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Peri-optic nerve infiltration during leukaemic relapse: MRI diagnosis

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Abstract *Background*. A 10-year-old boy with a history of acute lymphoblastic leukaemia (ALL), but without previous evidence of central nervous system involvement, presented with seizures 3 years after complete remission.
Materials and methods. MRI showed bilateral enlargement of the optic nerves despite normal ophthalmological examination.
Results. Only the third cerebrospinal fluid examination showed 2 % blasts without concomitant bone-marrow infiltration. Enlargement of the optic nerves was consistent with bilateral leukaemic peri-optic nerve infiltration. The appearances returned to normal after chemotherapy.
Conclusion. The optic nerves are a potential site of relapse in patients with systemic and meningeal ALL, even in the absence of ophthalmological signs.

Introduction

Bilateral optic nerve enlargement in children has numerous aetiologies, but in a context of previous history of ALL, optic nerve enlargement, enhancing after gadolinium, should suggest the diagnosis of leukaemic infiltration, even in the absence of previous leukaemic CNS involvement.

Case report

A 10-year-old boy was admitted because of generalised tonic-clonic seizures. Five years before the present admission, he had been treated for early B-lineage acute lymphoblastic leukaemia (ALL). At that time, there was no evidence of central nervous system (CNS) involvement. He achieved complete remission after four-drug induction therapy and remained on chemotherapy for 2 years according to protocol CLCG-EORTC no. 58881, which includes high doses of intravenous and intrathecal methotrexate for CNS prophylaxis.

On the present admission, general, neurological and ophthalmological examinations (including visual fields, acuity and fundoscopy) were normal. Laboratory studies showed normal haematological data. Bone-marrow aspirate was normal. EEG showed diffuse, high-amplitude delta activity. Cerebrospinal fluid (CSF) analysis showed high protein level (3.12 g/l) and pleocytosis (72 nucleated cells/mm^3) with 60 % neutrophils and 40 % lymphocytes. There were no blasts. Bacterial and viral cultures, as well as serology, remained negative. MRI showed bilateral asymmetrical enlargement of the optic nerves extending to the chiasm. After intravenous gadolinium, enhancement was observed, predominantly at the periphery of the nerves (Fig. 1).

Repeat CSF, obtained 7 days after the first sample, did not show any significant change. Two weeks after admission, seizures recurred and a third CSF examination showed 2 % blasts. Bone-marrow aspirate was still normal. The diagnosis of late, isolated, CNS leukaemic relapse in the form of carcinomatous meningitis with bilateral peri-optic nerve leukaemic infiltration was proposed, and chemotherapy was started. MRI showed gradual decrease of the optic nerve enlargement within 4 weeks after initiation of anti-leukaemic therapy (prednisone, dexamethasone, vincristine and methotrexate). The lesions disappeared completely after 2 months (Fig. 2). The child has been in complete remission for 2 years after this recurrence.

Discussion

Our patient most probably had bilateral peri-optic nerve leukaemic infiltration. It was detected by MRI performed in the context of a non-specific meningo-encephalitis. Bilateral optic nerve enlargement in children

