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Juvenile Xanthogranuloma in a Child: A Case Report

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Case Report

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Abstract

Background

Juvenile xanthogranuloma (JXG) is a rare non-Langerhans cell histiocytic disorder that predominantly affects infants and young children. It most commonly presents as a solitary cutaneous lesion, while extracutaneous involvement is considerably less frequent.

Case presentation:

We report the case of a 7 -year-old girl who presented with The patient presented with headache, weakness in the left upper and lower extremities, inability to walk independently, nausea, vomiting, dysphagia, shortness of breath, and generalized weakness for approximately 5 months. Clinical examination revealed Clinical examination revealed left-sided hemiparesis involving both the upper and lower extremities, impaired independent ambulation, and signs of dysphagia. The patient was generally weak, with reduced muscle strength in the left extremities. Magnetic resonance imaging demonstrated a mass lesion was identified in the right cerebral hemisphere. The patient underwent a right-sided pterional craniotomy with surgical resection of the right temporal lobe tumor. Histopathological and immunohistochemical examination demonstrated diffuse expression of CD68 and CD163 in macrophages and giant cells, with focal expression of Factor XIIIa and S100. Immunohistochemical staining for CD1a was negative. The morphological and immunophenotypic findings were consistent with juvenile xanthogranuloma (JXG).No data regarding cerebrospinal fluid (CSF) analysis obtained by lumbar puncture were available. During the course of treatment, the patient received CapmaXen (capmatinib) for 2 days and Kotellic (cobimetinib) for 12 days.

Conclusion

JXG Juvenile xanthogranuloma should be considered in the differential diagnosis of intracranial mass lesions in pediatric patients, particularly in cases with atypical neurological manifestations and no characteristic cutaneous involvement. Histopathological and immunohistochemical evaluation is essential for establishing an accurate diagnosis, especially in patients with isolated or atypical intracranial disease.

Introduction

Juvenile xanthogranuloma (JXG) is an uncommon non-Langerhans cell histiocytic disorder that predominantly affects infants and young children. It most commonly presents as a solitary cutaneous lesion; however, extracutaneous and systemic involvement has also been described [1, 2]. Although extracutaneous JXG may involve several organs, involvement of the central nervous system (CNS) remains an uncommon and clinically challenging manifestation [2, 3].CNS JXG can occur as an isolated

lesion or as part of multisystem disease and may involve different anatomical compartments of the neuroaxis [3–5]. The clinical presentation is highly variable and depends largely on the location and extent of the lesion. Reported neurological manifestations include headache, seizures, ataxia, cranial nerve deficits, motor weakness, and other focal neurological abnormalities [3, 5]. Neuroimaging findings are also heterogeneous, and CNS JXG may mimic primary brain tumors, hematologic malignancies, other histiocytic disorders, infectious processes, or granulomatous diseases [5].Consequently, radiological findings alone are generally insufficient to establish a definitive diagnosis, and histopathological examination with immunohistochemical characterization plays a central role in confirming JXG [3, 4]. Typical immunophenotypic findings include expression of histiocytic markers such as CD68 and factor XIIIa, whereas CD1a is generally negative, supporting differentiation from Langerhans cell histiocytosis [3].Because intracranial JXG is rare, standardized therapeutic strategies have not been established, and management is generally individualized according to the anatomical location, extent of disease, clinical manifestations, and feasibility of surgical resection [2, 4, 6].

Here, we report a rare case of intracranial JXG presenting as a right temporal lobe mass associated with progressive neurological symptoms. The case highlights the diagnostic challenges of CNS JXG and the importance of integrating clinical, neuroimaging, histopathological, and immunohistochemical findings for accurate diagnosis.

Here, we describe a case of JXG in a 7-years-old girl presenting with unusual feature. We discuss the clinical presentation, imaging characteristics, pathological findings, differential diagnosis, treatment, and outcome.

Case Presentation

A 7-year-old girl was admitted to hospital with complaints of the patient presented with headache, left-sided upper and lower extremity weakness, inability to ambulate independently, nausea, vomiting, dysphagia, dyspnea, and generalized weakness.

