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CASE REPORT

Surgical considerations in a paediatric case of a large skull-base epithelioid haemangioendothelioma

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Abstract

Intracranial epithelioid haemangioendothelioma (EHE) is a rare intermediate grade vascular tumour with heterogeneous clinical and histopathological behaviour. We present the surgical considerations of an exceptionally large skull-based EHE in an 11-year old female who presented to our institution with headaches and a protuberance over the left parietal area. Magnetic resonance imaging (MRI) demonstrated a left sided 10.5 × 6.6 × 11.1 cm extra-axial tumour arising from the parieto-temporaloccipital region which was continuous with the calvarium. An initial biopsy confirmed EHE. Staged treatment involved preoperative angiography and embolization. The patient underwent an extensive tumour excision and acrylic cranioplasty. Residual tumour persists in the petrous temporal bone. No neurological deficit was sustained. Postoperatively, we proceeded to tumour surveillance rather than adjuvant therapies, and follow-up imaging up to 36 months postoperatively has shown no tumour progression. We illustrate our surgical management of this large EHE and review the literature of this rare pathological entity with variable tumour behaviour and potential role for adjuvant therapy.

Keywords Intracranial epithelioid haemangioendothelioma · Paediatric · Embolization

Abbreviations

EHE Epithelioid haemangioendothelioma

Introduction

Epithelioid haemangioendothelioma (EHE) is an intermediate grade vascular tumour of soft tissue with histological features resembling haemangioma and angiosarcoma [1, 2]. Of approximately 43 cases of primary intracranial EHE in the literature, we believe this is the 12th case of primary intracranial EHE described in a paediatric patient [3–20].

Due to the unpredictable nature of the tumour and its rarity, there is a lack of consensus in treatment strategy for intracranial EHE. In this case report, we describe our surgical management of an EHE and decision-making relating to its vascularity, size, and extent of calvarial and skull-base infiltration.

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Case report

The patient was an 11-year-old female presenting with a 4-month history of headaches and a protuberant mass over her left temporal area detected by her hairdresser. Her neurological and visual examination was otherwise unremarkable.

A non-contrast enhanced computed tomography (CT) brain scan revealed a large left sided parietal/temporal/occipital calcified mass arising from the calvarium down to the mastoid bone. It involved the tegmen mastoideum of the posterior petrous temporal bone but spared the tegmen tympani.

Contrast enhanced magnetic resonance imaging (MRI) demonstrated a 10.5 × 6.6 × 11.1 cm well-circumscribed extra-axial lesion with marked flow voids (Fig. 1a and b). The lesion demonstrated marked peripheral contrast enhancement and no diffusion restriction. There was subfalcine herniation to the right of approximately 10 mm, associated with early obstructive hydrocephalus and trans-ependymal oedema. Further investigations also included a positron emission tomography scan which did not reveal any extra-cranial fludeoxyglucose uptake.

An initial burr hole biopsy was performed which revealed a firm and very vascular lesion. Histopathology revealed EHE. In view of its size and vascularity, a staged approach with an

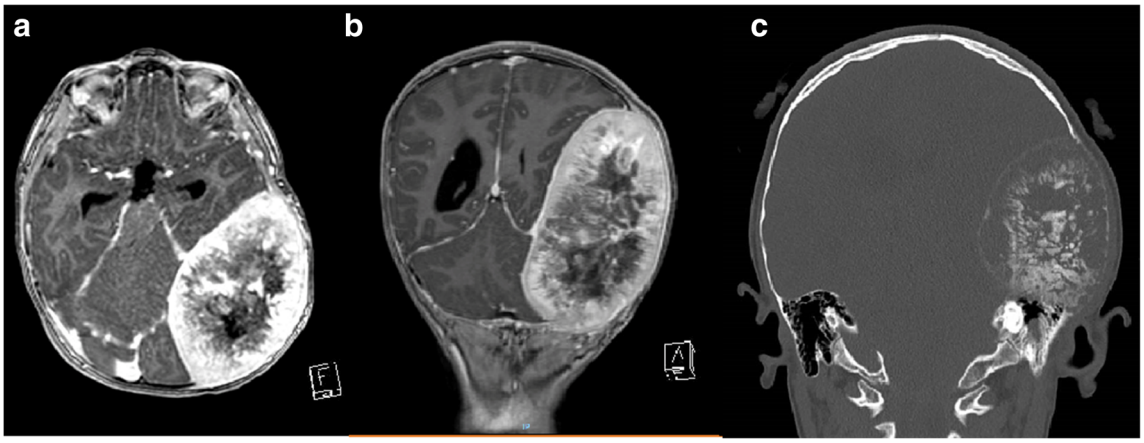

Fig. 1 **a**, **b** MRI scan with contrast demonstrating large extra-axial mass. **c** Preoperative CT-Brain, coronal bone views.

