International Journal of Surgery Case Reports 85 (2021) 106265

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.elsevier.com/locate/ijscr

Case report

Multiple intracranial juvenile xanthogranuloma not a straightforward diagnosis (a case report)

Chrystal Calderon [a,*], Amit Ramsingh [a], Rohini Pattron [a], Srikanth Umakanthan [b], Devindra Ramnarine [c]

[a] Department of Surgery, Eric Williams Medical Sciences Complex, North Central Regional Health Authority, Trinidad and Tobago
[b] Department of Paraclinical Sciences Pathology Unit, Faculty of Medical Sciences, University of the West Indies Eric Williams Medical Sciences Complex, North Central Regional Health Authority, Trinidad and Tobago
[c] Honorary Adult & Paediatric Neurosurgeon, Department of Paediatric Surgery, Eric Williams Medical Sciences Complex, North Central Regional Health Authority, Trinidad and Tobago

ARTICLE INFO

Keywords:
Intracranial lesion
Juvenile xanthogranuloma
Lateral ventricle
Pediatrics
Case report

ABSTRACT

Introduction and importance: Juvenile xanthogranuloma (JXG) rarely presents as multifocal intracranial disease in the paediatric population. Therefore, this case of extensive tumour burden, primarily within the lateral ventricles, presented a neurosurgical challenge on numerous fronts.

Presentation of case: This is the case of a 9-year-old male presenting with a 2-year history of visual disturbances. Radiographic imaging demonstrated extensive intracranial masses involving both lateral ventricles, the straight sinus and right cerebellum. A staged tumour resection was planned, targeting the lesions within the right lateral ventricle initially. Complete resection was achieved during surgery. Post-operative morbidity showed a decline in the patient's functional status with respect to mobility and communication, Glasgow outcome scale 3. Extensive immunohistochemical analysis ultimately revealed a diagnosis of JXG. The patient is undergoing chemotherapy, with subsequent surgical resection being dependent on overall recovery.

Clinical discussion: JXG is the most common form of non-Langerhans histiocytosis and typically arises as a cutaneous disorder during early childhood. It is a rare cause of extensive intracranial tumour burden, with limited publications of this kind in the literature. This is even more atypical given the absence of any of the classic cutaneous morphology seen in JXG.

Conclusion: JXG involving the central nervous system is a rare encounter. Therefore, a clear algorithm for the management of a case of extensive intracranial tumours resulting from JXG has not been defined. This only amplifies the difficulty in treating these cases.

1. Introduction

Juvenile xanthogranuloma (JXG) predominantly manifests as cutaneous lesions during childhood. A presentation of isolated, multiple intracranial lesions are extraordinary for this proliferative disorder [1,2]. Attempting to elucidate a histological diagnosis for this exceptional case presentation proved to be arduous. Broad immunohistochemical analysis was essential in attaining a diagnosis of JXG and hence distinguishing it from other pathologies. This was especially difficult in a developing country with low resources. This was a neurosurgical challenge from presentation to rehabilitation. Although JXG is a benign tumour, extensive intracranial disease as in this case, results in life altering morbidity [3].

This work has been reported in line with the SCARE 2020 criteria [4].

2. Presentation of case

A 9-year-old male, with no known medical conditions, presented to the neurosurgery clinic with a 2-year history of visual obscurations. Within the latter 6 months he also noted holocephalic headaches and gait imbalance. These symptoms progressively worsened over time. Initial examination findings demonstrated an ataxic gait on tandem walking without lateropulsion. A globally increased tone was noted with

* Corresponding author at: Savoie 5, French Village, Eric Williams Medical Sciences Complex, Mount Hope, Trinidad and Tobago.
E-mail address: ccalderon88@gmail.com (C. Calderon).

https://doi.org/10.1016/j.ijscr.2021.106265
Received 1 July 2021; Received in revised form 31 July 2021; Accepted 1 August 2021
Available online 3 August 2021

dysdiadochokinesia and multiple beats of clonus elicited at the ankles bilaterally. His Glasgow coma scale was 15 however, verbal responses were delayed on questioning. Of note, there was no relevant drug, social or family history to consider.

Magnetic resonance imaging (MRI) of the brain showed multiple, bilateral intraventricular masses. These were hypointense on T1-weighted imaging with homogenous enhancement depicted with contrast. Additionally, abnormal, enhancing signal foci was depicted along the posterior straight sinus, confluence of sinuses and right cerebellum (Fig. 1). The patient was admitted to the hospital for close neuromonitoring and the commencement of supportive care. Based on the tumour locations and the extent of disease, a staged resection was scheduled after thorough patient/parent counselling.

