



Cerebral Epithelioid Haemangioendothelioma

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Abstract

Epithelioid haemangioendothelioma (EHE) is a rare tumour of endothelial cell origin that arises from soft tissue, liver, lungs and rarely, the brain.

We present a case of cerebral EHE in a 43 year old previously well female, who suffered two generalised tonic-clonic seizures. Contrast enhanced CT and MRI brain showed a left frontal lobe vividly enhancing intra-axial lesion at the grey-white junction. Pathological examination revealed a circumscribed lesion with spindled to epithelioid cells, some exhibiting cytoplasmic vacuoles, within a myxoid stroma. Tumour cells demonstrated immunoreactivity with CD31 and patchily with epithelial membrane antigen. These findings were consistent with epithelioid haemangioendothelioma. Follow up MRIs showed no recurrence at 28 months post surgery.

Cerebral EHEs frequently display imaging features that correlate with the underlying pathology and cystic degeneration. Tumours are hypervascular, with a variable pattern of enhancement, but the degree of enhancement is usually vivid, best shown on angiography. Large intralesional large flow voids and rCBV elevation are common.

EHE exhibits malignant potential intermediate between benign haemangiomas and conventional angiosarcoma, and is differentiated histologically. "Malignant EHE" describes tumours exhibiting greater nuclear atypia, tumour cell spindling, necrosis and excessive mitotic activity. These atypical features, present in approximately 33%, correlate with propensity for metastasis.

Current standard of treatment is total surgical excision. Adjuvant and neoadjuvant therapy remain controversial.

Cerebral EHE should be considered a differential if imaging features demonstrate a hypervascular lesion.

Introduction

Epithelioid haemangioendothelioma (EHE) is a rare tumour of endothelial cell origin that arise from soft tissue, liver and lungs [1,2]. Intracranial EHE's are extremely rare, accounting for <0.02% of all brain tumours. The clinical presentation is often non specific and imaging features may mimic other more common entities. The definitive diagnosis is made by pathological examination. It is important to recognise this entity as some may be described as "malignant epithelioid haemangioendothelioma", which correlate with propensity for metastasis. We present a case of cerebral EHE in a 43 year old previously well female.

Case Presentation

A 43 year old previously well female presented to emergency with two episodes of generalised tonic-clonic seizure with no post ictal neurological deficit.

CT brain (Figure 1) demonstrated a solitary 18 mm intra-axial left frontal lobe lesion located at the grey-white junction, hypodense pre-contrast and vividly and homogeneously enhancing. There was associated perilesional vasogenic oedema with moderate mass effect.

Contrast enhanced MR brain (Figure 2) showed the lesion to be T2 hyperintense, T1 hypointense with vivid enhancement and associated vasogenic oedema. Flow voids were not identified within the lesion.

At surgery, a pink gelatinous lobulated tissue was found 2 mm beneath the cortex. Post operative

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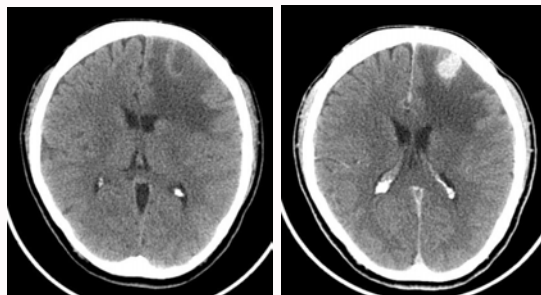


Figure 1: Pre (left) and post (right) contrast CT brain showing hypoattenuating lesion with vasogenic oedema and vivid enhancement.

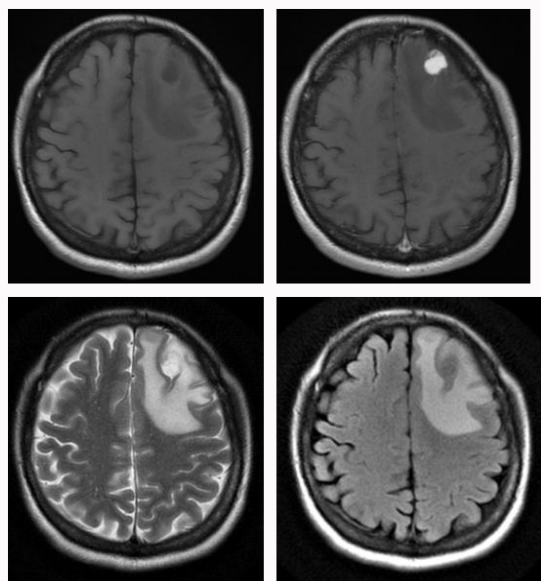


Figure 2: Multisequence MRI – T1 pre (top left) and post (top right) gadolinium T1; T2 (bottom left) and FLAIR (bottom right) demonstrating T1 hypointense/T2 hyperintense intra-axial left frontal lobe lesion with vivid, homogenous enhancement with large amount of perilesional vasogenic oedema.

course was unremarkable.

