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CASE REPORT

Systemic Mastocytosis presents as a solitary skull lesion in a child

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ABSTRACT

Mastocytosis arises from the abnormal growth and accumulation of mast cells within the body's organ systems. Within the pediatric age group, systemic mastocytosis is exceptionally rare, with only a few reported cases in the medical literature. Here, we report a case detailing a solitary skull lesion in a 10-year-old child as the sole identified manifestation of systemic mastocytosis. She presented with neurologic symptoms without any allergic or systemic manifestation. The child was initially diagnosed with hemangiopericytoma, with the differential diagnosis of atypical meningioma. The patient underwent surgery and histopathological examination confirmed the diagnosis of systemic mastocytosis. Unfortunately, the patient presented with recurrence, necessitating another surgery that again confirmed the diagnosis. Multidisciplinary team collaboration integrating clinical, radiographic, and immunophenotypic correlations is vital in the diagnosis and management of this sporadic condition.

INTRODUCTION

Systemic mastocytosis is a rare condition, with an estimated global prevalence of 1 in 10000 individuals. It is due to the abnormal growth of mast cells which can affect the bone marrow, skin, or extracutaneous organs such as the liver, spleen, lymph nodes and gastrointestinal tract (George et al., 2011; Theoharides et al., 2015). While it can manifest at any age, it is more commonly observed in adults and can affect both sexes with a slight predominance in

males. KIT mutations have been demonstrated in over 95% of adults with mastocytosis (Valent, 2015), but less so in children, with recent literature indicating mutations in 25 to 64.3% of pediatric-onset mastocytosis (Verzijl et al., 2007; Yanagihori et al., 2005).

Due to its rarity in the pediatric population, there have been very few reported cases in the literature (Castells, 2006; Guenther et al., 2001). These cases are classified as mast cell neoplasms with lytic bone lesions and do not meet the diagnostic criteria for SM. Conversely, our case report presents a tumor that fulfils the criteria for SM, despite lacking systemic involvement. Thus, we describe a unique case of a child with a solitary skull lesion as the sole identified manifestation of systemic mastocytosis.

CASE PRESENTATION

A previously well 10-year-old Asian girl presented with headache, vomiting and left-sided visual loss. There was no history of urticaria or allergic manifestation. On examination, she had left temporal inferior quadrant hemianopia. The rest of the neurological examination was unremarkable. No cutaneous or other organ involvement was identified.

The initial non-contrast-enhanced CT scan of the brain (Figure 1) showed a solitary lytic bone lesion in the right occipital skull with an extra-axial mass causing adjacent cerebral vasogenic oedema. Contrast-enhanced MRI scan of the brain (Figure 2) confirmed the presence of an extra-axial mass which was isointense on T1- and T2-weighted sequences, with post-contrast enhancement and associated dural enhancement. No other intracranial abnormality was detected. The initial provisional diagnosis was meningeal hemangiopericytoma because of the locally aggressive enhancing extra-axial tumour with bone erosion.

Differential diagnosis included atypical meningioma or bone malignancy such as skull osteosarcoma with intracranial extension. Meningiomas are dural-based extra-axial tumours which show avid post-contrast enhancement with dural tail; these are commonly associated with calcification and adjacent bony hyperostosis, instead of erosion. Osteosarcoma typically exhibits permeative or moth-eaten appearance with aggressive periosteal reactions such as the sunburst-type, onion-skin or Codman triangle, which is not seen in this case.

The patient underwent right posterior craniotomy and excision of the tumour with titanium mesh cranioplasty. Intraoperatively, the tumour was noted to arise from the dura with involvement of both the outer and inner tables of the skull.

Histopathological examination (Figure 3) of tumour, skull and dura showed densely packed sheets of neoplastic cells with cytoplasm ranging from abundant eosinophilic to vacuolated in appearance. These neoplastic cells had round to oval nuclei, exhibiting clumped chromatin and some with small nucleoli. Mitoses were occasionally seen. Intermingled were scattered cells with irregular lobulated to reniform nuclear contours as well as multinucleated cells. A small number of neutrophils and eosinophils were present. There was no marked nuclear pleomorphism.

Immunohistochemical studies demonstrated diffuse positivity for CD117, CD43, CD25, CD68 and CD2. Additionally, there was focal positivity for tryptase, CD45 and CD30. Immunostains for CD163, myeloperoxidase (MPO), lysozyme, CD15, CD34, CD56, Langerin, S100, CD1a, epithelial membrane antigen (EMA), pan-cytokeratin (PanCK), glial fibrillary acidic protein (GFAP), D2-40, and E-cadherin all yielded negative results. The Ki67 proliferative index was approximately 10 percent. Toluidine blue staining revealed metachromatic granules in numerous neoplastic cells. Based

on the histological features and ancillary testing, the features were indicative of a mast cell neoplasm consistent with systemic mastocytosis.

