CASE REPORT

Acute myeloid leukaemia masquerading as a primary CNS tumour

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SUMMARY

In children with newly diagnosed acute myeloid leukaemia (AML), myeloid sarcomas (MS) of the central nervous system (CNS) are rare. Since MS involving the CNS are potentially curable, timely recognition is paramount. Establishing a diagnosis may be problematic as they can easily mimic primary CNS neoplasms. We report the case of a 5-year-old boy with AML with t(8;21)(q22;q22) rearrangement who presented with a massive intracranial MS and rapid clinical deterioration suggestive of a meningioma or a primitive neuroectodermal tumour. The peripheral smear showed blasts with Auer rods. Urgent chemotherapy was started for AML with presumptive CNS MS. The mass resolved with chemotherapy, and treatment was consolidated with radiotherapy. Although exceedingly rare, this case highlights the potential for MS to present similarly to a primary CNS tumour. MS should be part of the differential diagnosis as part of a CNS mass, particularly if the complete blood count is abnormal.

BACKGROUND

Myeloid sarcomas (MS) are extramedullary lesions composed of myeloid lineage blasts that typically form tumorous masses and may precede, follow or accompany systemic acute myeloid leukaemia (AML).^{1,2} MS are commonly associated with the translocation t(8;21)(q22;q22). Other chromosomal aberrations such as monosomy 7, trisomy 8 and mixed lineage leukaemia have also been reported.^{2,3} In children with newly diagnosed AML, extramedullary involvement is most common in the skin with orbital involvement being the second most common site.⁴ MS involving the central nervous system (CNS) are rare, accounting for approximately 3% of all cases.⁵ When CNS disease occurs, patients can display a heterogeneous clinical picture ranging from minor headaches and paraesthesia to pronounced stupor and hemiplegia.⁶ Since MS involving the CNS are potentially curable, timely recognition is paramount. Frequently, establishing a diagnosis is problematic as these masses can easily mimic primary CNS neoplasms.⁷

We report the case of a 5-year-old boy with AML with t(8;21)(q22;q22) rearrangement who presented with a massive intracranial MS and rapid clinical deterioration suggestive of a meningioma or a primitive neuroectodermal tumour (PNET). Following, the peripheral smear showed blasts with Auer rods confirming the diagnosis. Although exceedingly rare, this case highlights the

potential for MS to present similarly to a primary CNS tumour. MS should be part of the differential diagnosis as part of a CNS mass, particularly if the complete blood count (CBC) is abnormal. Here we discuss the diagnosis and treatment of challenging AML cases with intracranial MS.

CASE PRESENTATION

A 5-year-old boy presented with a 1-month history of worsening headaches and emesis. As per his mother, the patient had gradually developed proptosis, periorbital oedema and significant left lower extremity weakness that presented as a limp. One day prior to admission, he suddenly developed worsening projectile emesis and progressive lethargy and was taken to the emergency department of an outside institution for further evaluation. Physical examination revealed bilateral periorbital oedema, proptosis and a significantly altered mental state. Immediate CT scan (CT) of the brain revealed a 9.2 cm × 5.7 cm × 4.7 cm mass arising from the midline falx suggesting a meningioma or a PNET. Emergent MRI of the brain with and without contrast exhibited intermediate signal intensity on both T1 and T2 and showed restricted diffusion and homogenous enhancement following contrast administration. Secondary mass effect on the underlying brain parenchyma with associated vasogenic oedema was appreciated (figure 1A,B).

TREATMENT

Hydration and intravenous steroids were immediately initiated, and a neurosurgery consult was obtained for consideration of an emergent decompressive craniotomy. While awaiting neurosurgical assessment, CBC came back showing leucocytosis of 24 × 10⁹/L with numerous blasts (63%) displaying Auer rods (figure 1C, arrow). Following, a bone marrow aspirate differential revealed 32% blasts. Flow cytometry analysis showed an aberrant population with positive immunophenotype for CD13, CD25 (partial), CD33 (partial), CD34, CD38 (bright), CD56 (subset), CD117, CD123, MPO and HLA-DR.

Fluorescence in situ hybridization (FISH) was positive for t(8;21)(q22;q22) rearrangement. Molecular expression of RUNX1–RUNX1T1 (AML1–ETO) fusion transcript associated with t(8;21) by quantitative real-time RT-PCR was reported. Additionally, two internal tandem duplications (ITD) in the FLT3 gene were detected by PCR-based DNA analysis with ITD ratios of 0.242 and 0.008. The

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Figure 1 (A) Sagittal and (B) axial planes of the brain CT scan showing a 9.2 cm×5.7 cm×4.7 cm mass arising from the midline falx with associated vasogenic oedema. (C) Acute myeloid leukaemia blasts with Auer rods found in peripheral blood. (D) Resolution of the intracranial mass after induction chemotherapy.

morphological, immunophenotypic and cytogenetic findings were diagnostic of AML with t(8;21); *RUNX1/RUNX1T1* (WHO 2008 classification). By French-American-British (FAB) classification, this was best classified as AML-M2. A diagnosis of AML with CNS MS was made. No initial lumbar puncture (LP) was obtained due to the risk of CNS herniation.

