

# Multiple calcified primary central nervous system lymphoma with immunodeficiency in a child

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**Background:** Multiple calcified primary central nervous system lymphoma (PCNSL) is extremely rare in childhood.

**Methods:** We report a 4-year-old boy suffering from multiple calcified B-cell lymphoma in the brain with immunodeficiency.

**Results:** The boy had a history of walking weakness and seizure for 4 months. The serum levels of immunoglobulin G, A and M were decreased. Brain MRI showed multiple lesions which had ring enhancement. CT showed calcification in all of the lesions. The boy was firstly misdiagnosed with multiple chronic brain abscesses. Pathological analysis of biopsy confirmed the diagnosis of anaplastic diffuse large B-cell lymphoma.

**Conclusion:** PCNSL should be included in the differential diagnosis of intracranial mass with calcification.

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**Key words:** calcification;  
immunodeficiency;  
primary central nervous system lymphoma

## Introduction

Primary central nervous system lymphoma (PCNSL) is a rare disease, accounting for 0.3%-6% of all primary brain tumors.<sup>[1-4]</sup> It frequently occurs in 40-60 year old adults,<sup>[1,4,5]</sup> but rarely in children.<sup>[1]</sup> Herein we report a case of multiple calcified PCNSL with immunodeficiency in a 4-year-old boy.

## Case report

The boy was referred to the Pediatric Department, complaining of walking weakness and seizure for 4 months. He had no history of organ transplantation or immunosuppressive therapy but a history of recurrent respiratory infection. Physical examination on admission showed no fever, lymphadenopathy, rales in the lung or hepatosplenomegaly. His left muscle strength was of III grade. White blood cell count was 8060/ $\mu$ L with normal differential, hemoglobin 11.1 g/dL and platelets 274 000/ $\mu$ L. The serum immunoglobulin (Ig) levels were decreased (IgG level, 279 mg/dL, reference range: 660-1039 mg/dL; IgA level, 24 mg/dL, reference range: 58-100 mg/dL; IgM level, 19 mg/dL, reference range: 110-180 mg/dL). Lumbar puncture showed leukocytes of 42/ $\mu$ L without neoplastic cells, protein 95.1 mg/dL, and glucose 53.5 mg/dL. Bone marrow aspiration showed hyperplasia image, obviously in granulocyte series. Skin test to purified protein derivative of tuberculin was negative. Serum antibody IgM to Epstein-Barr virus was positive. Serum antibodies to human immunodeficiency virus and tubercule bacillus were negative. Serum and cerebrospinal fluid antibodies to parasite were negative.

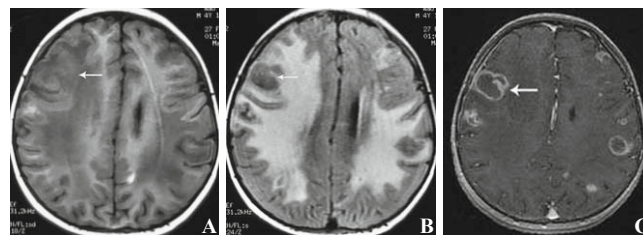
MRI demonstrated that the bilateral cerebral hemispheres, right cerebellar hemisphere and bridge of varolius had multiple abnormal signals with edema. The mass effect of the lesion was little. The lesion was hypointense and hyperintense on T1-weighted and fluid-attenuated inversion recovery images respectively (Fig. 1 A, B). Contrast-enhanced T1-weighted images showed that the lesion had notable ring enhancement

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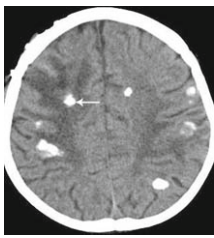
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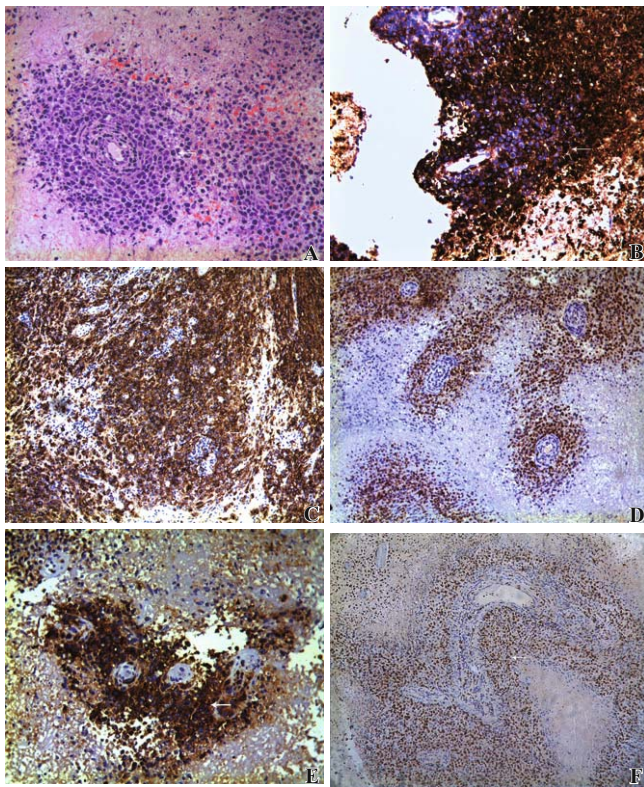


**Fig. 1.** MRI demonstrating multiple lesions in the bilateral cerebral hemispheres. **A:** T1-weighted; **B:** fluid-attenuated inversion recovery; **C:** contrast-enhanced T1-weighted.