The patient underwent re-craniotomy and tumour excision, during which a thin film of tissue was observed growing over the titanium mesh, which was also removed to

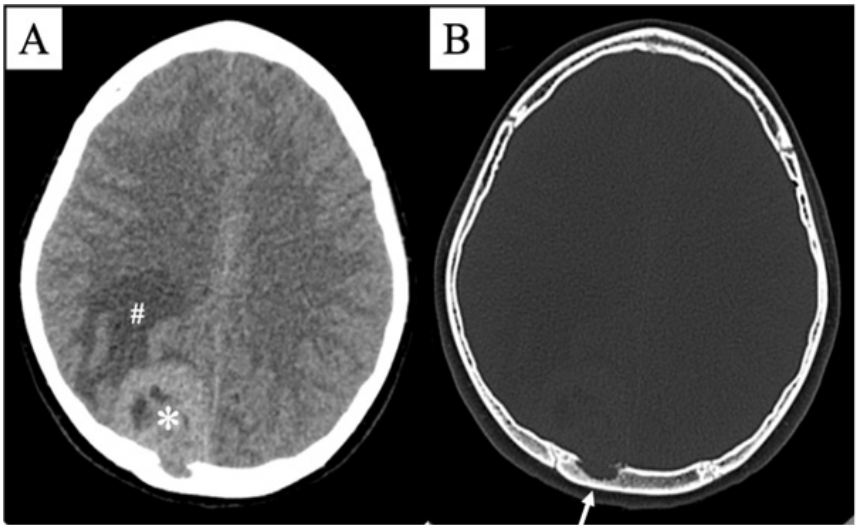

Figure 1: Non-contrast enhanced axial CT images of the brain at presentation. (A) Soft tissue window and (B) bone window showed a solitary right occipital extra-axial mass (asterisk) associated with cerebral vasogenic (hashtag) and adjacent bone erosion (arrow).

Bone marrow aspiration and trephine biopsy, along with immunophenotyping did not reveal any evidence of marrow infiltration. Genetic study for cKIT D816V mutation analysis was negative. Serum Tryptase were within the normal range. Full blood count was unremarkable with no signs of eosinophilia.

The patient's symptoms resolved after the surgery. Immediate post-operative CT brain study did not show residual tumour. Post-operative whole-body PET/CT scan did not show FDG-avid uptake to suggest another site of disease involvement. Following a multidisciplinary team discussion, the patient was followed up clinically without adjuvant chemotherapy or radiotherapy as she was asymptomatic.

However, two months after the surgery, the patient complained of headache. Subsequent contrast-enhanced MRI scan (Figure 4) revealed tumour recurrence.

prevent future recurrence necessitating re-surgery. Histopathological examination again confirmed tumour recurrence.

DISCUSSION

The 2022 World Health Organization (WHO) categorised mastocytosis into three major types: cutaneous mastocytosis (CM), SM, and mast cell sarcoma (MCS). The SM is further divided into bone marrow mastocytosis (BMM), indolent (ISM), smoldering (SSM), aggressive (ASM), SM with an associated hematologic neoplasm (SM-AHN), and mast cell leukaemia (MCL).

Cutaneous mastocytosis is predominantly observed in the pediatric age group, constituting 90% of cases with a bimodal distribution pattern. It typically peaks in the first three years of life, with a second smaller peak occurring after 15 years of age (Klaiber et al., 2017). Systemic mastocytosis makes up less than 10 per cent of the

