Primary intraosseous xanthoma of the frontal bone in a child: illustrative case

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BACKGROUND Skull lesions are a common finding in children, with dermoid cysts and eosinophilic granulomas observed most frequently. However, primary intraosseous xanthomas of the calvaria, which are lytic, expansile lesions that develop without underlying hyperlipidemic disease, are rare in children, with only one prior case reported.

OBSERVATIONS The authors describe the case of a healthy 6-year-old male who presented with a 2-month history of an enlarging midline skull mass that developed after a recent minor trauma. Imaging showed a full-thickness, lytic frontal bone lesion with an aggressive appearance and heterogeneous contrast enhancement. The patient underwent gross-total resection of the lesion with placement of a mesh cranioplasty. Histopathology revealed a primary intraosseous xanthoma. The patient was discharged on postoperative day 2 and required no further treatment at the 1-month follow-up.

LESSONS This is the first reported case of a primary intraosseous xanthoma in the frontal bone of a pediatric patient. It emphasizes the need to include primary xanthomas in the differential diagnosis for pediatric skull lesions, particularly when the lesion has an aggressive radiographic appearance or the patient has a history of focal trauma. Furthermore, our findings indicate that resection, together with subsequent monitoring for lesion recurrence, is an adequate first-line treatment.

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or new neurological phenomena. On physical examination, he was neurologically intact, and the lesion was soft and nontender to palpation. In addition, the overlying skin was intact without erythema or drainage. Computed tomography (CT) scanning of the head revealed a full-thickness, 3 × 3 cm isodense lesion located within the frontal bone (Fig. 1). T1-weighted magnetic resonance imaging (MRI) demonstrated the same 3 × 3 cm mass with a heterogeneous appearance and heterogeneous contrast enhancement (Fig. 2A–C). T2-weighted MRI similarly showed distinct areas of hypo- and hyperintensity within the lesion as well as possible dural displacement without superior sagittal sinus involvement. All laboratory tests, including the patient’s lipid panel, were within normal limits.

The patient was taken to the operating room for resection. During exposure, it was noted that the lesion appeared to invade the outermost layer of dura. The lesion, including the impacted dura, was completely excised, and the surrounding bone was drilled away until healthy bone was encountered. The cranial defect was repaired with titanium mesh. Tissue from the lesion was sent for histopathological analysis, which demonstrated findings characteristic of an intraossous xanthoma (e.g., abundant foam cells, multinucleated giant cells). Postoperative MRI was performed immediately after surgery and showed gross-total resection, as well as an intact cranioplasty and superior sagittal sinus (Fig. 3).

The remainder of the patient’s hospital course was uncomplicated, with no postoperative concerns and well-controlled pain. He was discharged home on postoperative day 2 with instructions to follow-up in 1 month. At the follow-up, the patient reported no new symptoms. Physical examination at that time revealed no neurological deficits and an intact incision.

Patient Informed Consent
The necessary patient informed consent was obtained in this study.

Discussion
Observations
We reported on the first primary intraosseous xanthoma of the frontal bone in a pediatric patient, which had developed over months after an initial traumatic event. The patient was asymptomatic and fully recovered following gross-total resection, with no known recurrence to date. In the literature, only one other pediatric patient has been diagnosed with a calvarial intraosseous xanthoma. The patient, a 9-year-old male, was similarly asymptomatic and only presented in the setting of a bump on the right upper occipital region of his skull.1 This patient was treated via subtotal surgical curettage, with no progression of the disease at the 1-year follow-up.1 Interestingly, although the patient had no history of a hyperlipidemic disorder, and thus was also given the diagnosis of a primary calvarial xanthoma, he had Hodgkin lymphoma at the time of diagnosis.1 Although it is unclear if the patient was actively undergoing treatment for his malignancy at this time, it is important to note certain chemotherapy agents have been associated with an increased...
such as diplopia, vertigo, and an unsteady gait to otalgia, tinnitus, bone erosion. For instance, patients with temporal bone xanthomas are asymptomatic, and most lesions are nontender to palpation. When symptoms are present, they are unsurprisingly dependent on the location of the lesion and are likely caused by either mass effect or abnormal lipid accumulation in the bone.10,18 However, it is unknown how much of an insult is required to cause xanthoma formation, albeit not of boney origin.14–16 Thus, although infrequently seen, primary intraosseous xanthomas should be considered as a potential diagnosis in children with skull masses.

Lessons
Primary intraosseous xanthomas are exceedingly rare, with fewer than 50 cases documented in the literature since the lesion was first characterized in the 1980s.12,17 Although the pathogenesis of a secondary intraosseous xanthoma is fairly well understood, being attributed to elevated cholesterol levels that then abnormally deposit into bone, the mechanism underlying a primary lesion is more obscure. As was the case in our normo-lipidemic patient, it is believed that local trauma or infection may play a key role in primary intraosseous xanthoma development. The hypothesized underlying mechanism is a robust local inflammatory response due to trauma or infection, leading to an increase in vascular permeability and abnormal lipid accumulation in the bone.10,18 However, it is unknown how much of an insult is required to cause xanthoma formation, and other young, healthy patients have developed such lesions with no recollected history of trauma or infection.