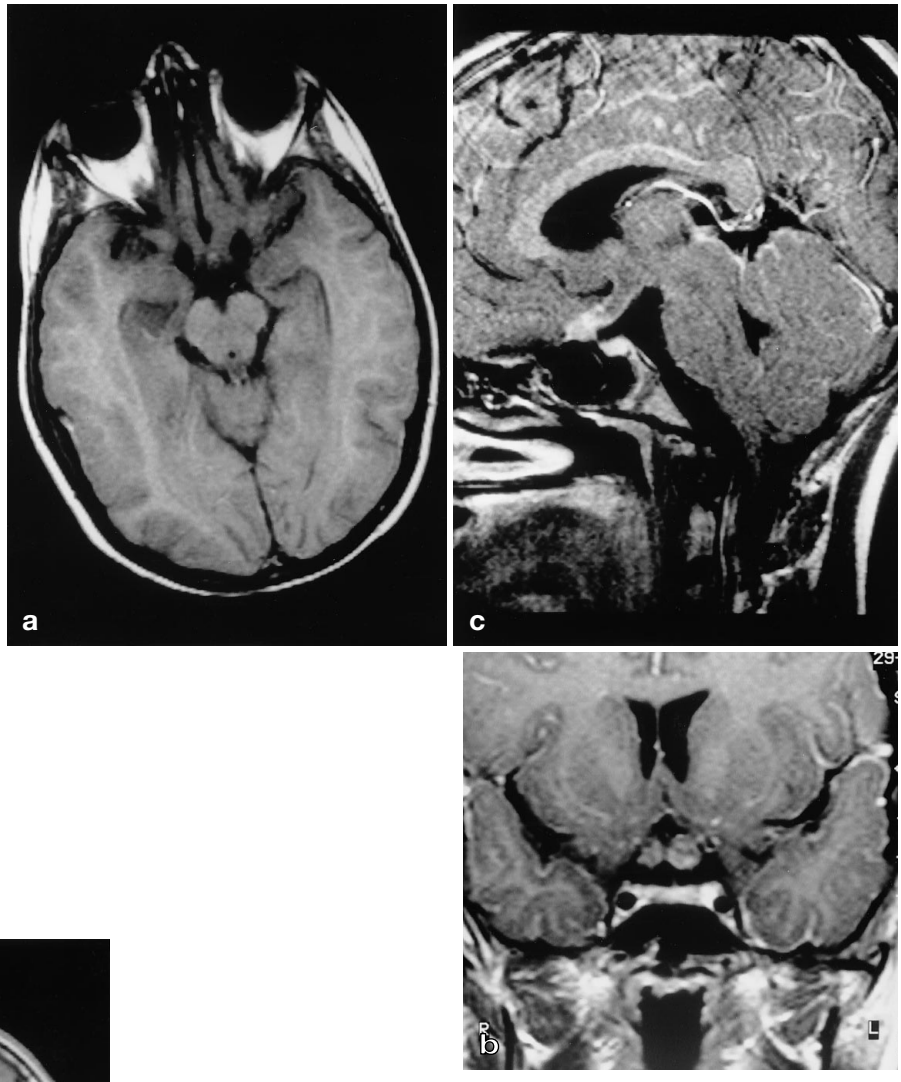

Fig. 1a–c MRI at presentation. **a** Unenhanced axial, **b** contrast-enhanced coronal and **c** contrast-enhanced sagittal T1-W spin echo images showing bilateral asymmetrical enlargement of the optic nerves and enhancement after contrast medium

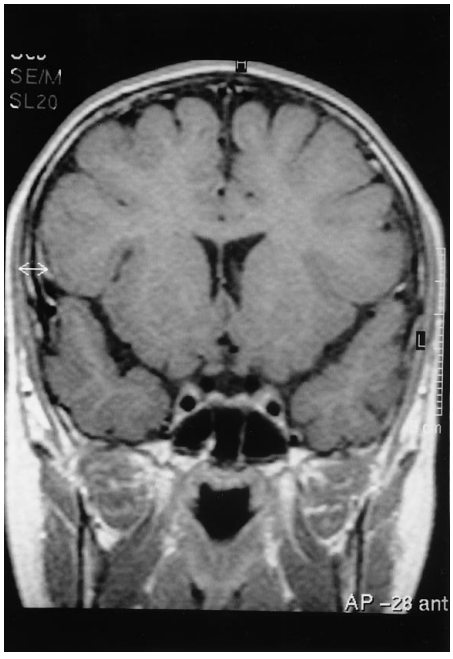

Fig. 2 Contrast-enhanced coronal T1-W spin echo MRI showing complete regression of leukaemic infiltration of the optic nerves 2 months after chemotherapy

should arouse suspicion of glioma (which may be isolated or associated with neurofibromatosis type 1), inflammatory lesions, meningioma (which is very rare in children), granulocytic sarcoma or leukaemic infiltration. Granulocytic sarcoma is a manifestation of acute myelogenous or myelomonocytic leukaemia [1]. In a context of previous history of ALL, optic nerve enlargement, enhancing after gadolinium, should suggest the diagnosis of leukaemic infiltration, even in the absence of previous leukaemic CNS involvement. This location of leukaemic infiltration is found in 13–16 % of patients who die from leukaemia [2]. It occurs most frequently in children with ALL, but has been reported in adults and in acute myeloblastic leukaemia [2]. Histopathologically, a small tumoral mass may be seen, but perivascular infiltration is more common [2].

The presence of isolated relapse around the optic nerves suggests that this area might be a sanctuary for

leukaemic cells. This may be due to suboptimal penetration of antileukaemic chemotherapy in the retrobulbar optic nerve; some authors have proposed that invasion of leukaemic cells (with or without inflammatory swelling of the optic nerve) in the optic canal acts as an anatomical barrier [3]. It has therefore been proposed that follow-up examinations of the optic disks should be performed in all patients with previous history of ALL, since leukaemic infiltration may be asymptomatic [2, 4].

Leukaemic infiltration of the optic nerve usually affects the optic disk and presents clinically as a pale grey swelling, sometimes associated with haemorrhages within the disk or the surrounding retina. As the disease progresses, irreversible visual loss can occur, resulting from compression necrosis or vascular occlusion if adequate therapy is not started. Early diagnosis is particularly important because of the dramatic response to treatment with complete resolution and good long-term survival [4, 5].

This report emphasises that bilateral peri-optic nerve leukaemic infiltration may be seen on MRI despite normal visual acuity, visual fields and fundi. MRI may, however, be negative. Camera et al. [6] proposed orbital ultrasonography as an alternative imaging technique. We conclude that in children with previous history of ALL, unexplained neurological presentation should prompt consideration of CNS ALL recurrence. In this context, MRI should be performed, with special attention to the optic nerves, even in the absence of blasts in the CSF or optic disk abnormalities.

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