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(CASE REPORT)

Optic nerve infiltration revealing an extramedullary relapse of acute lymphoblastic leukemia in a child: A case report and review of the literature

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Abstract

Orbital involvement represents a relatively common manifestation in leukemia, in contrast to involvement of the optic nerve, uveal tract, and retina, which remains uncommon. Ocular manifestations are most often related to direct infiltration of ocular structures by leukemic cells. However, associated hematologic abnormalities, particularly anemia and hyperviscosity syndromes, may also contribute to ophthalmic complications.

Optic nerve infiltration is increasingly recognized as a significant manifestation of central nervous system (CNS) involvement in leukemia.

We report the case of a 15-year-old male patient with T-cell acute lymphoblastic leukemia (T-ALL), who developed an early neuromeningeal relapse five months after initiation of chemotherapy according to the MARALL 2006 protocol.

Clinically, the course was marked by the onset of right-sided unilateral blindness associated with ophthalmoplegia involving the superior and lateral rectus muscles, along with absent pupillary light reflexes. Bone marrow examination revealed 2% blasts, leading to classification of this relapse as early, group S2.

Brain computed tomography demonstrated passive tetra-ventricular hydrocephalus, associated with a thickened, enlarged, and tortuous appearance of the right optic nerve.

Salvage therapy was initiated according to the COPRALL 2007 relapse protocol. However, follow-up magnetic resonance imaging revealed progression of the intraorbital tumor process, with intracranial extension into the cavernous sinus.

Following disease progression, palliative chemotherapy was initiated.

Keywords: Optic nerve; Lymphoblastic leukemia; Chemotherapy; Radiotherapy; Extramedullary Relapse

1. Introduction

Extramedullary leukemia remains an important complication of acute lymphoblastic leukemia (ALL). Leukemic infiltration of the eye is rare and most often occurs concomitantly with central nervous system (CNS) relapse [3].

Orbital involvement in leukemia may be related either to the disease itself or to its treatment [4].

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Leukemia can affect virtually all ocular tissues, either through direct infiltration, hemorrhage, or ischemic mechanisms [1].

Papilledema is not uncommon in patients with leukemia. Swelling of the optic nerve head in these patients may be related to five different mechanisms: intracranial hypertension secondary to leukemic infiltration of the CNS, prolonged corticosteroid therapy, tumor infiltration of the orbit or optic nerve leading to ischemic papillitis, perivascular infiltration causing venous congestion, or direct leukemic infiltration of the optic nerve head, with or without increased intracranial pressure, as in our patient [2].

Intrathecal chemotherapy alone has become a first-line treatment for orbital and leptomeningeal involvement in chronic lymphocytic leukemia (CLL) due to its rapid antitumor effect on central nervous system dissemination, its prolonged duration of action, and the extended survival it provides [5-6-7].

2. Case presentation

We report the case of a 15-year-old male patient followed for T-cell acute lymphoblastic leukemia (T-ALL), confirmed by cervical lymph node biopsy.

At initial diagnosis, cerebrospinal fluid (CSF) examination by cytospin was negative. The patient was corticosteroid-sensitive, with regression of the tumor syndrome by day 8 of corticosteroid therapy. He was treated according to the MARALL 2006 protocol, with a good initial clinical response.

Five months later, the patient presented with a progressive decrease in right visual acuity, evolving to complete blindness in the right eye, associated with paralysis of the superior and lateral extraocular muscles and ipsilateral abolition of the pupillary light reflex.

Ophthalmologic examination of the right eye revealed no light perception, a normal anterior segment, and stage III optic disc atrophy, consistent with advanced papilledema.

Brain computed tomography demonstrated passive tetraventricular hydrocephalus associated with a swollen and tortuous appearance of the right optic nerve **(Figure 1).**

Brain MRI with axial T2-weighted and coronal contrast-enhanced T1-weighted sequences showed a swollen appearance of the right optic nerve, associated with dilation of its perineural sheaths, extending to the prechiasmatic segment **(Figure 2).**

CSF analysis revealed an abnormal population of lymphoid cells on a hemorrhagic background. Bone marrow examination showed 2% blasts.

