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Authors

Chen, Dillon

Crawford, John

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CASE REPORT

Hodgkin's lymphoma in an adolescent previously treated with surgical resection of third ventricular juvenile pilocytic astrocytoma

Dillon Y Chen, John Ross Crawford

Department of Neurosciences and Pediatrics, University of California San Diego, San Diego, California, USA

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

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SUMMARY

We present a case of a 19-year-old man with cervical lymphadenopathy diagnosed with classical Hodgkin's lymphoma 9 years after gross total resection of a third ventricular juvenile pilocytic astrocytoma (JPA). Chemotherapy or radiation therapy was not a part of his initial JPA treatment. Owing to his two primary neoplasms, genetic testing was performed, which revealed heterozygous polymorphisms of unknown significance for CDH1 and p53, and negative BRAF mutation analysis. Our case reports development of classical Hodgkin's lymphoma after JPA in the absence of antecedent radiation and/or chemotherapy, and identifiable genetic predisposition.

BACKGROUND

Central nervous system (CNS) tumours are the most common solid tumours in children.[1] Long-term side effects after the initial treatment with CNS tumours represent a large burden for these patients and their families. Second malignant neoplasms (SMNs) are among the most serious long-term complications.[2 3] SMNs are most commonly associated with radiation and/or chemotherapy.[4–6] Additionally, several genetic syndromes, including neurofibromatosis type 1 (NF1) and Gorlin syndrome, as well as mutations in oncogenes such as BRAF and tumour suppressor genes tumour protein p53 (TP53) have been linked to higher incidence of secondary malignant neoplasms.[2 7]

We report a case of a 19-year-old man who was diagnosed with classical Hodgkin's lymphoma nearly 9 years after surgical resection of a third ventricular juvenile pilocytic astrocytoma (JPA). Neither constitutional nor tumour genetic testing identified specific mutations to explain the presumed predisposition to secondary neoplasm.

CASE PRESENTATION

The patient was diagnosed with third ventricular JPAwhen he was 10 years old. He initially presented with a 1-month history of headache, emesis, ataxia and diplopia. MRI of the brain demonstrated a cystic lesion in his third ventricle (figure 1). He underwent gross total resection and histopathology confirmed the diagnosis of pilocytic astrocytoma (figure 2). He did not require chemotherapy or radiation therapy. His postoperative course was uncomplicated and he was monitored with serial imaging and had no evidence of tumour recurrence. Approximately 9 years after the resection, he presented to the emergency department with painless lymphadenopathy on his neck. No associated constitutional symptoms were reported. MRI of the neck, chest and abdomen revealed extensive lymphadenopathy. Given that the patient had no constitutional symptoms, an infectious aetiology was initially favoured. An extensive infectious work up revealed negative HIV, Epstein-Barr virus (EBV), cytomegalovirus (CMV), tuberculosis (TB), bartonella, toxoplasma, lyme, mycoplasma and West Nile virus tests. Repeat MRI showed interval worsening of the adenopathy, thus a node biopsy was performed. The biopsy confirmed the diagnosis of stage 2A classical Hodgkin's lymphoma (figure 3A, B) with the largest node measuring 5.9 cm. Importantly, the patient's adult brother had a history of non-Hodgkin's lymphoma (NHL), which, however, was presumed to be secondary to his immunosuppression. The patient has no other significant family history of cancer or other significant medical or surgical history, and physical examination revealed no cutaneous or other clinical findings of neurofibromatosis.

The patient was started with chemotherapy and completed four cycles of chemotherapy. Positron

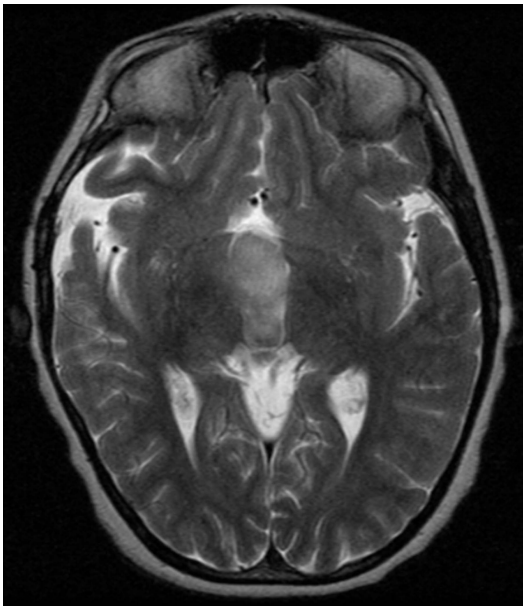

Figure 1 Axial T2-weighted MRI demonstrates juvenile pilocytic astrocytoma at diagnosis filling the third ventricle.

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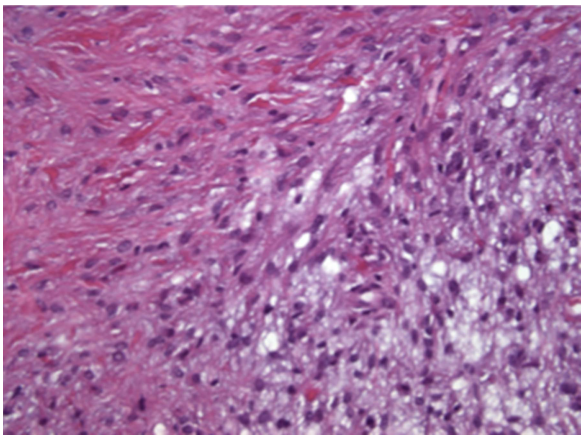

Figure 2 Histopathology of third ventricular tumour reveals a biphasic glial neoplasm with abundant Rosenthal fibres consistent with juvenile pilocytic astrocytoma (200× magnification).

emission tomography CT (PET/CT) imaging studies carried out at the completion of chemotherapy showed lingering quiescent lymphadenopathy. After extensive discussion of the risk of a second malignant neoplasm after radiation therapy, the patient was further treated with involved field radiation therapy.