initial preoperative angiographic assessment and subsequent embolization with Onyx glue was deemed appropriate to minimise blood loss (Fig. 2). The proposed extent of surgery was aimed at balancing the proposed benefits of possible cure with attempting total excision, against the risks of hearing loss and other neurological compromise by excising tumour invading the posterior petrous bone and adjacent transverse dural sinus. Recommendation from ear, nose, and throat surgeons was for a partial temporal bone resection with likely skeletalisation of the facial nerve being required. Consent was provided by the

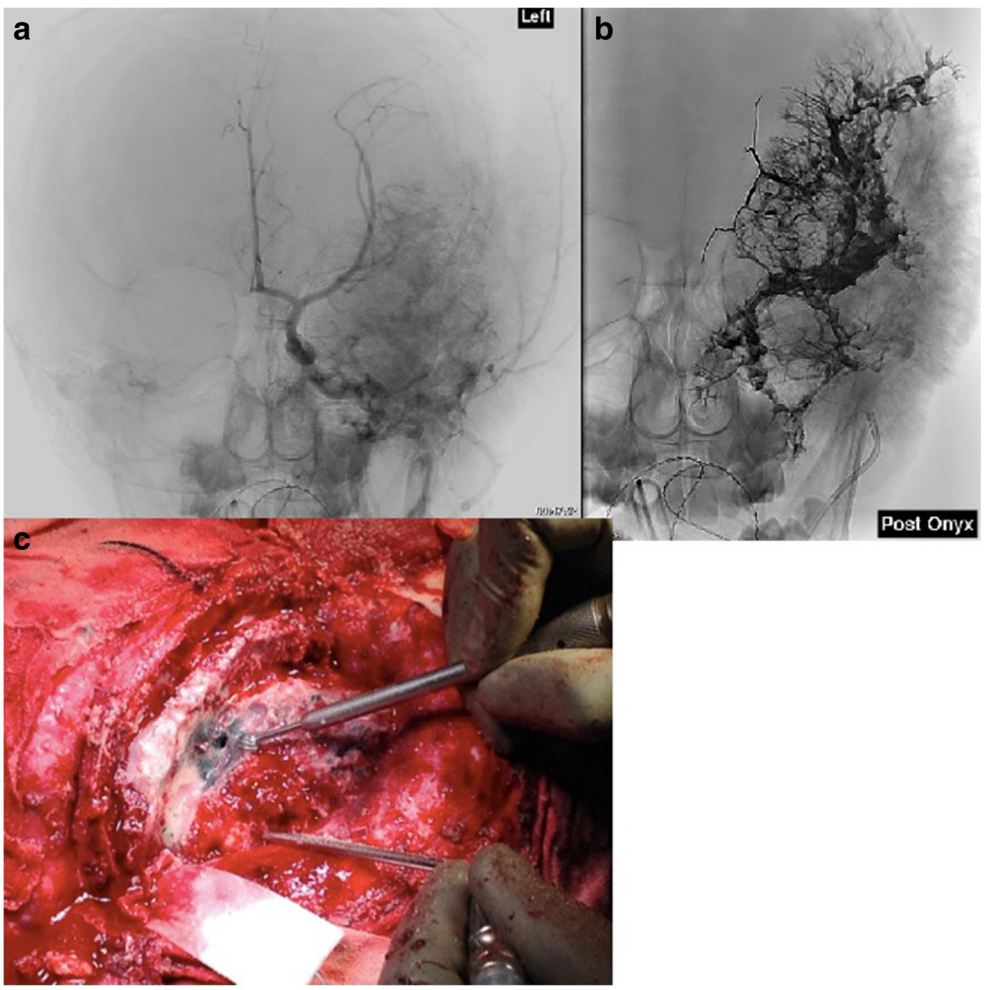

Fig. 2 **a**, **b** Preoperative angiography and Onyx embolization. **c** Intraoperative tumour resection