According to the parents, the symptoms had first appeared approximately 5 months before admission and were characterized by the patient initially experienced intermittent episodes of weakness in the left upper and lower extremities. Over time, the left-sided weakness became progressively more pronounced. Subsequently, severe headaches developed, accompanied by further progression of the motor weakness, eventually resulting in an inability to walk independently.

The patient was born from the mother’s third pregnancy and third delivery, at term via spontaneous vaginal delivery. Living and socioeconomic conditions were satisfactory. The patient had no known history of chronic medical conditions.

Neurological examination revealed the patient was conscious, with a Glasgow Coma Scale score of 15. During the examination, the patient was distressed and crying because of severe headache and was poorly cooperative with the examination. Commands were followed within the limitations imposed by

the neurological deficits. Mild nuchal rigidity was noted. Voluntary movements of the upper extremities were preserved, whereas voluntary movements of the lower extremities were absent. Bladder and bowel function remained intact. Serial magnetic resonance imaging demonstrated rapid tumor progression, multifocal dissemination, and an increasing mass effect.

Laboratory investigations revealed a hemoglobin level of 118 g/L and an erythrocyte count of 5.29 × 10^{12}/L. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were 16 U/L and 23 U/L, respectively. Serum creatinine was 71 μmol/L, and blood urea was 2.4 mmol/L. Urinalysis revealed no pathological abnormalities.

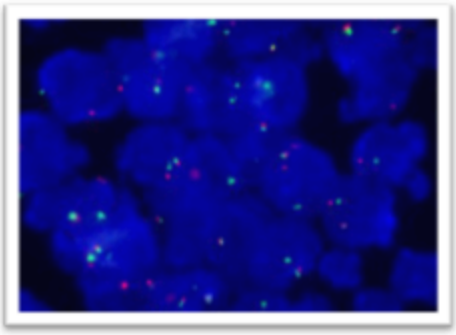
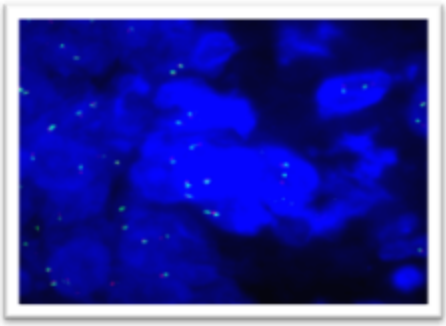
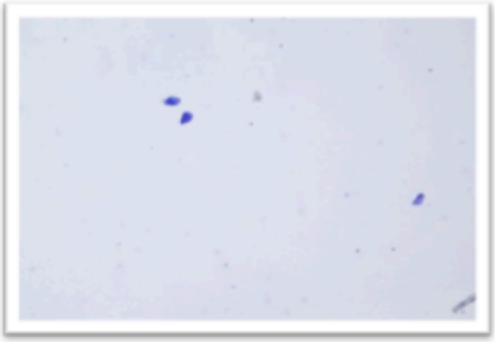
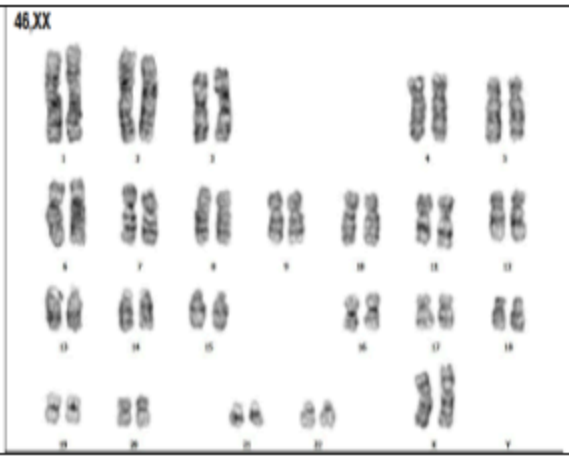
Imaging Findings

2.1Histopathological and Immunohistochemical Findings

Histopathological and immunohistochemical examination of the resected intracranial lesion demonstrated a histiocytic proliferation characterized by macrophages and multinucleated giant cells. Immunohistochemical analysis showed diffuse expression of CD68 and CD163 in macrophages and giant cells, with focal expression of factor XIIIa and S100. CD1a staining was negative. The overall morphological and immunophenotypic profile was considered consistent with juvenile xanthogranuloma (JXG).