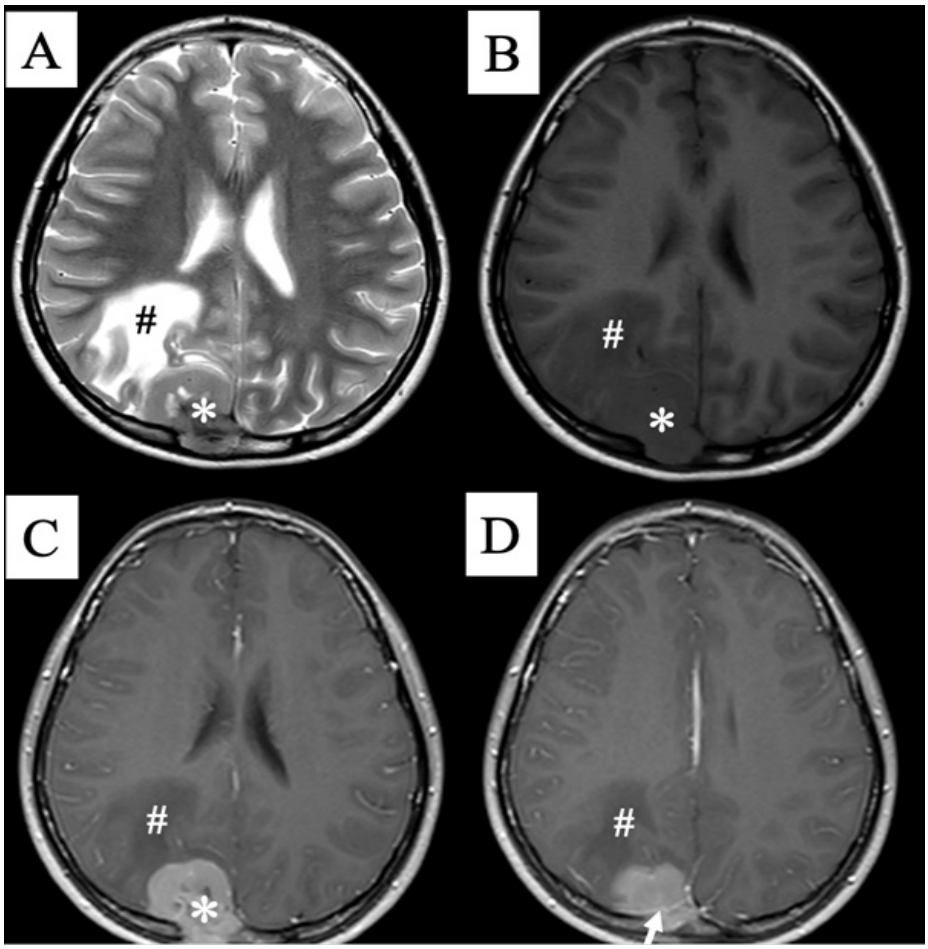

Figure 2: Pre-operative axial MR images of the brain. (A) T2-weighted and (B) pre-contrast enhanced T1-weighted images depicted an isointense right occipital extra-axial mass (asterisk) with adjacent cerebral vasogenic oedema (hashtag). (C, D) Post-contrast enhanced T1-weighted images showed the mass to be heterogeneously enhancing, associated with dural enhancement (arrow).

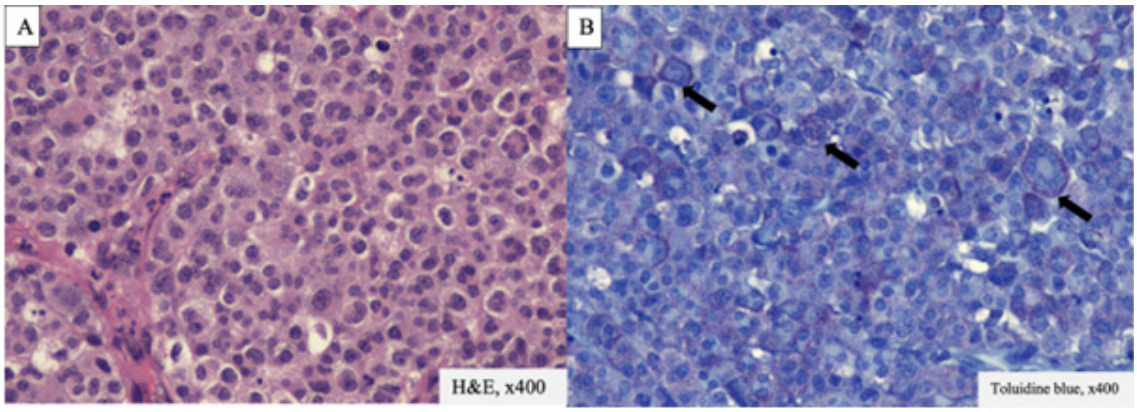

Figure 3: Light Microscopy High power view x400 magnification. (A) Haematoxylin and eosin staining (H&E) of extra-axial mass depicted hypercellular sheets of neoplastic cells displaying variable round, oval, and reniform nuclei with scattered interspersed multinucleated foms. (B) Toludine blue highlighted metachromatic granules (arrows) in the neoplastic cells.