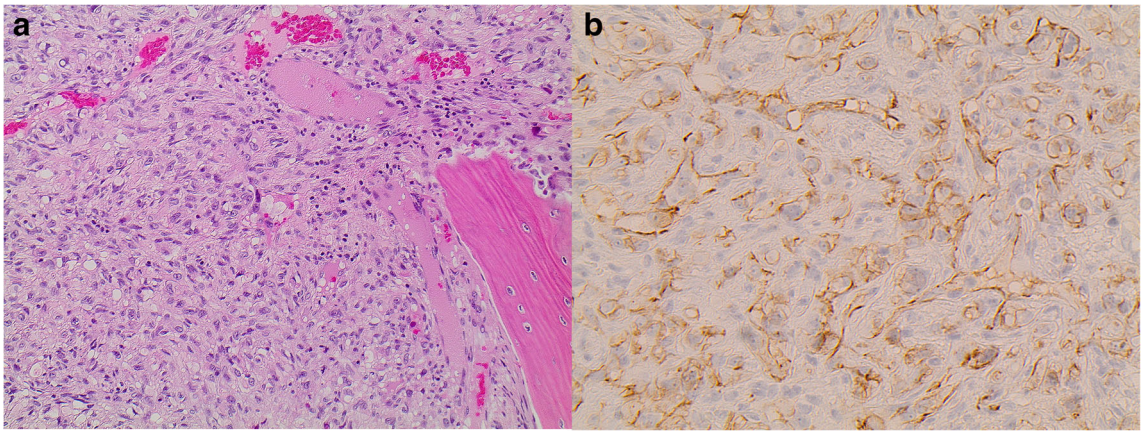

Fig. 3 **a**, **b** Histopathology

patient and family for a subtotal excision with the specific decision made to not perform petrous bone and base of skull excision at this time due to potential morbidity concerns.

Craniotomy and substantial debulking procedure were undertaken. Intraoperatively, the tumour was moderately vascular and very firm requiring extensive drilling. Tumour was able to be mobilised slowly off dura which was not breached. At the level of the petrous bone, tumour invasion was confirmed with large vascular tumour spaces and occluded with bone wax and a pericranial graft. Per the family decision, we did not proceed with temporal bone excision. An acrylic cranioplasty planned preoperatively with CT scan three-dimensional modelling was inserted for a satisfactory cosmetic result. Total operating time was over 7 h. The patient required 1053 ml blood transfusion in total for an estimated 2500 ml blood loss during the case.

Postoperatively, the patient made an uneventful recovery with no focal neurological deficits. MRI and CT imaging demonstrated significant brain re-expansion with an expected small residual tumour mass in the petrous bone.

Microscopically, the tumour had infiltrated mature bone with a mix of viable and necrotic tumour. Tumour cells were polygonal to elongated, often forming vascular channels with rare mitotic figures. Variable nuclear membrane irregularities were seen with some discernible nucleoli. Many cells showed degenerate type nuclear enlargement and hyperchromasia and a moderate amount of ampophilic cytoplasm was seen intracellularly. The background stroma was that of chondromyxoid nature. Immunoperoxidase staining of tumour cells with the endothelial marker CD31 and cytokeratin was positive. Staining with S100, CD68, calcitonin, and epithelial membrane antigen was negative.

Given the mitotic figures were rare, it was concluded the lesion was consistent with a minimally aggressive tumour (Fig. 3).

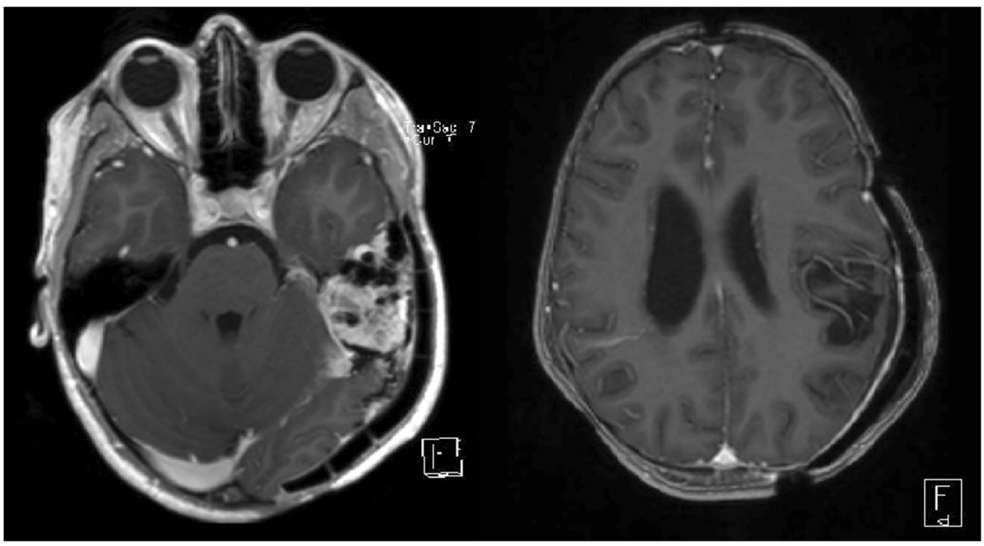

Fig. 4 MRI scan—postoperative with residual temporal tumour

Discussion

This case illustrates a large intracranial EHE in a paediatric patient and describes the necessary treatment considerations due to size, location, and vascularity. The use of preoperative embolization has been described in previous adult intracranial EHE cases [9, 13, 21], and is recommended due to tumour vascularity. In our case, despite embolization, the firmness of tumour and duration of operation still led to ongoing blood loss and required intraoperative blood transfusion.