The patient underwent a right parietal craniotomy and resection of tumour within the atrium, frontal and temporal horns of the right lateral ventricle by the paediatric neurosurgery consultant. During the procedure, there was minimal blood loss, and the tumour was only mildly adherent to the surrounding ventricle wall. Following resection, the patient was admitted to the intensive care unit and computed tomography of the brain was done. Imaging showed satisfactory resection of tumour from the right lateral ventricle with no other significant post-operative changes (Fig. 2). However, on day 3 post-operation, clinical examination revealed significant upper motor neuron lesion signs. There was increased tone throughout and spastic weakness of the left upper and lower limbs. Additionally, his speech showed further significant delay. Repeat imaging showed subtle oedema of the posterior limb of the right internal capsule but no areas of infarction were highlighted.

Histopathology reporting revealed a diagnosis of WHO grade 2 pleomorphic xanthoastrocytoma (PXA), with no significant mitotic activity (<5/hpf) (Fig. 3). Tissue sampling was sent for further immunohistochemistry analysis and demonstrated a negative GFAP, and diffuse strong positive FXIIIa, CD68 and CD163. Based on this evaluation, a final diagnosis of juvenile xanthogranuloma (JXG) was made. After extensive multi-disciplinary team meetings, a long-term adjuvant chemotherapy regime was decided, initiated with vinblastine by oncology. An interdisciplinary approach with oncology, neurosurgery, nutrition enhancement, speech and physical rehabilitation ensues with the aim of patient optimisation.

At 6 months following surgery, he has a Glasgow outcome scale of 3, with slow progress being noted with speech and mobility. Further surgical intervention on the left ventricular tumour is to be determined pending recovery in the future. There has been no change in size or characteristics of the residual tumours at this time.

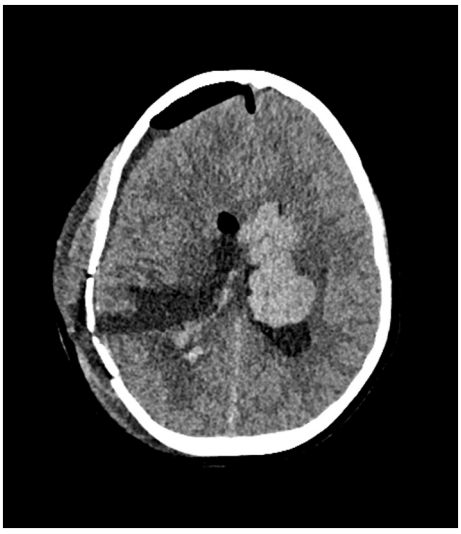

Fig. 2. Computed tomography of the brain axial view showing surgical trajectory and gross total resection of tumour within the right lateral ventricle. Residual tumour noted within left lateral ventricle.

3. Discussion

Juvenile xanthogranuloma (JXG) is considered a proliferative disorder involving monoclonal histiocytes, reminiscent of dermal dendrocytes [5,6]. The estimated prevalence of JXG is 1 case per million children and accounts for 1.5% of neoplastic lesions, with an overall male predominance [2,7]. It is a rare, benign, predominantly cutaneous histiocytic condition. Approximately 15–20% of the characteristic cutaneous lesions of JXG appear at birth and then the majority during the first year of life [1,6]. Extra-cutaneous manifestations are possible in numerous locations such as the eyes, liver, spleen, retroperitoneum and central nervous system (CNS) [2,6]. However, systemic presentations are an atypical form of the disease, being represented in 4% of cases [6,8].

CNS-JXG in the absence of the distinctive dermal features is extremely uncommon, as depicted in this case [3]. Furthermore, there is a paucity of cases of CNS-JXG in the literature, with an incidence of 1–2.3% [1]. It is estimated that 50% of intracranial manifestations will be multifocal, with predominant locations being intra-parenchymal, ventricular and dural-cortical regions [8–10]. Noteworthy, most of the patients with CNS involvement are usually male and of younger age compared to those patients with peripheral involvement [9,11].

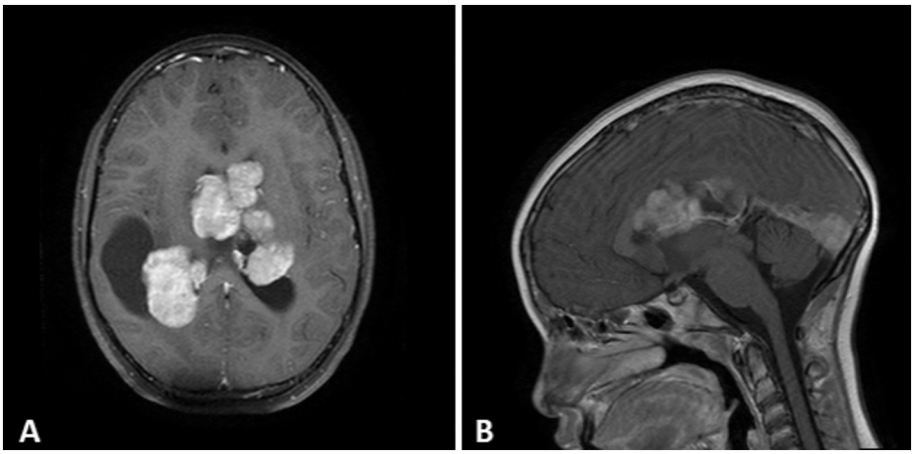

Fig. 1. MRI Brain (A) axial images showing multifocal lesions within the bilateral ventricles, demonstrating gadolinium enhancement; sagittal image (B) demonstrating additional neoplastic disease along the straight sinus.