(Fig. 1C). Unenhanced CT images showed that all the lesions had calcification (Fig. 2). Contrast-enhanced CT scans of the chest and abdomen showed no signs of lymphoma or lymphnode enlargement. The boy was diagnosed with multiple chronic brain abscesses initially. He did not receive any corticosteroids before CT scan, MRI scan and brain biopsy. Mannitol was used to manage intracranial hypertension. Anti-infection therapy with ceftriaxone, mepem, cefotaxime



**Fig. 2.** Unenhanced brain CT scan demonstrating all of the lesions with calcification.



**Fig. 3.** **A:** Photomicrograph of biopsy specimen demonstrating a characteristic angiocentric pattern, forming cuffs of tumor cells within and around cerebral blood vessels (original magnification  $\times 200$ ); **B:** Immunohistochemistry indicating leukocyte common antigen (+) (original magnification  $\times 200$ ); **C:** Immunohistochemistry indicating L26 (+) (original magnification  $\times 100$ ); **D:** Immunohistochemistry indicating CD79a (+) (original magnification  $\times 100$ ); **E:** Immunohistochemistry indicating CD30 (+) (original magnification  $\times 200$ ); **F:** Immunohistochemistry indicating Ki67 (+) (original magnification  $\times 100$ ).

and vancomycin was given for 2 months. But the lesions did not shrink in size. So a biopsy of the lesion was performed. Histobiologic analysis showed a characteristic angiocentric pattern, forming cuffs of tumor cells within and around cerebral blood vessels (Fig. 3A), and immunohistochemistry staining was positive for Ki67, leukocyte common antigen (LCA), L26, BCL2, CD79a and CD30 antibodies (Fig. 3B-3F). Ki67 labeling index of the tumor cells was 50%. Pathologic analysis confirmed the diagnosis of anaplastic diffuse large B-cell lymphoma (DLBCL). The parents refused continued treatment for the boy because of economic burden.

### Discussion

It is very difficult to determine the true incidence for PCNSL. Because of the rarity of this condition, much of the available information is derived from small pediatric case series or extrapolated from larger adult studies. No more than 30 cases have been reported over the past two or three decades.<sup>[2,6,7]</sup> The incidence of PCNSL remains stable in the immunocompetent population, but is decreasing in the immunosuppressed population.<sup>[8]</sup> Primary immunodeficiencies are genetic defects of some components of immune response. They are characterized by no or low response to infectious agents and a high prevalence of autoimmune manifestation and lymphoproliferative diseases. It can present at any age in patients with a history of recurrent infections.<sup>[9]</sup> Epstein-Barr virus has been implicated as an effector for lymphomagenesis in immunosuppressed individuals.<sup>[10]</sup>

PCNSL is a most common DLBCL which may appear as a nodule, solitary or multiple neoplasm, or as a diffusely infiltrative perivascular neoplasm. Primary and secondary central nervous system lymphoma is morphologically indistinguishable on CT or MRI, including T- and B-cell PCNSL. The identification of PCNSL mainly depends on pathological examinations. The tumor cells are composed of densely packed lymphoma cells with a characteristic pattern of dense concentric cuffing along the perivascular spaces. Immunohistochemistry examination was usually positive for LCA, L26 and CD79a antibodies, but anaplastic DLBCL expresses CD30 antigen.<sup>[4]</sup>

On CT scan, PCNSL demonstrates as iso- or hyperdense to grey matter, with little surrounding edema and disproportionately little mass effect. Calcification is accepted as being a rare feature of PCNSL which occurs most frequently after radiotherapy or chemotherapy.<sup>[11]</sup> To our knowledge, only two reports described calcification of untreated PCNSL in adults.<sup>[1,11]</sup> The present case is the first

to report a multiple calcified untreated PCNSL in children. Radiographically, all PCNSLs show contrast enhancement on CT or MRI. The majority of immunocompetent patients show dense, homogeneous enhancement. The frequency of ring enhancement is rare in such immunocompetent patients before treatment.<sup>[11]</sup> This pattern of enhancement is more frequently seen in the posterior fossa and immunocompromised patients.<sup>[12,13]</sup> The administration of corticosteroids must be avoided because the lympholytic properties of PCNSL may render a brain biopsy non-diagnostic. Also corticosteroids can modify the enhancement pattern, and should not be administered prior to CT and MRI (except in case of severe intracranial hypertension).<sup>[11]</sup>

It is difficult to make a correct diagnosis of PCNSL before biopsy. It would be differentiated from glioma, metastases, meningioma, vasculitis, abscess, parasitic disease, multiple sclerosis and secondary central nervous system lymphoma.<sup>[3,4]</sup> Early brain biopsy is essential to the diagnosis of PCNSL.

It is also difficult to determine the best therapeutic strategy for PCNSL in childhood. Except for human immunodeficiency virus-related PCNSL, the prognosis of this tumor type is significantly better in children than in adults. The majority of children with PCNSL can achieve long-term remissions after intensive chemotherapy (high-dose methotrexate and cytarabine) alone without cranial irradiation (an estimated 5-year event-free survival rate of 70%), and cranial irradiation can induce relapse of the disease.<sup>[6]</sup>

In summary, PCNSL with multiple calcifications is unusual. Pediatricians and radiologists should include PCNSL in the differential diagnosis of intracranial mass with calcification.

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**Ethical approval:** Not needed.

**Competing interest:** None declared.

**Contributors:** Zhu JQ wrote the main body of the article. All authors contributed to the design and interpretation of the study.

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