

have reviewed 20 patients with partial 11q trisomy where CC aplasia was confirmed in 2/4 patients, and with growth and mental retardation in almost all patients.¹⁴

Magnetic resonance imaging is the best modality for evaluation of the CC.¹⁵ Agenesis has been described in 1.6% of consecutive MRI undertaken at a pediatric reference centre,¹⁶ while in other nonpediatric institutions the prevalence of CC aplasia in MRIs done for various nonurgent indications, has been 0.07%.¹² Another series by Marzal et al. found evidence of CC aplasia in seven out of 135 children who had been referred with structural defects in the central nervous system.¹⁰

In some cases a partial agenesis of the CC is accompanied by enlargement of the anterior commissure or the hippocampal commissure that may mimic an isolated callosal splenium.¹⁷ Whether isolated callosal hypogenesis is of clinical importance, and to what degree, is debatable as there are asymptomatic patients where the anomaly is detected by cerebral imaging, and neither developmental disabilities nor interhemispheric transfer dysfunction are observed in these patients.¹⁸

In conclusion, a very young patient with parathyroid adenoma and an incidental CC aplasia has been presented. To our knowledge a relationship between CC aplasia and parathyroid adenoma has not been established. However, from our discussion above there is evidence that a proportion of parathyroid adenomas and corpus callosal aplasias are caused by genetic abnormalities of the same chromosome, that is chromosome 11. Our patient and his family refused genetic analysis. Whether 11q trisomy or monosomy or other types of chromosomal defects related to asymptomatic CC aplasia could lead to gene alterations on chromosome 11 that might trigger parathyroid cell replication, is to be further evaluated by appropriate epidemiological studies. We advise that patients with CC aplasia should be screened for primary hyperparathyroidism, until the possible association of the two abnormalities is clarified.

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Prolonged interval between sentinel pseudotumoral demyelination and development of primary CNS lymphoma

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Abstract

Primary central nervous system lymphoma (PCNSL) can be associated with preceding demyelinating pseudotumoral brain lesions. The ‘sentinel’ demyelinating lesions recede spontaneously or with corticosteroid, and are followed by development of PCNSL typically within 12 months. This report describes a 29 year-old post-partum woman who developed PCNSL 4 years after a biopsy-proven pseudotumoral demyelinating episode. She presented with focal seizures in February 2005. She subsequently developed hemiparesis and raised intracranial pressure. MRI showed two contrast enhancing lesions in the right frontal lobe, which were hypermetabolic on ^{18}F -FDG PET. A provisional diagnosis of tumefactive multiple sclerosis was made. Symptoms recurred despite multiple courses of high dose corticosteroid. Brain biopsy confirmed large B-cell non-Hodgkin’s lymphoma. This patient illustrates the importance of considering PCNSL in patients presenting with a space-occupying lesion, even with previously confirmed demyelination, and that the interval between the two events may be several years.

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1. Case report

A 29-year-old woman initially presented in 2001 with 6 weeks of headache and lethargy, and 4 days of left-sided facial droop and limb weakness. MRI revealed a left heterogenous 4×3 cm contrast-enhancing lesion near the basal ganglia and the posterior limb of the internal capsule (Fig. 1). Clinically, she responded rapidly to a course of oral dexamethasone. A frameless stereotactic-guided brain biopsy of the lesion a week later showed evidence of inflammatory demyelination (Fig. 2). For the following 3 years, she remained healthy, and there was almost complete resolution of the lesion on subsequent MRI studies.

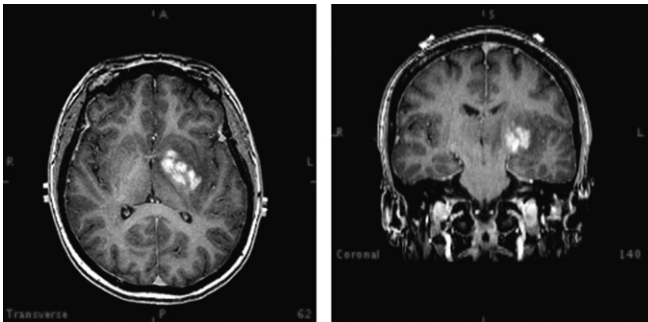


Fig. 1. T1-weighted axial (left) and coronal (right) MRI with intravenous contrast showing a heterogenous mass lesion in the left basal ganglia and posterior limb of the internal capsule.

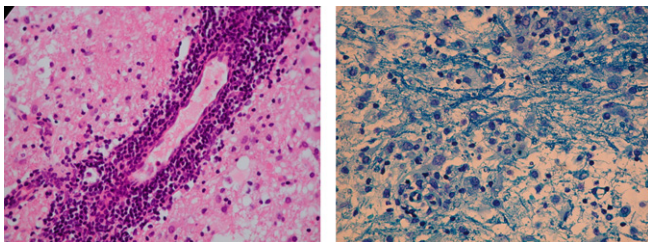


Fig. 2. Haematoxylin and eosin section $\times 400$ (left) showing perivascular cuffing by small lymphocytes, together with reactive changes in the adjacent cerebral tissue. Luxol fast blue stained section $\times 400$ (right) showing some fibres with preserved myelin sheaths in the upper half of the illustration. The lower half shows extensive myelin destruction, with a macrophage infiltrate.