The term EHE was first described in 1982 as an intermediate grade vascular tumour of soft tissue with features between haemangioma and angiosarcoma [1]. EHE is a rare diagnosis comprising of less than 0.02% of all brain tumours [22]. In the central nervous system, EHE can affect all ages [5, 23]. Intracranial sites previously described include the suprasellar cistern [11, 23], clivus [12], sphenoid wing [13], occipital bone [4], infratemporal fossa [14], parietal lobe [15], tentorium [16], cavernous sinus [17], cervicomedullary junction, and gasserion ganglion [11]. Despite the potential for EHE to be locally aggressive and even metastasise, intracranial EHE tends to be unifocal [23]. EHE has also been reported in infancy affecting the calvarium [20], as well as in older children with multiple skull lesions [18].

Histopathologically, EHE is characterised by loose aggregates of endothelial cells with an epithelioid appearance, embedded in an extra-cellular matrix that is myxoid or rich in hyaluronic acid [2, 23]. Capillary-sized vascular channels are lined by these abnormal endothelial cells which typically contain abundant intracytoplasmic vacuoles, eosinophils, and erythrocytes [6, 8, 24, 25]. Tumour cell atypia increased mitosis and necrosis in conjunction with angioblast differentiation and morphology form the basis of the classification of EHE [26].

EHE can be differentiated from other tumours of endothelial cells such as cavernous haemangioma and angiosarcoma by the lack of dilated vascular space and the microscopic haemorrhage and aggressive cytological features seen in cavernous haemangioma and angiosarcoma respectively [27]. Multiple reports recommend total surgical excision of EHE as the preferred treatment option with the potential for cure, with doubts persisting regarding the usefulness of adjuvant radiotherapy and chemotherapy [13, 18, 20]. In cases where complete resection is not possible, adjuvant radiotherapy and immunotherapy with interferon alpha 2 has led to a reduction of residual tumour in systemic and intracranial EHE cases, although complete resolution with interferon has not been demonstrated in patients without total resection [5, 19, 26]. The use of adjuvant monotherapy bevacizumab, a monoclonal antibody against vascular endothelial growth factor (VEGF) resulted in stable disease over a period of 11, 7, and 12 months respectively for advanced stage lung, liver and bone EHE [8]. Other case reports of EHE describe an indolent course after total resection obviating the need for adjuvant treatment [28].

In our case, in view of the patient's indolent presentation, the lack of preoperative neurological dysfunction and the absence of an elevated mitotic rate, our strategy is that of postoperative surveillance of the residual tumour. Postoperative MRI at 3, 12, 24, and 36 months demonstrated stable appearances of the tumour remnant involving the left petrous temporal bone (Fig. 4). In the event of clinical or radiological progression, consideration of repeat surgical intervention as primary treatment as well as adjuvant therapies is still an available option.

Conclusion

In this case of an exceptionally large intracranial EHE in a paediatric patient, an initial biopsy and the use of preoperative angiography and embolization were utilised. In contrast to previous case reports which have described a combination of surgical excision and adjunctive chemo-radiotherapy, we performed a substantial debulking procedure and acrylic cranioplasty alone. There is an invasive petrous temporal component of the tumour remaining, as per the parent's wishes due to morbidity concerns. In the absence of an elevated mitotic rate, our postoperative strategy is one of clinical and radiological surveillance, with the option of further surgery and adjuvant therapies if progression occurs.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose.

References

1. Weiss SW, Enzinger FM (1982) Epithelioid hemangioendothelioma: a vascular tumor often mistaken for a carcinoma. Cancer 50(5):970–981
2. Goldblum, J.R., Folpe A.L., Weiss S.W., ed. *Enzinger and Weiss's Soft Tissue Tumurs*. 6th ed., ed J.R. Goldblum. 2014, Elsevier Saunders: Philadelphia
3. Zhang J, Wang Y, Geng D Intracranial epithelioid hemangioendothelioma: an unusual CTA finding in one case. Br J Neurosurg 24(3):294–295
4. Amit A et al (2012) Malignant hemangioendothelioma of occipital bone. Chin J Cancer Res 24(2):161–163
5. Zheng J, Liu L, Wang J, Wang S, Cao Y, Zhao J (2012) Primary intracranial epithelioid hemangioendothelioma: a low-proliferation tumor exhibiting clinically malignant behavior. J Neuro-Oncol 110(1):119–127
6. Oliveira PCR, Alcantara FP, Souza-Vianna PE, Brito AP (2012) Cerebral epithelioid hemangioendothelioma with thoracic simultaneous involvement: advanced MRI features. Arq Neuropsiquiatr 70:637–638

