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Case Study

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Unilateral optic nerve relapse after acute lymphoblastic leukaemia remission

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Abstract

Background: The aim of this case report is to describe the clinical presentation and imaging features of a patient with optic nerve leukaemic infiltration as the first site of relapse after complete response to systemic treatment.
Materials and methods: We report the case of a 23-year-old man with history of acute lymphoblastic leukaemia (ALL) in complete remission. Six months later, the ocular examination revealed decreased visual acuity. Fundus examination showed a pale optic disk with blurred margins and multiple flame-shaped and dot and blot retinal haemorrhages in his left eye. A diagnosis of leukaemic infiltration to the optic nerve was made by magnetic resonance imaging (MRI). Cytological analysis of the cerebrospinal fluid did not show any abnormal cells or blasts.
Results: A course of oral corticosteroid therapy was prescribed and 20 Gy of radiation was administered to the whole brain including the left orbit. Vision was improved dramatically in the left eye. Isolated optic nerve relapse of leukaemic infiltration is of paramount importance to early diagnosis, as vision can be saved if treatment with orbital radiotherapy is initiated promptly.

Introduction

The relapse in ocular structures without systemic involvement is extremely rare in acute lymphoblastic leukaemia (ALL). Active bone marrow disease is usually associated with optic nerve infiltration (ONI).[1] However, ONI is rarely reported as an initial site of relapse after complete systemic remission. This relapse, if diagnosed and treated promptly deterioration of vision may be prevented.[2] We describe an adult patient with ALL whose disease relapsed with unilateral left-sided optic nerve infiltration of leukaemic cells, who suffered sudden vision loss 6 months after complete remission. We discuss the implications of early diagnostic and the optimal treatment for a good vision prognosis.

Case Presentation

A 23-year old man was diagnosed with T-cell ALL and treated with conventional chemotherapy including vincristine 2 mg/m^2 associated to prednisolone 70 mg/m^2 and L-asparaginase 6,000 U/m^2. Prophylactic intrathecal therapy was administered with methotrexate. The cerebrospinal fluid (CSF) examination was carried out prior to each intrathecal-therapy drug instillation without any central nerve system (CNS) suspicious disease. Complete remission was achieved. The patient refused the intracranial prophylactic treatment. Six months later, he complained of dimness of vision for 25 days in his left eye. A cerebral magnetic resonance imaging (MRI) showed an isolated thickening of the left optic nerve with increased perineural gadolinium enhancement (Figure 1). Fundoscopic investigation, left-sided optic disc edema and peripapillary nerve fiber layer edema were detected (Figure 2). There was peripapillary retinal haemorrhage but vitreous, macula and retinal vessels were normal. The optical coherence tomography (OCT) indicated inflammation of the left optic nerve (Figure 3). CSF was normal at morphologic and immunophenotypic studies. The CSF viral studies (CMV, EBV, HHV-6, HSV1, HSV2) were performed without abnormalities. We delivered 20 Gy of radiation to the whole brain including the left orbit in a curative intent. Conformal radiotherapy (RT) was delivered using 6 MV photons with a target dose of 2 Gy in 10 fractions.

An improvement in vision was reported after the first few sessions. Consolidation chemotherapy was continued. Fundoscopic examination showed a complete resolve of the haemorrhage. After follow up, he remained stable for 12 months until he developed an intramedullary progression and unfortunately, he did not survive.

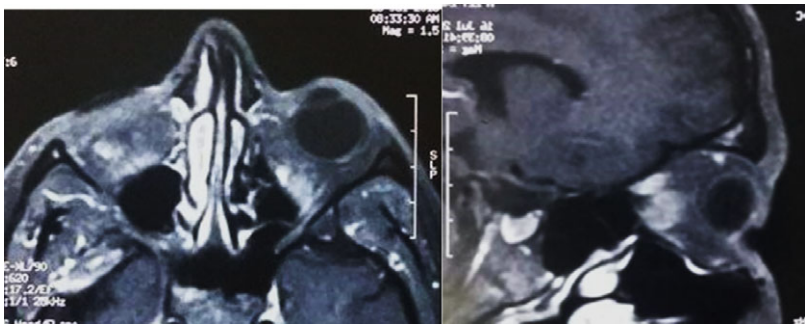


Figure 1. Magnetic resonance imaging (MRI) of the left orbit showing thickened left optic nerve.

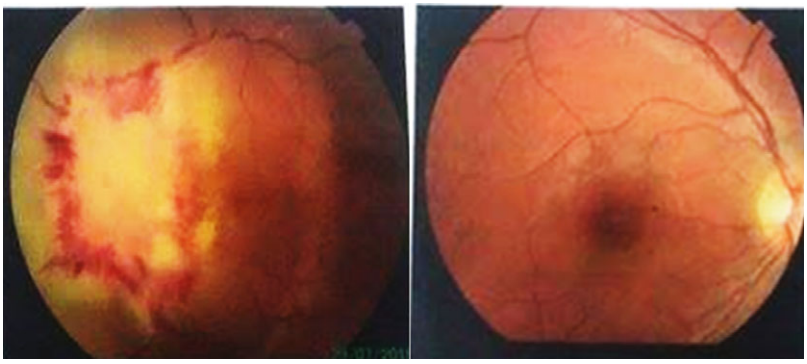


Figure 2. Left optic nerve fluorangiography showing a papillary infiltration with haemorrhage around the lesion associated with macular edema.