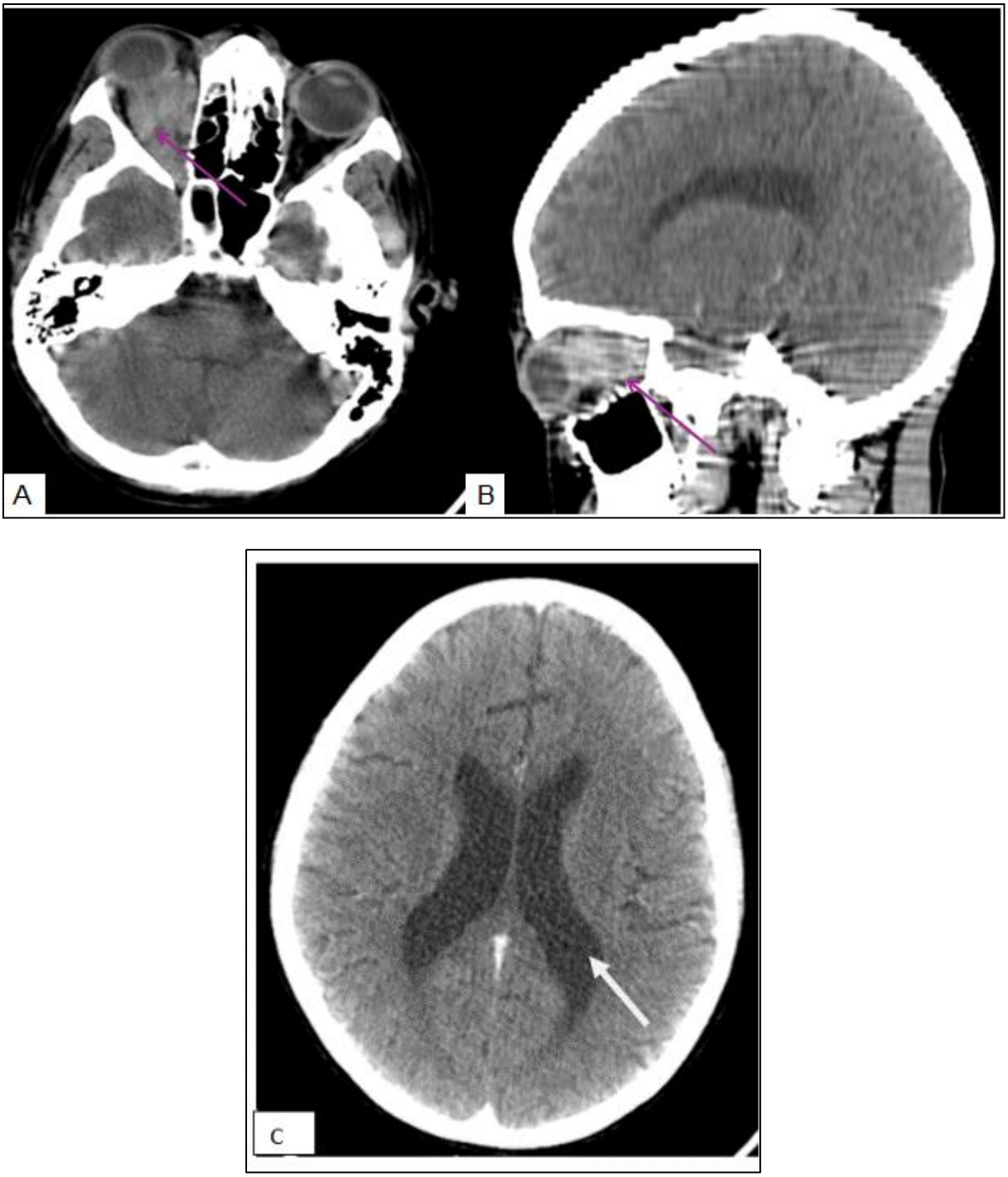
A diagnosis of neuromeningeal relapse was established based on clinical and biological findings, and relapse treatment was initiated according to the COPRALL 2007 protocol.

Two months later, follow-up magnetic resonance imaging (MRI) showed progression of the lesion centered on the right optic nerve, appearing hyperintense on T2-weighted images, hypointense on T1-weighted images with diffusion restriction, and showing mild enhancement after contrast administration. The lesion occupied the entire intraorbital region, encasing the optic nerve, which appeared stretched, as well as the medial rectus muscle.

The lesion extended posteriorly into the carotid canal, which was enlarged, with infiltration of the ipsilateral cavernous sinus showing a convex contour. Right temporal meningeal thickening with contrast enhancement was also noted **(Figure 3).**