7. Aniba K et al (2012) A tragical paediatric case history of intraorbital and intracranial epithelioid hemangioendothelioma. Case Rep Neurol Med 2012:396097
8. Merikas E, Grapsa D, Dikoudi E, Gkiozos I, Boura P, Charpidou A, Kainis E, Syrigos K (2015) Epithelioid hemangioendothelioma treated with bevacizumab: a case series. Cancer Treatment Communications 4:59–64
9. Raheja A, Suri A, Singh S, Kumar R, Kumar R, Nambirajan A, Sharma MC (2015) Multimodality management of a giant skull base hemangioendothelioma of the sphenopetroclival region. J Clin Neurosci 22(9):1495–1498
10. Pacheco JM, Goodman JC, Mandel J (2015) Intracranial epithelioid hemangioendothelioma causing subacute loss of vision. Neurology 85(8):735–736
11. Chen TC, Gonzalez-Gomez I, Gilles FH, McComb JG (1997) Pediatric intracranial hemangioendotheliomas: case report. Neurosurgery 40(2):410–414
12. Rushing EJ et al (1998) Primary epithelioid hemangioendothelioma of the clivus. Clin Neuropathol 17(2):110–114
13. Koh Y-C, Yoo H (2001) Epithelioid haemangioendothelioma of the sphenoid bone. J Clin Neurosci 8(4, Part A):63–66
14. Fernandes AL, Ratilal B, Mafra M, Magalhaes C (2006) Aggressive intracranial and extra-cranial epithelioid hemangioendothelioma: a case report and review of the literature. Neuropathology 26(3):201–205
15. Taratuto AL, Zurbriggen G, Sevlever G, Saccoliti M (1988) Epithelioid hemangioendothelioma of the central nervous system. Pediatr Neurosurg 14(1):11–14
16. Kubota T, Sato K, Takeuchi H, Handa Y (2004) Successful removal after radiotherapy and vascular embolization in a huge tentorial epithelioid hemangioendothelioma: a case report. J Neuro-Oncol 68(2):177–183
17. Phookan G, Davis AT, Holmes B (1998) Hemangioendothelioma of the cavernous sinus: case report. Neurosurgery 42(5):1153–1155
18. Zhu Y, Fan M, Pandey S, Liang W, Chang D (2016) Multiple epithelioid hemangioedothelioma of the skull in a child. Medicine 95(30):e4081
19. Tammam AG, Lewis PD, Crockard HA (1997) Cerebello-pontine angle epithelioid haemangioendothelioma in a 4-year-old boy. Childs Nerv Syst 13(11–12):648–650
20. Carlotti C, Jay V, Rulka J (Jan 2000) Infantile haemangioendothelioma of the pericranium presenting as an occipital mass lesion. J Neurosurg 92(1):156–160
21. Puca A, Meglio M, Rollo M, Zannoni GF (1996) Intracranial epithelioid hemangioendothelioma: case report. Neurosurgery 38(2): 399–401
22. Yeo SK et al (2007) Intracranial epithelioid hemangioendothelioma. J Korean Neurosurg Soc 42(2):129–131
23. Baehring JM, Dickey PS, Bannykh SI (2004) Epithelioid hemangioendothelioma of the suprasellar area. Arch Pathol Lab Med 128:1289–1293
24. Mohan SM et al (2008) Intracranial epithelioid hemangioendothelioma. Childs Nerv Syst 24(7):863–868
25. Rubin, R., Strayer, D. , ed. Rubin's pathology: clinicopathologic foundations of medicine. 6th ed. 2012, Lippincott Williams and Wilkins: Baltimore. 1450
26. Unni KK, Ivins JC, Beabout JW, Dahlin DC (1971) Haemangioma, haemangiopericytoma, and haemangioendothelioma (angiosarcoma) of bone. Cancer 27:1403–1414
27. Chen Y, Chen JQ, Katz RL (2015) Epithelioid hemangioendothelioma: a study of 14 cytopathology cases. Journal of the American Society of Cytopathology 4(3):148–159
28. Chow LT, Chow W, Fong DT (1992) Epithelioid hemangioendothelioma of the brain. Am J Surg Pathol 16(6): 619–625