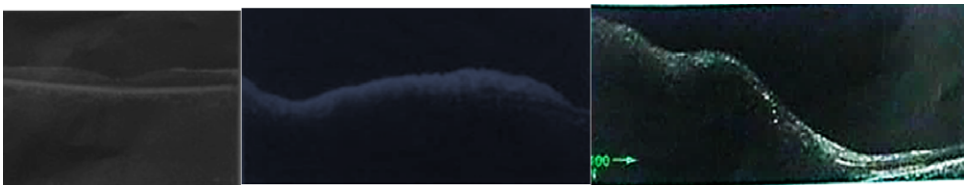


Figure 3. Optical coherence tomography (OCT) of optic nerve head (ONH) showing swollen left optic nerve head.

Discussion

The estimating incidence of ocular infiltration in ALL varied between 5 and 13%.[3] The largest series of 657 children identified a 4·4% rate of infiltration of the optic nerve, retina, iris or orbit.[4] Intracranial irradiation and intrathecal chemotherapy are required to prevent recurrence of ALL and to attain the complete remission. The orbital cavity and optic nerve are potential sanctuaries for leukaemic relapse after conventional central nervous system prophylaxis because these structures are shielded during brain irradiation.[3] Clinicians should be aware of these possible manifestations even after achieving disease remission. The CNS relapse and ocular involvement in ALL usually indicate refractory disease and a poor prognosis.[5] ALL patient have an eye-meningeal risk of relapse and this is more common than in acute myeloid leukaemia and should receive prophylactic treatment of CNS by repeated intrathecal injections of cytotoxic chemotherapy.[6] Early limited relapse without systemic involvement is a challenge issue for clinical management because the optic nerve is relatively unaffected by systemic chemotherapy and serves as a sanctuary of ALL.[7,8] To confirm the diagnosis of ONI, other causes of decreased visual acuity in ALL have to be excluded like infection, vasculitis, radiation optic neuropathy or side effects of chemotherapeutic agents.[2] The typical appearance was an infiltration of the entire papillary region by a tumour mass, accompanied by exudates and haemorrhages and forming a projection into the vitreous cavity. Sometimes bilateral, but often asymmetrical, it must be differentiated from papilledema on intracranial pressure.[9] Decreased visual acuity, perivascular infiltration and parapapillary retinal, an asymmetrical involvement and the absence of clinical signs of intracranial hypertension or meningitis argue for a blast infiltration of the optic nerve. The occurrence of papilledema mechanism is a consecutive venous obstruction to the invasion perivascular by leukaemic cells.[9] The efficacy of intrathecal chemotherapy is limited because the drug is unlikely to reach the optic nerve located in an optical channel obstructed by tumour infiltration. The most effective treatment is irradiation of the orbit at a dose of 20–24 Gy over 2 weeks.[9] Early administration of focal radiotherapy allows the cytotoxic drugs to reach the CSF to attack the neoplastic cells. The optic nerve is relatively less sensitive to RT whereas leukaemic cells are quite radiosensitive. It must be done as early as possible to observe a rapid regression and improvement of visual function. Treatment should be instituted before irreversible optic nerve damage occurs. The target volume should involve the posterior poles of the globes with or without whole brain treatment.[10] Despite intensive treatment, the prognosis is poor and is related to other risk factors of bone marrow with CSF involvement and the length of initial haematological remission. Overall survival in cases where the ocular structures are infiltrated with disease is less than 24 months (9). Two large retrospectives multicentre

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studies included a total of 59 patients with leukaemic orbital infiltration, most of whom also had bone marrow or CNS involvement.[11,12] Results suggested that patients treated with RT were more likely to achieve remission. The authors recommended doses of greater than 20 Gy to the affected eye.[11] RT to the orbital structures is associated with the risk of long-term morbidity. However, considering that radiation-induced cataracts can be surgically removed, an inadequate RT dose may increase the risk of progression.[3] Intravitreal methotrexate administration can be another option therapy in this case relapse.[13]

Conclusion

In this case, the intracranial and orbital irradiation was delivered simultaneously with a complete recovery of left eye sight. The optic nerve leukaemic infiltration should be kept in mind in high-risk patients with T-cell ALL. The accurate ophthalmologist and MRI can suggest early diagnosis of ONI. Prompt irradiation should be given to prevent irreversible visual loss.

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Conflict of Interest. The authors have no conflicts of interest to declare.

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