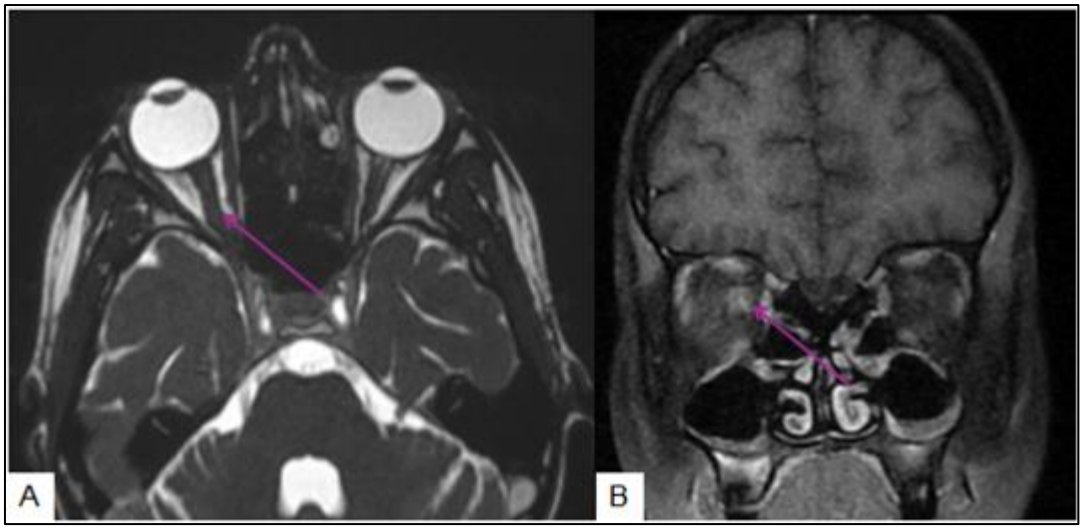
This process resulted in anterior displacement of the globe, causing grade II exophthalmos. It was associated with both lateral and medial retinal detachment, with subretinal material and mild contrast enhancement at this level **(Figure 3).**

Given the progression of the intraorbital tumor and its extension to the cavernous sinus, palliative chemotherapy was initiated.



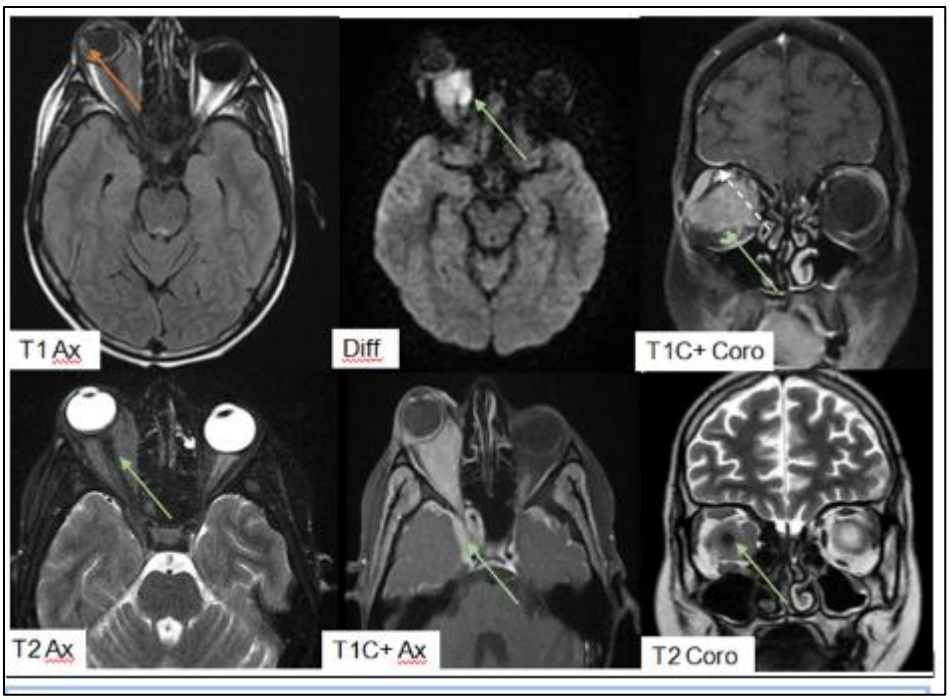
Reference: Radiology department CHU HASSAN II, FEZ, Morocco

Figure 1 Brain CT in axial and sagittal planes (A,B,C) demonstrated passive tetraventricular hydrocephalus (white arrow) associated with a swollen and tortuous appearance of the right optic nerve (purple arrow)



Reference: Radiology department CHU HASSAN II, FEZ, Morocco

Figure 2 Brain MRI with axial T2-weighted and coronal contrast-enhanced T1-weighted sequences showed a swollen appearance of the right optic nerve, associated with dilation of its perineural sheaths, extending to the prechiasmatic segment



Reference: Radiology department CHU HASSAN II, FEZ, Morocco

Figure 3 Progression of the lesion centered on the right optic nerve, appearing hyperintense on T2-weighted sequences, hypointense on T1-weighted sequences with diffusion restriction, and showing mild enhancement after contrast administration (green arrow). The lesion occupied the entire intraorbital region, encasing the optic nerve, which appeared stretched, as well as the medial rectus muscle.