PCR analysis of the CSF was negative for cytomegalovirus, herpes simplex virus types 1/2, Epstein–Barr virus, and human herpesvirus 6.

Bacterial culture of the CSF yielded no pathogenic organisms.

Additional molecular testing was performed on the tumor tissue. Fluorescence in situ hybridization (FISH) demonstrated a KIAA1549::BRAF rearrangement in 48% of tumor cells, whereas 52% of tumor cells showed no rearrangement.	
FISH analysis for ALK rearrangement was negative, with rearrangement detected in only 5% of tumor cells, below the laboratory-defined positivity threshold.	
Cerebrospinal fluid (CSF) cytological examination showed an acellular specimen with occasional proteinaceous casts and no identifiable cellular elements.	
Conventional cytogenetic analysis demonstrated a normal female karyotype, 46,XX.	

Based on the morphological and immunohistochemical findings, a diagnosis of **juvenile xanthogranuloma** was established.

2.2 Clinical Course and Outcomes

The patient subsequently received systemic therapy consisting of cytarabine at 100 mg/m² (75 mg per dose; cumulative dose, 750 mg), administered every 12 hours on days 1–5, and cladribine at 6 mg/m²

(4.5 mg per dose; cumulative dose, 22.5 mg) on days 1–5. Cobimetinib was administered orally at a dose of 20 mg once daily on days 1–9.

During treatment, a noticeable clinical improvement was observed, with an improvement in the patient's overall condition and neurological symptoms. However, shortly after completion of therapy, the patient experienced a rapid clinical deterioration.. Despite intensive medical management and ongoing supportive care, no sustained clinical improvement was achieved. The disease continued to progress, accompanied by a gradual worsening of the patient's general condition. Ultimately, despite all therapeutic measures undertaken, the patient died due to progressive disease and associated complications.

Discussion

Juvenile xanthogranuloma (JXG) is an uncommon non-Langerhans cell histiocytic disorder that predominantly affects infants and young children. The disease most frequently manifests as a solitary cutaneous lesion, whereas extracutaneous involvement is considerably less common. Central nervous system (CNS) involvement represents a particularly rare manifestation and may occur either as an isolated intracranial lesion or as part of multisystem disease. In a systematic review of systemic JXG, the CNS was the most frequently involved extracutaneous site, accounting for 40.9% of reported systemic cases. [7]

The clinical manifestations of CNS JXG are highly variable and depend primarily on the anatomical location, size, and extent of the lesion. Unlike cutaneous JXG, which often follows a self-limiting course, intracranial disease may cause substantial neurological morbidity because of local mass effect and involvement of functionally critical structures. Previous reports have described headache, seizures, cranial nerve dysfunction, motor deficits, and other focal neurological abnormalities. Furthermore, neuroimaging findings are nonspecific, making reliable preoperative differentiation of JXG from other intracranial neoplasms difficult. Consequently, tissue examination remains essential for definitive diagnosis. [8]

Histopathological and immunohistochemical evaluation is central to the diagnosis of JXG. The histological spectrum may include histiocytes, foamy macrophages, inflammatory cells, and multinucleated giant cells. Although Touton giant cells are considered characteristic, their absence does not exclude the diagnosis. Immunophenotypically, JXG typically expresses histiocytic markers, including CD68 and factor XIIIa, whereas CD1a is generally absent, an immunophenotypic pattern that helps distinguish JXG from Langerhans cell histiocytosis. [9]

In the present case, histopathological and immunohistochemical examination demonstrated a histiocytic proliferation with macrophages and giant cells showing diffuse CD68 and CD163 expression and focal factor XIIIa and S100 expression, while CD1a was negative. This morphological and immunophenotypic profile supported the diagnosis of JXG. The absence of CD1a expression was particularly useful in the differential diagnosis from Langerhans cell histiocytosis.

A particularly noteworthy finding in our patient was the detection of a **KIAA1549::BRAF rearrangement by fluorescence in situ hybridization (FISH), involving 48% of tumor cells**, whereas ALK rearrangement was not detected. This molecular finding warrants careful interpretation because KIAA1549::BRAF is classically associated with MAPK-pathway activation in certain glial neoplasms and is not, by itself, diagnostic of JXG. Therefore, in the present case, the molecular result should be interpreted in conjunction with the morphological and immunophenotypic findings rather than as an isolated diagnostic marker.