The patient was stabilised and was given his first course of induction chemotherapy with high dose cytarabine, daunorubicin and etoposide resulting in an almost complete reduction in the intracranial mass (figure 1D) and resolution of neurological symptoms. Two weeks later, a LP with intrathecal cytarabine was then administered, and no malignant cells were identified in the cerebrospinal fluid (CSF). A repeat bone marrow aspiration after count recovery following the first cycle of induction demonstrated morphological remission; however, minimal residual disease was detected by flow cytometry (0.1%), and FISH remained positive for t(8;21)(q22;q22) rearrangement at a low level.

OUTCOME AND FOLLOW-UP

The patient completed AML therapy over 4 months and underwent consolidative radiotherapy with 2400 cGy to the residual mass. Bone marrow studies at the end of treatment showed FISH to be negative for the translocation, and the molecular expression of *RUNX1-RUNX1T1* (AML1-ETO) fusion transcript associated with t(8;21) by quantitative real-time RT-PCR was found to be 0.01%.

At 12 months postdiagnosis, the patient remains in remission and is active, playful and otherwise neurologically asymptomatic.

DISCUSSION

We present the case of a paediatric patient with acute neurological deterioration, who was found to have a massive CNS

mass concurrently with peripheral blasts that exhibited Auer rods. This pointed towards a diagnosis of a CNS MS. A biopsy or cranial surgery would have delayed therapy, contaminated the CSF and potentially led to lethal complications. We assumed that the patient had CNS AML and proceeded with treatment. In this case, increased clinical suspicion and an experienced radiologist were crucial for proper diagnosis.

At radiological presentation on CT, MS may exhibit intermediate or high attenuation on unenhanced scans, with surrounding oedema and typical uniform contrast enhancement.⁸ On MRI, lesions are usually hypointense to isointense on T1- and T2-weighted images.⁵ When presenting as dural-based mass lesions, radiological differential diagnosis includes haematoma, brain abscess, meningioma, metastatic neuroblastoma and lymphoma.^{9 10} Perfusion-weighted MRI may be helpful in differentiating MS from meningiomas.⁹ Spectroscopy does not reliably demonstrate differences in metabolic activity.⁵

AML induction therapy is recommended in the great majority of cases even in rare and the most difficult cases where patients present with MS as an isolated mass, with no evidence of AML after extensive work-up.^{11–13} Radiotherapy continues to be a topic of debate. Combined chemotherapy with radiation therapy has shown to improve overall failure-free survival compared with single modalities.¹⁴ Other studies focused mainly on large paediatric populations have demonstrated that localised radiotherapy to the site of extra-medullary involvement at the end of induction chemotherapy did not improve outcomes.⁴ For patients who present with life-threatening or organ-threatening MS, low dose emergency radiotherapy (1.5–2.0 Gy for 3–5 fractions) may be extremely effective at relieving symptoms and preserving organ function.⁴

Initially, intracranial MS can cause dramatic mental deterioration. Risk factors for their development include high lactate dehydrogenase, African-American ethnicity and young age.¹⁵ Surprisingly, intracranial involvement seems to be related to favourable prognoses when compared with patients with MS of the skin and those without MS at all.^{4 16} Of course, an alternative explanation for the better outcome is the association of these cases with the presence of the t(8;21)(q22;q22) cytogenetic abnormality, which is known to be a favourable prognostic factor.¹⁷ Irrespective of the above, when evaluating a patient with these clinical and radiological findings, it is critical to consider MS in the differential diagnosis, as an unnecessary surgical intervention in the setting of a newly diagnosed AML could lead to substantial complications.

Learning points

- ▶ Myeloid sarcomas (MS) should be part of the differential diagnosis as part of a central nervous system mass, particularly if the complete blood count is abnormal.
- ▶ Radiologically, MS may mimic haematomas, brain abscesses, meningiomas, metastatic neuroblastoma and lymphomas.
- ▶ Intracranial MS seem to be related to favourable prognoses when compared with patients with MS of the skin and those without MS at all.
- ▶ Acute myeloid leukaemia (AML) induction therapy is recommended in all cases even in rare cases where patients present with MS as an isolated mass, with no evidence of AML after extensive work-up.

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