The process extended posteriorly into the carotid canal, which was enlarged, with infiltration of the ipsilateral cavernous sinus showing a convex contour (green arrow). Right temporal meningeal thickening with contrast enhancement was also noted (white arrow).

This process resulted in anterior displacement of the globe, causing grade II exophthalmos. It was associated with both lateral and medial retinal detachment, with subretinal material and mild contrast enhancement at this level (orange arrow).

3. Discussion

Acute lymphoblastic leukemia (ALL) is characterized by bone marrow failure syndrome associated with a tumor syndrome, resulting from the accumulation of blast cells in various tissues of the body.

Compared with other, more common ocular leukemic manifestations, optic nerve involvement remains rare. It is reported in approximately 18% of cases in autopsy studies [8] and occurs predominantly in children with ALL.

The mechanisms of leukemic infiltration of the optic nerve are multiple and include direct invasion by leukemic cells, extension from the meninges in the setting of leukemic leptomeningitis, perivascular infiltration, and central nervous system involvement with extension along the optic nerve.

This infiltration may involve different anatomical portions, including the optic nerve head (optic disc), the intraorbital segment, and the meningeal sheaths.

The eye represents a true sanctuary site, protected by the blood–ocular barrier, which limits the penetration of chemotherapeutic agents [9]. This explains the possibility of isolated ocular relapses despite apparent systemic remission [10].

Clinically, this condition most often presents with a rapid decrease in visual acuity, sometimes associated with a central scotoma and, in some cases, orbital pain.

From a clinical perspective, patients usually present with reduced visual acuity. An asymmetric pattern of visual impairment, in the absence of clinical features suggestive of intracranial hypertension or meningitis, favors the diagnosis of leukemic involvement of the optic nerve [12].

On ophthalmologic examination, findings may include papilledema, an infiltrated optic disc with a whitish or yellowish appearance, dilation of retinal veins, and associated retinal hemorrhages. In advanced stages, secondary optic atrophy may develop, either following treatment or due to disease progression [10].

The typical appearance consists of a diffuse tumoral infiltration of the optic disc, accompanied by retinal exudation and hemorrhagic changes, often extending anteriorly into the vitreous cavity. Although bilateral cases may occur, the involvement is more commonly asymmetric and should be distinguished from papilledema secondary to intracranial hypertension [11].

In the past, management primarily relied on irradiation of the optic nerve or whole-brain radiotherapy, approaches that carried a significant risk of neurocognitive toxicity, particularly in older individuals. More recently, intrathecal chemotherapy alone has become the preferred first-line treatment for leptomeningeal involvement in chronic lymphocytic leukemia. This shift is explained by its rapid efficacy against central nervous system spread, sustained therapeutic activity, and its association with improved survival compared with combined radiotherapy approaches [5-6–7].

Commonly administered intrathecal agents include methotrexate, cytarabine, and corticosteroids [6,13,14].

Despite therapeutic advances, leukemic infiltration of the optic nerve head is associated with an unfavorable prognosis, with overall survival in cases of ocular involvement typically not exceeding 24 months [15].

This manifestation generally results from direct extension of central nervous system disease. Preventive strategies rely on intensification of both systemic and intrathecal chemotherapy in patients with identified risk factors. Acute lymphoblastic leukemia is associated with a higher likelihood of oculo-meningeal dissemination compared with acute myeloid leukemia, and therefore routinely requires central nervous system prophylaxis using repeated intrathecal administration of cytotoxic agents. In adults, this prophylactic approach is often combined with cranial irradiation encompassing the extraorbital segment of the optic nerve, whereas in pediatric patients, radiotherapy is reserved for selected high-risk cases [16].

4. Conclusion

Optic nerve infiltration in acute lymphoblastic leukemia is a rare but serious complication.

It should be suspected in any leukemic patient presenting with visual impairment, even during remission.

Prompt management, combining intrathecal chemotherapy and, in some cases, radiotherapy, is essential to limit long-term sequelae.

List of abreviations:

- **CT** : Computed tomography
- **ALL**: Acute Lymphoblastic leukemia
- **MRI** : Magnetic resonance imaging
- **CNS** : Central nervous system
- **CSF :** Cerebrospinal fluid
- **CLL :** Chronic lymphocytic leukemia

Compliance with ethical standards

Disclosure of conflict of interest

The authors do not declare any conflict of interest

Statement of ethical approval

Not applicable

Statement of informed consent

Written informed consent was obtained from the patient. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

The data sets are generated on the data system of the CHU Hassan II of Fes, including the biological and radiological data.

Author's contribution

- KL Is the corresponding author, she participated in the organization and writing of the article.
- Professor MB supervised the working and validated the figures.
- Professor and chief of department of radiology MB and MM red and allowed the article for publication.

All authors read and approved the final manuscript.

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