The clinical course in our patient was also notable for aggressive neurological progression. The patient initially developed intermittent left-sided weakness, which subsequently progressed to marked hemiparesis and loss of independent ambulation, accompanied by severe headache and other neurological manifestations. Serial neuroimaging demonstrated progressive intracranial disease with increasing mass effect. Such behavior contrasts with the frequently self-limited natural history of cutaneous JXG and illustrates the potentially aggressive course of CNS involvement. Previous reports have similarly documented progressive, recurrent, and occasionally fatal intracranial JXG, although outcomes vary considerably among patients. [10]

Management of CNS JXG remains challenging because of its rarity and the absence of standardized treatment protocols. Complete surgical resection may provide durable disease control when the lesion is anatomically accessible; however, surgery may be limited by lesion location, multifocal disease, or involvement of eloquent CNS structures. Published cases have described the use of systemic chemotherapy and, less commonly, radiotherapy for unresectable, recurrent, or progressive disease. A review of 43 pediatric intracranial JXG cases emphasized the heterogeneity of presentation and management and did not identify a single clinical or surgical factor that reliably predicted outcome.

Systemic therapy in the present patient included cytarabine and cladribine, together with the MEK inhibitor cobimetinib. A previous report described successful treatment of CNS JXG with cladribine, resulting in radiological resolution after failure of vinblastine-based therapy, although evidence remains limited to individual cases and small series. **[11]** In our patient, clinical improvement was observed during therapy; however, rapid deterioration occurred shortly after treatment completion. Given the observational nature of a single case, this temporal association cannot establish either treatment efficacy or a causal relationship between treatment cessation and subsequent deterioration.

Overall, this case highlights the diagnostic and therapeutic complexity of intracranial JXG. The combination of an uncommon CNS presentation, aggressive clinical behavior, characteristic histiocytic immunophenotype, and the unusual detection of a KIAA1549::BRAF rearrangement makes the case particularly informative. It also underscores the importance of integrating clinical presentation, serial neuroimaging, histopathology, immunohistochemistry, and molecular findings when evaluating atypical intracranial histiocytic lesions. Further accumulation of molecularly characterized CNS JXG cases is needed to clarify the biological significance of MAPK-pathway alterations and to define optimal therapeutic strategies.

This case emphasizes the importance of including JXG in the differential diagnosis of [specific presentation], particularly in pediatric patients.

Conclusion

Juvenile xanthogranuloma is an uncommon non-Langerhans cell histiocytic disorder with a broad spectrum of clinical manifestations. Although cutaneous disease is the most frequent presentation, isolated or atypical central nervous system involvement may present a significant diagnostic and therapeutic challenge.

Accurate diagnosis requires integration of clinical presentation, neuroimaging, histopathological, immunohistochemical, and, when available, molecular findings. JXG should therefore be considered in the differential diagnosis of **intracranial mass lesions in pediatric patients, particularly in the absence of characteristic cutaneous manifestations**.

The present case highlights the potentially aggressive clinical course of intracranial JXG and the challenges associated with its management. The unusual molecular findings and the transient clinical improvement observed during systemic and targeted therapy further emphasize the need for molecular characterization and long-term clinical and radiological monitoring. Additional studies and accumulation of molecularly characterized cases are required to better define the biological behavior of CNS JXG and establish optimal treatment strategies.

Declarations

Conflict of Interest

The authors declare that they have no conflicts of interest related to this publication.

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The authors have nothing to report.

Author Contribution

S.X. collected the clinical data and followed the patient. J.B. wrote the main manuscript text and was responsible for the pathological and molecular data interpretation. A.B. performed the neurosurgical operation and prepared the imaging figures. All authors reviewed and approved the final manuscript.

Patient Consent

Written informed consent for publication of the clinical information and accompanying images was obtained from the patient's parent/legal guardian.

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Figures

Figure 1.