In February 2005, 2 months after giving birth to her first child, she developed frequent seizures characterised by rapid left-to-right eye movement, head-shaking, and occasionally focal jerking of the left limbs. MRI showed three gadolinium-enhancing lesions in the right frontal sub-cortical area and post-ictal EEG revealed an ictal focus in the right frontal lobe. Serology for human immunodeficiency virus (HIV) and vasculitis were unremarkable. A provisional diagnosis of tumefactive multiple sclerosis (MS) was made and she was commenced on high-dose intravenous (IV) methylprednisolone and carbamazepine.

During her stay, she developed severe headache, vomiting, and left hemiparesis over a period of 3 days. CT scan demonstrated two contrast-enhancing masses in the anterior right frontal lobe with extensive vasogenic oedema, and evidence of raised intracranial pressure. One gram IV methylprednisolone was given daily for 5 days. Her neurological symptoms resolved rapidly. A repeat MRI showed persistent oedema and mass effect from the two frontal lobe lesions. She underwent ^{201}Tl -thallium-chloride single photon emission computed tomography (SPECT) which showed two right-sided homogenous frontal hyperintense lesions. Three days later, an ^{18}F -fluorodeoxyglucose (FDG) positron emission tomography (PET) scan showed two intensely FDG avid frontal lesions which correspond to the lesions on the MRI (Fig. 3). Temporal evolution of the lesions was considered to be more consistent with MS, rather than other differentials such as lymphoma, or high-grade glioma. She was discharged home after 10 days.

Two weeks later, focal seizures recurred and she was recommenced on high-dose steroids, and the dose of carbamazepine was increased.

Her seizure control remained poor, and she presented again in June 2005 with left hemiparesis. CT scan showed persistent frontal lesions with 5 mm midline shift. High-dose dexamethasone was commenced, and an urgent brain biopsy was performed. This revealed large B-cell non-Hodgkin’s lymphoma (Fig. 4). She was commenced on methotrexate with dramatic clinical and radiological response. Subsequent pathologic tests and imaging studies did not show involvement of other organs, and a formal

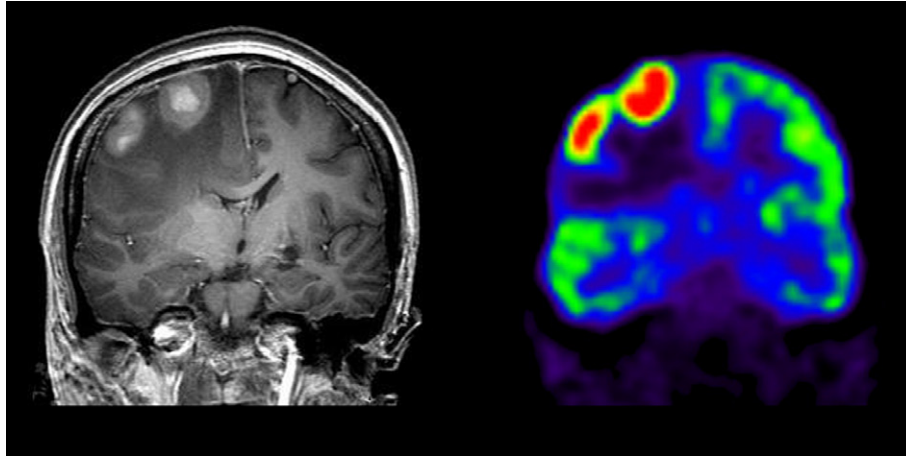


Fig. 3. Coronal T1-weighted MRI (left) and ^{18}F -fluorodeoxyglucose (FDG) positron emission tomography (PET) (right) showing two gadolinium enhancing, hypermetabolic space-occupying lesions in the right frontal region.

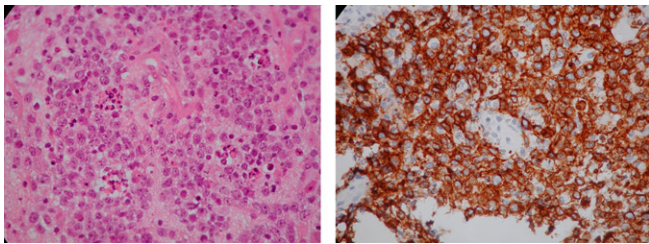


Fig. 4. Haematoxylin and eosin section $\times 400$ (left) showing vascular, perivascular and infiltrating large cell non-Hodgkin lymphoma. Immunohistochemical stain (right) for CD 79a, indicating a B immunophenotype of the tumour cells.

diagnosis of primary central nervous system lymphoma (PCNSL) was made.

