sectional (**a**, **b**) and longitudinal (**c**) T1-weighted magnetic resonance imaging of the brain 15 days after the operation showed multiple enhanced nodules **a** in the right temporal lobe homogenous enhancement, **b** bilateral cerebral hemisphere, **c** cerebellar hemisphere and meninges, which indicated intracranial multiple metastases

Table 1 Summary of the previously reported cases of intracranial MS in infancy

Author	Age (months), sex	Presenting symptoms	Hematologic neoplasia	CNS involvement	Imaging findings	Treatment	Outcome
Psiachou-Leonard et al. (2001) [8]	11, male	Vomiting + lethargy	AML/M5	Left cerebellum	Intraparenchymal mass	Systemic chemotherapy	Death
Olar et al. (2016) [9]	At birth, female	Poor respiratory effort	AML	Cerebral and cerebellar, pituitary gland	Subdural hematoma	None	Death
Olar et al. (2016) [9]	5, male	Not available	AML	Left frontal and parietal lobes	Subdural hematoma	Autologous stem cell transplantation	Death

CNS central nervous system, *AML* acute myeloid leukemia, *M5* monocytic leukemia

Conclusion

Isolated intracranial MS occurs only rarely in infants. Intracranial MS has certain imaging characteristics. Special attention should be paid to metastatic spread and timely chemotherapy even if there is no evidence of leukemia. Pathological and immunohistochemical examinations are still needed to confirm the diagnosis. As isolated MS is rare, further investigations and research are required to achieve an improved understanding about its pathogenesis, image findings and treatment.

Conflict of interest J. Zhu, S. Thapa, X. Wang, C. Jiang, Y. Qu and Z. Wen declare that they have no competing interests.

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