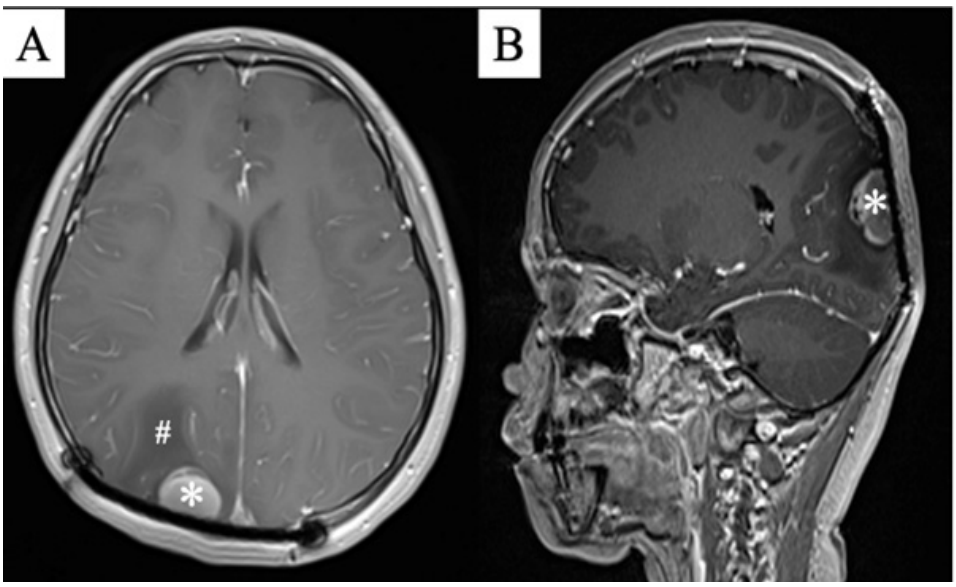

Figure 4: Post-operative contrast-enhanced MR images of the brain. (A) Axial and (B) Sagittal plane showed tumour recurrence (asterisk) with cerebral vasogenic oedema (hashtag).

pediatric mastocytosis cases. Most follow a benign course, often exhibiting spontaneous improvement or resolution before reaching the prepubescent stage (Carter et al., 2015). The majority of children with SM tend to have indolent SM, with the more aggressive or advanced forms of the disease being rare. Additionally, in comparison to adult mastocytosis, the pediatric disease is less likely to be associated with haematological, bone marrow or gastrointestinal involvement; similar as noted in this case report (Cooper et al., 1982; Horan et al., 1991; Parker, 2000).
Meanwhile, mastocytosis in adults tends to present in the 5th decade of life or later (Arber et al., 2016) and persist throughout life. Bone abnormalities are prevalent in approximately 50% of adult patients with systemic mastocytosis (Barete et al., 2010). These abnormalities can manifest in various forms, including diffuse or focal, lytic, sclerotic or mixed patterns (Rossini et al., 2011; Van der Veer et al., 2012). Unlike adult mastocytosis, bone involvement in childhood-onset mastocytosis is rare, with only a few reported cases (Castells, 2006; Guenther, 2001). Most of them do not meet the criteria for SM and are instead described as solitary mast cell neoplasms with lytic bone lesions.

The 2022 WHO diagnosis of SM needs the presence of one major and one minor criterion, OR three minor criteria for confirmation:

a.The major diagnostic criterion for SM is the presence of multifocal mast cell aggregates (15 or more mast cells) in the bone marrow or other extracutaneous organs.
b.The minor criteria for SM include the presence of atypical mast cells of more than 25 per cent, the activation of KIT codon 816 mutations, the expression of one or more surface markers (CD2, CD25, CD30), and the elevation in serum tryptase levels exceeding 20 ng/mL.

The patient in this case report met the diagnostic criteria for systemic mastocytosis, based on histopathological analysis. The specimen exhibited one major criterion and two minor criteria, characterized by multifocal dense aggregates of mast cells exceeding 15, with more than 25% of all mast cells being of the atypical type II variety and expressing CD2 and CD25 antigens.

CONCLUSION

Paediatric-onset systemic mastocytosis is a sporadic condition with distinctive and often

atypical presentation compared to its adult counterpart. Clinicians, radiologists, and pathologists must recognise that solitary mast cell neoplasm may indicate an underlying systemic disease. Multidisciplinary team collaboration integrating clinical, radiographic, and immunophenotypic correlations is vital in the diagnosis and management of this condition.

CONFLICT OF INTEREST

All authors affirm that they have no affiliations with or involvement in any organisation or entity that may have financial or non-financial interests in the subject matter or materials discussed in this manuscript.

CONSENTS

Written informed consent was acquired from the child's father.

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