2. Discussion

Primary CNS lymphoma is a rare high-grade non-Hodgkin's lymphoma. In immunocompetent patients, they are almost exclusively of B-cell type. The mean age at diagnosis is 60 years, with slight predominance in men. Mortality is high, and recurrence is common despite high-dose chemoradiotherapy.

Primary CNS lymphoma can be associated with preceding demyelinating pseudotumoral lesions, as briefly described in several case reports.^{1–3} However, little is known about this rare occurrence. The 'sentinel' demyelinating lesions recede spontaneously or with corticosteroid, and are followed by the diagnosis of PCNSL typically within 6–12 months.² It has been postulated that the resolution of the sentinel lesion may represent a host immune response to the lymphoma.²

In retrospect, the patient's presentation was consistent with PCNSL with preceding demyelinating pseudotumoral lesions. A unique feature of this case was the relatively long delay of 4 years before the onset of the lymphoma in contrast to previously described cases where PCNSL developed in under 1 year. Although it is possible that the initial lesion

was steroid-treated PCNSL, it is very unlikely for lymphoma to have such a long period of remission.

Another interesting observation is that the PCNSL developed post partum. Very little is known about the effect of pregnancy and childbirth on PCNSL. In general, similar to MS, non-Hodgkin's lymphoma is reported to worsen during the post partum period.^{4,5} It is thought that during pregnancy, hormonal and immune system changes have an immunomodulating effect on these diseases.⁵ The sudden withdrawal of such effects during the post partum period then results in acute exacerbation.

Diagnosing new brain lesions in patients with a preceding history of demyelination is often challenging. While most represent another episode of steroid responsive demyelination, a small number, as in this case, are malignant lesions.

In retrospect, there were several clinical and radiologic features that suggest PCNSL rather than MS in this patient.

An acute neurologic presentation with a space-occupying lesion in a young adult suggests a diagnosis of lymphoma, high-grade glioma, or less likely, tumefactive MS. An initial diagnosis of tumefactive MS was made in our patient given the history of biopsy-proven demyelination, and a rapid initial clinical response to corticosteroid. However, glioma and lymphoma may respond equally well to steroids,⁶ and clinical remission can be achieved occasionally in lymphoma.⁷ Other differential diagnoses include CNS infection such as cytomegalovirus, toxoplasmosis, and brain abscess, but these were thought unlikely given the patient's negative HIV status. Metastatic tumour was unlikely given her age and absence of other symptoms. Vasculitis was unlikely given absence of inflammatory or autoimmune markers.

Several imaging studies were performed in this patient but they did not contribute significantly to the diagnosis. Common to MS, PCNSL, and glioma, the lesions were hypointense on T1-weighted MRI sequence, hyperintense on T2-weighted MRI sequence, and contrast enhancing.⁸ The vasogenic oedema associated with MS is reported to be less extensive compared with high-grade tumours.⁸ The presence of multiple lesions that are typical of MS plaque distribu-

tion, such as in periventricular white matter, may be more supportive of MS.⁸ Therefore, the MRI findings of extensive oedema in our patient and the absence of typical MS white matter lesions did not support the diagnosis of MS.

At present, the role of MRI is confined to monitoring disease progression and treatment response. Serial MRI performed over a period of months without obvious progression is more likely to be MS. A lack of radiologic resolution with corticosteroid, suggests malignant tumour.

²⁰¹thallium SPECT, and ¹⁸F-FDG PET usually show metabolically active lesions in PCNSL. However, neither is specific, with glioma, metastases and infection having a similar appearance, although studies have reported that lymphoma is more FDG-avid than glioma and infection in HIV patients.⁹ ¹⁸F-FDG PET is not performed commonly on patients with active MS. In general, MS lesions have reduced metabolic activity during remission,¹⁰ while the opposite may be seen during a relapse.¹¹

Our patient's ¹⁸F-FDG PET showed persistent hyperintense lesions 3 days after completion of IV methylprednisolone. It has been reported that corticosteroid treatment does not significantly alter FDG uptake in PCNSL.¹²

In summary, it is important to consider PCNSL in patients presenting with space-occupying lesions even with previously confirmed pseudotumoral demyelination. There is no specific imaging method to differentiate PCNSL from aggressive MS, and biopsy may be required for definitive diagnosis. This patient illustrates that the interval between the episode of sentinel pseudotumoral demyelination and development of PCNSL may be several years.

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Solitary cerebral metastasis from transitional cell carcinoma of the urinary tract

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Abstract

We present a patient with a solitary cerebral metastasis from a transitional cell carcinoma of the right renal pelvis in the right occipital lobe with intratumoral hemorrhage. Despite aggressive multimodality management the patient died within 3 months of presentation due to widespread systemic disease.

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