Microscopic examination (Figure 3a) showed a well circumscribed lesion comprised of spindled to epithelioid cells, some exhibiting cytoplasmic vacuoles, arranged within a myxoid stroma. There was no significant nuclear atypia. Mitotic figures were not identified. The cells were arranged about a prominent fine calibre vasculature lined by plump endothelial cells. Necrosis was not a feature.

Tumour cells showed immunoreactivity with antibodies against the vascular endothelial marker CD31 (Figure 3b) and patchy immunoreactivity of weak to moderate intensity with antibodies against epithelial membrane antigen (EMA). Immunohistochemistry with antibodies against glial fibrillary acidic protein (GFAP), neurofilament, S100 and Melan-A was negative.

Tumour morphology and immunoprofile were in keeping with a diagnosis of epithelioid haemangioendothelioma.

The patient was recurrence free on MRI brain 28 months post discharge.

Discussion

EHE, first described by Enzinger and Weiss et al. [1] in 1982,

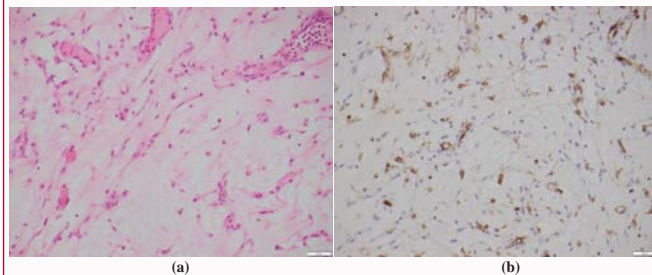


Figure 3: Epithelioid Haemangioendothelioma showing (a) spindled to epithelioid cells, some exhibiting cytoplasmic vacuoles, within a myxoid stroma that are (b) CD31 immunoreactive (CD31 image) x 200 magnification.

is a rare tumour of endothelial cell origin, most often arising in the superficial or deep soft tissue of the extremities, but also well documented in bone, liver and lungs [1,2]. Cerebral examples are extremely rare, accounting for <0.02% of all brain tumours [3-5]. Intracranial EHE may affect individuals of any age, although case reports have demonstrated a bimodal distribution, with a peak in younger children < 1 year of age and another in adults. There is a slight male predilection 1.6:1 in all age populations, although a higher male predominance of 9:2 is observed in the paediatric cohort.

Intra-cranial EHE's display non specific imaging features that correlate with the underlying pathology [6]. On non contrast CT, the lesion is isodense or hyperdense with variable homogeneity. On MRI, it may be hypointense or isointense on T1 and hyperintense on T2. Cystic components are frequently present due to cystic degeneration. These tumours demonstrate hypervascularity on imaging, with variable pattern of enhancement – homogenous or heterogenous, tumoural or nodular – and the degree of enhancement is usually vivid. Large intralesional large flow voids [7-9] and rCBV elevations are common findings, although the latter was not present in our case. Haemorrhage may occur, with subsequent hemosiderin deposits [6]. Radiological differential diagnoses of intra-axial EHE include primary neoplasm such as glioma or lymphoma, metastases, infection or haemorrhage. Extra-axial EHE are often misdiagnosed as meningioma.

Angiography often demonstrates a highly vascular tumour with variable single or multiple arterial supply [3,4,8,10-13].

EHEs exhibit a malignant potential intermediate between that of benign haemangiomas and conventional angiosarcoma [1,2]. The tumour is characterised by a recurrent t(1;3) translocation resulting in a WWTR1-CAMTA1 fusion gene [14-16]. More recently, an alternate YAP1-TFE3 fusion gene has been described in a small subset of EHE, occurring in young adults and showing some distinct morphological features [17]. Approximately 50% of tumours demonstrate origin within or adjacent to a vessel, usually a small vein [2,18]. The primitive vascular differentiation demonstrated in EHE distinguishes it from benign haemangiomas and the conventional angiosarcomas [19]. “Malignant epithelioid haemangioendothelioma” has been used to describe those tumours that exhibit greater nuclear atypia, tumour cell spindling, necrosis and mitotic activity exceeding 1 per 10 high power fields. These atypical features, seen in approximately one third of tumours, correlate with propensity for metastasis [2].

Current standard of treatment is total surgical excision. Recommendation for adjuvant and neoadjuvant chemoradiotherapy remains controversial.

Conclusion

Epithelioid haemangioendothelioma is an extremely rare brain tumour of intermediate grade that can exhibit certain imaging characteristics, particularly large flow voids and vivid enhancement. These features should raise the possibility of the diagnosis.

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