INVESTIGATIONS

Given the patient's history of JPA and the family history of NHL, several genetic tests were ordered. He was found to be heterozygous for a polymorphism of unknown clinical significance of P53 gene, and CDH1 testing also revealed a variant of unknown clinical significance. Testing for CMMR-D/Lynch syndrome gene was negative as was BRAF mutation for the tumour. Notably, BRAFV600E mutation has been associated with 10–15% of JPA.[8 9]

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for generalised lymphadenopathy is broad. The most common causes of generalised lymphadenopathy are bacterial or viral infections. Other infectious agents such as mycobacteria, fungi, protozoa and spirochetes can also cause lymphadenopathy. Furthermore, although less common, non-infectious aetiologies such as malignancy, autoimmune and lymphoproliferative disorders, and other immunological causes also need to be considered.

TREATMENT

The third ventricular JPA was treated with gross total resection. No chemotherapy or radiation therapy was required following the resection. The patient was followed clinically as well as with serial imaging for recurrence postoperatively. In terms of his treatment for Hodgkin's lymphoma, he completed four cycles of chemotherapy (APVE-PC doxorubicin, bleomycin, vincristine, etoposide, prednisone and cyclophosphamide). He responded well to the chemotherapy, however, PET/CT imaging at the completion of chemotherapy showed quiescent cervical lymphadenopathy, for which he underwent involved field radiation therapy and remains disease-free more than 1 year post-therapy.

OUTCOME AND FOLLOW-UP

The patient remains in remission more than 1 year post-therapy.

DISCUSSION

Central nervous system tumours are the most common solid tumours in the paediatric population.[1] Of the CNS tumours in children, JPAs are the most common. They are usually slow growing, well circumscribed and associated with an excellent prognosis, especially following gross total resection.[10] Mortality associated with CNS tumours has improved over the years due to the advancement of cancer treatments. Thus, increasingly, we are recognising the late effects associated with long-term survivorship, including SMN.[2 11] SMNs after primary CNS tumours are relatively rare; the 10-year estimated cumulative incidence of secondary neoplasm for patients with primary CNS tumours was 1.4–1.7%[2 3] and 25-year cumulative incidence was 6%.[12] However, virtually all cases of SMNs were associated with radiation therapy and/or chemotherapy as part of primary CNS tumour treatment. There was one case where a SMN was reported without antecedent radiation or chemotherapy: the patient was diagnosed with malignant melanoma 3 months after surgical resection of the primary fibrillary astrocytoma.[11] Other risk factors for SMN include genetic predisposition, young age (<2 years) and the type of primary CNS tumour.[2 3 11] Our case demonstrates a rare presentation of classical Hodgkin's lymphoma in a man after the initial complete resection of his JPA in the absence of prior radiation or chemotherapy and identified genetic predisposition. Given the significant mortality and morbidity of secondary neoplasm, and the likelihood that the incidence of SMN will continue to increase as cancer therapy improves, rigorous longitudinal studies are warranted.

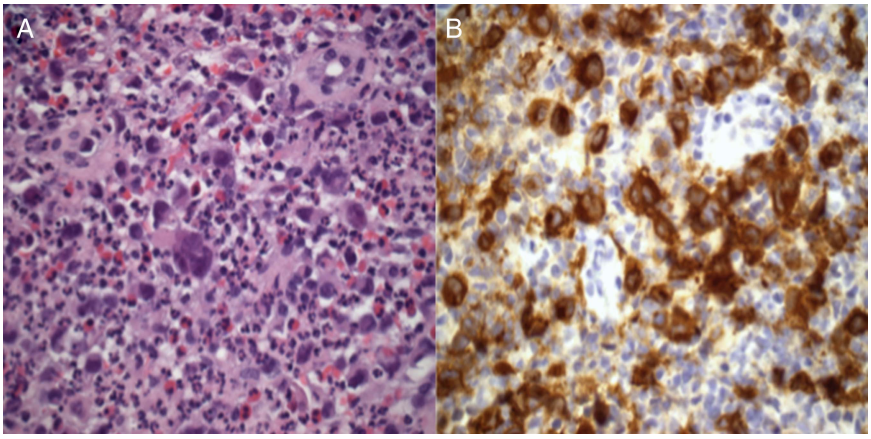

Figure 3 Histopathology reveals characteristic multinucleated giant cells within an inflammatory milieu (A) confirmed by positive CD30 positive staining (B) consistent with a diagnosis of classic Hodgkin's lymphoma (600× magnification).

Learning points

- Long-term complications of cancer therapy, including secondary malignant neoplasm, are becoming more prevalent as survivorship improves.
- Secondary malignant neoplasms can arise after primary central nervous system (CNS) tumours in the absence of therapy.
- Identifiable genetic predisposition syndromes should be considered in patients with previous history of CNS tumours and a secondary malignancy.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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