Novel cavernous sinus TSC2/JAK3 mutant hemangioendothelioma in a teenager

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DESCRIPTION

A 14-year-old girl presented with a 2-week history of right-sided facial pain and maxillary region numbness of the teeth and jaw. Neurological examination at presentation revealed right-sided V2 distribution paraesthesia. MRI demonstrated a middle cranial fossa mass abutting the dura of the right cavernous sinus residing in the area of Meckel’s cave (figure 1). Differential considerations at the time included a trigeminal schwannoma, meningioma or a vascular lesion. The patient underwent subtotal resection of the mass, where pathology revealed a moderately cellular vascular lesion composed of cells with small round to oval nuclei with moderate hyperchromasia most consistent with a diagnosis of hemangioendothelioma (figure 2). A follow-up MRI performed 3 months postsurgery showed extensive regrowth of the lesion and the patient underwent a second near-total resection. Repeat pathology demonstrated similar findings, however, the Ki67 staining was upwards of 40%. A next generation DNA sequencing panel consisting of 397 cancer-related genes (table 1) performed on paraffin-embedded formalin fixed tumour of the hemangioendothelioma revealed novel TSC2 (V241I) and JAK3 (R887C) mutations. Germline testing for TSC2 mutations was negative. Given the rapid recurrence and high mitotic index, the patient underwent focal proton radiation therapy. MRI performed 5 years postsurgery and proton therapy shows no recurrent or residual disease and the patient has very minimal V2 distribution trigeminal paraesthesia.

Central nervous system (CNS) hemangioendotheliomas are an extremely rare, low grade, vascular neoplasms, occurring in less than 0.02% of all brain tumours.1 2 Its pathology is composed of aggregates of round-shaped cells with abundant eosinophilic cytoplasm.3 While hemangioendotheliomas are well reported outside the CNS, not much is known about the behaviour of hemangioendotheliomas within the CNS. Neuroimaging findings have been reported for only a few cases making it difficult to diagnose by preoperative imaging alone. A distinction that can be made is that hemangioendotheliomas develop intracellular...

Figure 1 MRI features of central nervous system hemangioendothelioma. Initial preoperative T1-weighted images with gadolinium contrast (A, B) show right middle cranial fossa mass lesion (arrows). Postoperative contrast-enhanced T1-weighted images (C, D) show subtotal resection of the mass (arrows). Follow-up contrast-enhanced T1-weighted imaging (E, F) 3 months after initial surgery show re-expansion of the lesion (arrows). Postoperative contrast-enhanced T1-weighted images (G, H) show subtotal resection of the mass (arrows). Follow-up contrast-enhanced T1-weighted imaging (I, J) 5 years after second surgery and proton therapy reveals no evidence of disease.

Figure 2 Histological features of central nervous system hemangioendothelioma. Neuropathology of the central portion of the tumour (1000×) reveals a moderately cellular vascular lesion composed of cells with small round to oval nuclei with moderate hyperchromasia most consistent with a diagnosis of hemangioendothelioma.

Learning points

► Central nervous system hemangioendothelioma is extremely rare neoplasm that should be included in the differential diagnosis of cavernous sinus tumours.
► The novel TSC2 (V241I) and JAK3 (R887C) mutations reported may provide the potential for non-invasive targeted based therapies.

Table 1  Next generation cancer gene panel

<table>
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<tr>
<th>Genes for which entire coding panel is interrogated</th>
<th>Genes for which potential rearrangements are evaluated</th>
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<tbody>
<tr>
<td>ABL1, ABL2, ACVR1B, AKAP9, AKT1, AKT2, AKT3, ALK, AMED1, APC, AR, ARAF</td>
<td>ABL1, ASPSCR1, BRAF, EGFR, ETV1, ETV4, ETV6, EWSR1</td>
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Images in contrast to hemangiomas with well-formed vascular channels. In summary, the presence of novel TSC2 and JAK3 gene mutations reported in a CNS hemangioendothelioma indicates possible implications for novel biologic based therapies as an alternative to chemotherapy or radiation in the case of tumour recurrence.

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REFERENCES

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