

Rare case of *BRAF V600E* mutant anaplastic pleomorphic xanthoastrocytoma in a 5-year survivor of acute lymphoblastic leukaemia

Jennifer H Yang,¹ Suzanne M Tucker,² Michael L Levy,³ John Ross Crawford⁴

¹Department of Neurosciences, University of California San Diego, La Jolla, California, USA
²Department of Pathology, Rady Children's Hospital, San Diego, California, USA
³Neurosurgery, University of California San Diego, San Diego, California, USA
⁴Neurosciences and Pediatrics, University of California San Diego, La Jolla, California, USA

Correspondence to
 Dr John Ross Crawford;
 jrcrawford@ucsd.edu

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DESCRIPTION

A 20-year-old woman with a history of acute lymphoblastic leukaemia treated at 13 years old with radiation and chemotherapy and a benign cystic mature ovarian teratoma diagnosed at 18 years old presented with 6 weeks of headaches and vomiting. She did not report vision changes or other constitutional symptoms, and her neurological examination was normal. MRI of the brain showed a large right frontal lobe mass with extensive surrounding vasogenic oedema and mass effect with an additional enhancing nodule along the right lateral temporal lobe (figure 1). She underwent gross total resection, and frozen sections demonstrated a hypercellular glial neoplasm with atypical cells, hyperchromatic and pleomorphic nuclei and eosinophilic granular bodies with peak count of 5 mitotic figures per 10 high-power fields (HPF) consistent with an anaplastic pleomorphic xanthoastrocytoma (PXA) WHO grade III (figure 2).¹ Additional areas especially at the interface of the leptomeninges showed papillary growth pattern. Next-generation sequencing of the tumour detected clinically significant variants in *BRAF V600E*, *ATRX*, *CDKN2A*, *CDKN2B* and variants of uncertain clinical significance in *ROS1*, *WT1* and *KMT2D*. The microarray showed a homozygous loss of 9p21.3, which encompasses *CDKN2A* and *CDKN2B*, and high copy gain (x4) of chromosome

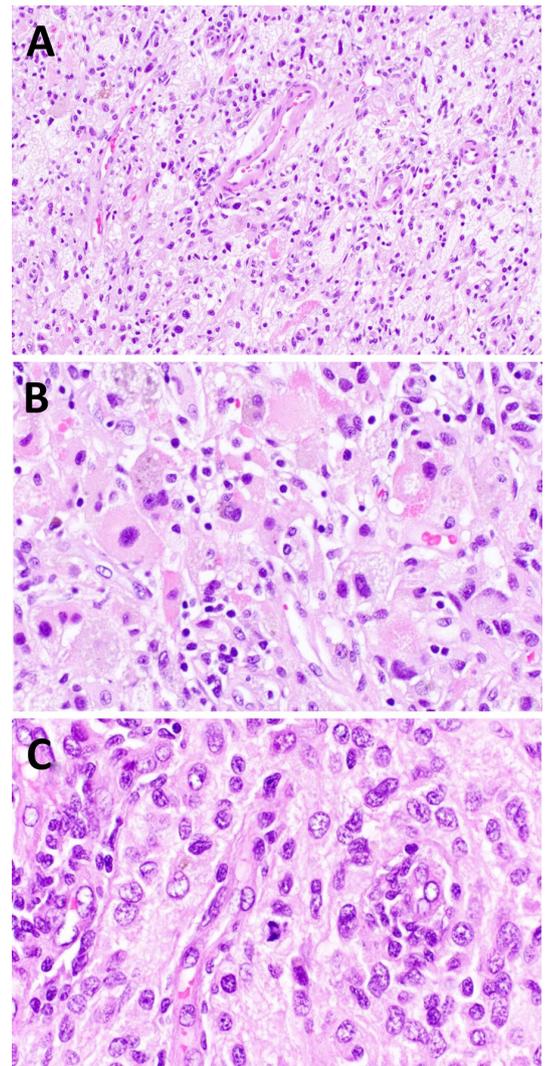


Figure 2 H&E stained sections showing xanthomatous cells, eosinophilic granular bodies with pleomorphic nuclei (A), pleomorphic cells, eosinophilic granular bodies and lymphocytes (B) and mitotic figure with 5/10 HPF (C). HPF, high-power fields.

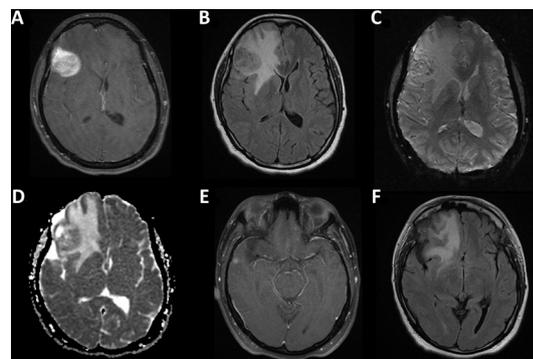


Figure 1 MRI showing mixed solid and cystic mass in the right frontal lobe with extensive vasogenic oedema noted on apparent diffusion coefficient (A) and T2 FLAIR (B and C) with contrast enhancement in the frontal lobe (D). There is additionally an enhancing nodule along the lateral right temporal lobe that may represent a satellite or metastatic nodule (E). There is no associated haemorrhage on susceptibility weight imaging (F). FLAIR, Fluid attenuation inversion recovery.

7. Additional findings include gains of chromosome 2, 3q26.1-q29 (17 cancer genes), chromosome 4, 5p15.33-q31.3 (20 cancer genes) and chromosomes 12, 15 and 20. There was also loss of 8p23.3-q12.1 (15 cancer genes), loss of heterozygosity at 5q31.3-q35.3 (13 cancer genes), 8q12.1-q24.3 (22 cancer genes) and chromosome 9.

PXAs are rare brain tumours seen more commonly in children with overall favourable outcomes.¹ PXA



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with anaplastic features, which are PXAs with mitotic indices $\geq 5/10$ HPF, are now recognised as a separate entity in the revised WHO classification in 2016.² *BRAF V600E* mutations are found in up to 80% of supratentorial grade II–III PXAs,³ although the incidence of *BRAF* mutations are less common in anaplastic PXAs.⁴ Deletions in tumour suppressor genes *CDKN2A* and *CDKN2B* are common in PXA, observed in 93% of anaplastic PXAs, and gains within chromosome 7 are seen in 57% of cases. Other findings include gains in chromosomes 2, 5, 21, 20, 12 and 15.³ Malignancies after treatment of childhood leukaemia have been well reported, and risk factors for developing central nervous system (CNS) tumours include prior CNS leukaemia and cranial irradiation in a dose-dependent manner.^{5–7} Our patient's PXA is most likely secondary malignancy related to her prior radiation therapy. Unfortunately, the molecular details regarding the patient's acute lymphoblastic leukaemia (ALL) and ovarian teratoma were unknown as her previous medical care

was obtained in another country. Nevertheless, this case adds to the current literature of the rare secondary malignancies associated with previously treated childhood cancer. We report the first case of an anaplastic PXA in association with therapy for acute lymphoblastic leukaemia.

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Learning points

- ▶ Pleomorphic xanthoastrocytomas with anaplastic features are WHO grade III tumours with overall favourable outcomes after surgery.
- ▶ *BRAF V600E* mutations and deletions in *CDKN2A* and *CDKN2B* are common mutations seen in patients with PXA.
- ▶ Patients with a history of childhood leukaemia especially those with radiation therapy should be monitored long term to monitor for development of secondary malignancies.

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