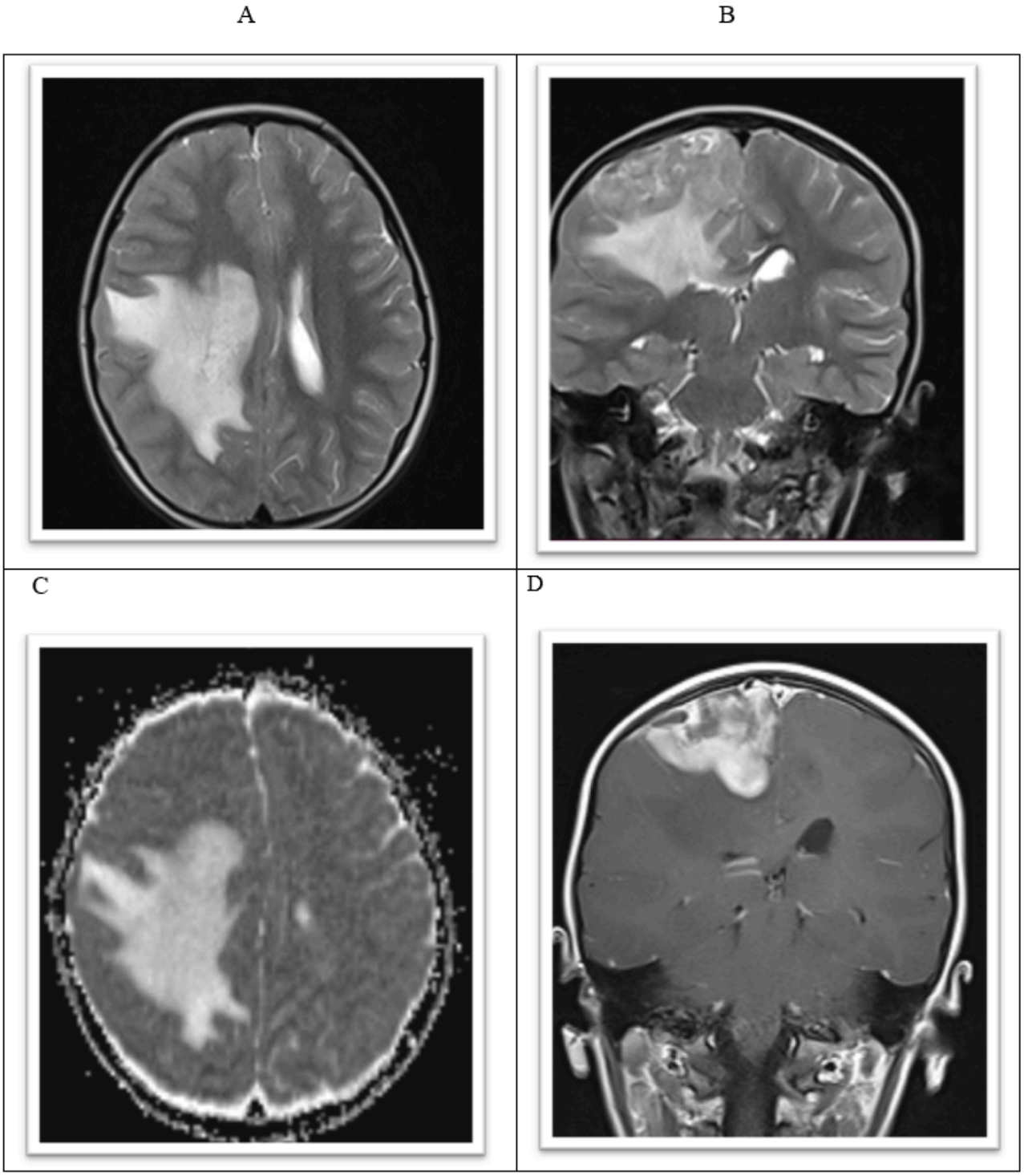


Figure 1

Brain magnetic resonance imaging findings in a patient with intracranial juvenile xanthogranuloma. T2-weighted axial (A) and coronal (B) images demonstrate a right frontoparietal intra-axial mass with extensive surrounding T2-hyperintense vasogenic edema and associated mass effect. The axial ADC map (C) demonstrates the diffusion characteristics of the lesion and surrounding abnormal signal.

Contrast-enhanced coronal T1-weighted imaging (D) demonstrates heterogeneous enhancement of the lesion.