The vast majority of patients with an intraosseous xanthoma are asymptomatic, and most lesions are nontender to palpation. When symptoms are present, they are unsurprisingly dependent on the location of the lesion and are likely caused by either mass effect or bone erosion. For instance, patients with temporal bone xanthomas have reported symptoms ranging from specific cranial nerve palsies such as diplopia, vertigo, and an unsteady gait to otalgia, tinnitus, and hearing loss when the mastoid and inner ear are involved.10 Such variability makes reliance on clinical symptoms difficult, especially in the pediatric population, which often has trouble appropriately verbalizing their ailments. Thus, clinical presentation often does little to aid in the diagnosis of an intraosseous xanthoma, and further workup is essential.

The radiographic appearance of intraosseous xanthomas is similar between children and adults. In the craniofacial region, the typical findings on a radiograph are a well-defined lytic lesion surrounded by a sclerotic margin.2,6,8 Less common, however, bone xanthomas can appear more aggressive with an irregular shape, ill-defined borders, or punched-out margins.2,5,8 CT images generally show an isodense or hypo- and hyperintensity on both T1- and T2-weighted imaging and heterogeneous contrast enhancement.9 In cases that involve the calvaria, careful attention on MRI should be given to the underlying dura and nearby sinuses to rule out possible invasion.2 Although imaging is an important step in lesion characterization, radiographic diagnosis of an intraosseous xanthoma is near impossible given the variability in findings and their often indistinguishable appearance from other lesions. Other similarly appearing masses include lytic boney metastases (e.g., clear cell carcinoma), primary malignant bone tumors, nonsclerosing fibromas, benign fibrous histiocytoma, extranodal Erdheim-Chester disease, Rosai-Dorfman disease, and xanthogranulomatous osteomyelitis.2,6,9,11 Although some of these diseases are less likely to be observed in pediatric patients (e.g., metastatic cancer), which can aid in diagnostic probability, all options should remain on the differential until a pathological diagnosis can be made.6,8

Given the lack of discernible clinical or radiographic findings, histopathological assessment is required for a correct diagnosis of an intraosseous xanthoma. Histologically, primary intraosseous xanthomas are characterized by macrophage-like mononuclear cells; foam cells with a granular, eosinophilic cytoplasm; multinucleated giant cells; and varying degrees of intertwined fibrous tissue.2,5,6,8–10,19 More specifically, positive CD68 and negative CD1a and S-100 staining is considered a hallmark for diagnosis, as it indicates the presence of abundant foam cells and simultaneously rules out Langerhan’s histiocytosis.5,8 Unlike other lesions on the differential, such as benign fibrous histiocytoma, which intraosseous xanthomas were long thought to be subset of, spindle cells are not a prominent feature of these lesions.2

For primary intraosseous xanthomas, excision or curettage is the gold-standard treatment for both children and adults, with no adjuvative therapies required. Although total resection is preferred, patients have equivocal outcomes with subtotal resections as well, with no reported cases of disease recurrence or progression in those who have undergone complete or partial removal of the lesion.6,11 Thus, although surgeons should strive for gross-total resection, it is not needed to achieve the desired outcome, and clinical judgement should be used in situations where further resection may compromise patient safety or quality of life. Furthermore, it is important to emphasize the need for a rigorous pathological diagnosis, as improper classification of these lesions can lead to over- or undertreatment of the patient’s condition. For instance, for similar lesions such as Langerhan’s histiocytosis, Rosai-Dorfman disease,
and Erdheim-Chester disease, surgery may or may not be recommended alongside a mixture of systemic steroids, chemotherapy, immunotherapy, or radiotherapy. On the other hand, for lesions such as a benign fibrous histiocytoma, observation may be all that is required.

Although primary intraosseous xanthomas are rare and typically do not involve pediatric patients or the calvaria, this report adds to the literature and emphasizes that the diagnosis must be considered when clinically indicated. Although diagnosis can be suggested by clinical or radiographic features, histopathological analysis is needed for definitive characterization and subsequent treatment planning. For patients with a confirmed primary xanthoma, total excision is recommended to eliminate the disease, although subtotal resection has had similar results according to the literature.

**References**


**Disclosures**
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**Author Contributions**

Conception and design: Kundishora, Reeves, Yang, Tucker. Acquisition of data: Reeves, Wong. Analysis and interpretation of data: Madsen, Coyle, Wong, Yang. Drafting the article: Kundishora, Madsen, Reeves, Coyle, Wong, Tucker. Critically revising the article: Madsen, Reeves, Coyle, Nagasawa, Wong, Tucker. Reviewed submitted version of the manuscript: Kundishora, Madsen, Reeves, Coyle, Wong, Yang, Tucker. Approved the final version of the manuscript on behalf of all authors: Kundishora. Administrative/technical/material support: Yang.

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