Short communication

Unilateral optic disk edema with central retinal artery and vein occlusions as the presenting signs of relapse in acute lymphoblastic leukemia

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Abstract

Clinical case: A 39-year-old man with Philadelphia chromosome-positive acute lymphoblastic leukemia (LAL Ph+) developed progressive vision loss to no light perception in his right eye. He had optic disk edema and later developed central artery and vein occlusions. Panphotocoagulation and radiotherapy of the whole brain were performed in several fractions. Unfortunately the patient died of hematological relapse 4 months later.

Discussion: Optic nerve infiltration may appear as an isolated sign of a leukemia relapse, even before a hematological relapse occurs. Leukemic optic neuropathy is a critical sign, not only for vision, but also for life, and radiotherapy should be immediately performed before irreversible optic nerve damage occurs.

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Edema de papila y obstrucción de arteria y vena central de la retina como manifestación inicial de una recaída leucémica

Resumen

Caso clínico: Varón con amaurosis en ojo derecho y diagnóstico previo de leucemia linfoblástica aguda con cromosoma Philadelphia positivo (LAL Ph+). Presenta edema sectorial del disco óptico y, posteriormente, obstrucción de arteria y vena central de la retina. Se realiza panfotocoagulación retiniana y tratamiento radioterápico holocraneal. A los 4 meses sufre recaída hematológica, siendo finalmente exitus.

Discusión: La afectación del nervio óptico puede presentarse como único hallazgo en una recurrencia de una LAL, precediendo incluso a la recaída hematológica. Constituye por tanto

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Introduction

The incidence of ophthalmological manifestations in patients with leukaemia has increased notably in recent years due to the longer patient survival resulting from the effectiveness of the available therapies.\(^1\)\(^-\)\(^3\) Despite longer remission periods, a relapse after a full remission continues to represent an unfavourable prognostic factor, especially in cases where the central nervous system (CNS) is involved.\(^4\)

The optic nerve (ON) is affected in 13–18\% of all patients with leukaemia. This may occur with any cytological variety and at any stage of the disease, even as the only finding of an extramedullary relapse, and even several months before a haematological relapse.\(^4\) Visual loss due to leukaemia infiltration of the ON constitutes an ophthalmological emergency and requires the urgent use of radiotherapy before irreversible neuronal damage occurs.\(^3\)

Clinical case

A 39-year-old male patient with a one-week course episode of loss of vision in the right eye (RE) and supraorbital pain. His medical history is notable for a diagnosis of Philadelphia chromosome-positive acute lymphoblastic leukaemia (Ph\(^+\) ALL) five years before. Chemotherapy was administered as per Pethema protocol and he later received an umbilical cord blood allotransplantation; he suffered two relapses following complete remission.

On the physical examination, the RE does not have light perception and the visual acuity in his left eye (LE) is 1.0. The intraocular pressure is normal and there is an afferent pupillary defect in the RE. The LE fundus does not show abnormalities (Fig. 1), whereas the RE displays some raised blurring of the optic nerve’s nasal edge (Fig. 2).

Fig. 1 – Funduscopic image at four days post-admission with diffuse retinal oedema, disruption of the blood column and cherry-red stain.

Fig. 2 – Funduscopic image at eight days post-admission, with blot haemorrhages appearing along the venous tracts.
Fig. 5 – Fluorescein angiography. Note the total absence of dye in the right eye, with a background choroidal filling.
The cranial and orbit CT scan does not reveal lesions whereas the magnetic resonance (MRI) shows that the periventricular white matter and the corpus callosum are affected. The echo Doppler of the supra-aortic trunks is normal and the evoked potentials suggest an axonal neuropathy of the left second cranial nerve and mixed (axonal and demyelinating) neuropathy of the right cranial nerve. The flow cytometry of cerebrospinal fluid reveals the presence of 0.13 blast cells/μL with undetectable DNA. The microbiological and immunological tests are normal and the bone marrow aspirate does not show blastosis.

Four days after his admission, the patient reported progressively increased pain that required gabapentin to be controlled. On the physical examination, the patient was found to have endotropia in his RE with paresis of the lateral rectus muscle, and the fundoscopy showed (Fig. 3) findings consistent with central retinal artery occlusion (CRAO). Afterwards, multiple blot haemorrhages appeared along the venous tract (Fig. 4), consistent with a central retinal vein occlusion. The angiography confirmed the suspected complete CRAO (Fig. 5). Given the progression to an ischaemic central retinal vein occlusion, retinal panphotocoagulation was initiated to prevent the development of neovascular glaucoma. At the systemic level, the decision was to administer holocranial radiotherapy with lateral and opposite fields. Following completion of radiotherapy sessions (Fig. 6), the patient was found to be stable, without pain and recovering motility.

Only four months after the episode, the patient was readmitted due to deteriorated general condition, with asthenia, anorexia and rectorrhagia. He had leucocytosis of 133,000 cells/μL with 95% blast cells, elevated ratio of BCR-ABL fusion gene copies and detection of the T315I mutation (which provides resistance to tyrosine-kinase inhibitors). Based on the poor prognosis, and with the family consent, analgesic and well-being measures were provided until the patient’s death.

**Discussion**

The most common findings in leukemic optic neuropathy include sectorial or diffuse optic disk oedema and secondary venous dilation. Occasionally, it may occur associated with vascular complications, such as CRAO, exceptionally combined with vein thrombosis. Such complications may be due to increased blood viscosity (due to blastosis or immune-mediated aggregation phenomena), a compressive phenomenon, or even the very infiltration into the arterial wall.

Because of its anatomical relation, the ON involvement represents an extension of the CNS leukaemia, which
necessitates the use of imaging tests as well as a lumbar puncture test to rule out the presence of blast cells, even though this finding is not constant and, often, hard to interpret. Thus, the diagnosis of leptomeningeal infiltration requires at least 5 cells/μL of cerebrospinal fluid; the clinical relevance of cell counts below that threshold—as in the case of our patient—is unknown. Likewise, even though the MRI constitutes the best imaging technique to explore the CNS, the orbit and the eye structures, it may be negative and the absence of enhancement of ON does not rule out the presence of microscopic infiltrates.

The ON, like the rest of the eyeball, is considered a pharmacological sanctuary in radiotherapy for leukaemia. Given the limitations of chemotherapy, local radiation is effective to reduce the tumour burden in the narrow optic canal, improving the impact and efficacy of chemotherapeutic agents on the residual cells.

In summary, the role of the ophthalmologist in leukaemia and other blood malignancies may be crucial. A rapid recognition of ocular manifestations as a sign of a potential relapse will allow, thanks to the early administration of radiotherapy, to improve not only the likelihood of visual recovery but also the possibility of prolonging the patient’s survival.

Conflicts of interest

The authors declare that they do not have any conflicts of interest.

REFERENCES