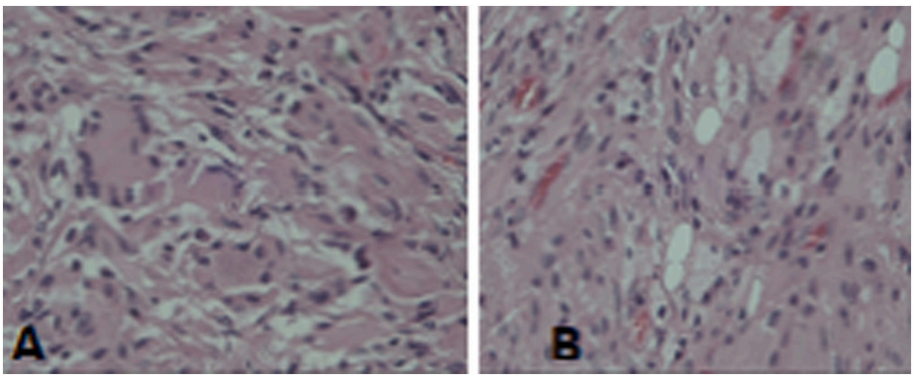

Fig. 3. Histopathology showing (A) tumour with multinucleated giant cells (H&E stained; original magnification, ×400); (B) tumour with xanthomatous change (H&E stained; original magnification, ×400).

Radiographic assessments of intracranial tumours generally aid in narrowing the possible differential diagnoses. This is not the case with JXG, which demonstrates varying manifestations on MRI and may easily mimic other pathologies [5,8].

The histological pattern noted in JXG is varied and can demonstrate multinucleated giant cells of the Touton type and abundant histiocytic monomorphic cells [12]. Interestingly, on inspection of older lesions, the histiocytes can become more xanthomatous and develop lipid in their cytoplasm. They have a foamier microscopic appearance, which can create a diagnostic dilemma with other lesions such as PXA [11,12]. This was demonstrated in the course of elucidating a histological diagnosis here. Most of the cells in JXG express markers of hematogenous origin namely CD45. This is also a positive marker of dendritic histiocytic differentiation [13,14]. The main markers are factor XIIIa, HAM56, CD68 and BRAFV600E. Important negative markers include GFAP, synaptophysin, Langerin (CD207) and CD1a which help to exclude closely related histiocytic conditions such as Langerhans cell Histiocytosis and Erdheim-Chester disease [13,15].

In this case of vast, bilateral ventricular lesions, a single procedure to clear the lateral ventricles in a young patient would likely lead to greater morbidity. We weighed the pros and cons of the increased operative time, requirement of separate surgical sites, neurological deficits, and haemorrhage risk. Consequently, working with the available information, a staged procedure was the best option in this scenario. Unlike the cutaneous form of JXG which is generally self-limiting, not requiring intervention, the management of extensive intracranial tumour burden differs [2,8]. A combination of treatment options exist for JXG such as surgical resection, radiation therapy, chemotherapy and immunotherapy [2,5,9].

A multi-disciplinary team effort continues to remain quintessential in this case, as there is multifocal disease present, some not amendable to surgical resection. Particularly, the tumour component noted at the straight sinus.

4. Conclusion

This rare entity of isolated, multifocal CNS- JXG provides a neurosurgical challenge on several fronts. Ascertaining a diagnosis is reliant on the use of wide immunohistochemistry analysis. Due to the low number of cases noted in clinical practice, deciding on the best surgical and oncological therapy may be daunting. This case demonstrated significant morbidity following the first stage of tumour resection due to the extensive tumour burden. Continued follow-up with a multidisciplinary team continues to be pivotal at this stage of management.

Sources of funding

None to declare.

Ethical approval

This report does not contain any personal information that could lead to the

identification of the patient. Therefore, it is exempt from ethical approval.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

- Dr Chrystal Calderon: conceptualisation, writing- original draft, writing- review and editing, visualisation, project administration
- Dr Amit Ramsingh: conceptualisation, validation, writing- original draft, writing- review and editing
- Dr Rohini Patron: conceptualisation, validation, writing- original draft, writing- review and editing
- Dr Srikanth Umakanthan: resources, validation, writing- review and editing
- Mr Devindra Ramnarine: conceptualisation, validation, investigation, resources, writing- review and editing, project administration

Registration of research studies

N/A.

Guarantor

Mr. Devindra Ramnarine.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

None to declare.

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