

Ocular Involvement in Acute Lymphoblastic Leukaemia

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Summary

A six-year-old boy, a known case of acute lymphoblastic leukaemia (ALL) on remission since 1991 presented with leukocoria and poor vision of the left eye for two days' duration. Examination revealed endophthalmitis in the left eye with raised intraocular pressure. Anterior chamber paracentesis with vitreous biopsy confirmed a diagnosis of ocular involvement. Further investigation revealed that he also had bone marrow and central nervous system relapse. Clinical manifestation and treatment modalities of ocular involvement in leukaemia are discussed.

Key Words: Endophthalmitis, Acute lymphoblastic leukaemia

Introduction

The clinical and pathological features of leukaemic infiltration of the eye are well established¹. Ocular involvement in leukaemia first described by Liebreich in 1861² may be an initial feature of the disease or the first manifestation of relapse after remission induced by chemotherapy.

There is often uncertainty about the diagnosis that can only be resolved by histological or cytological examination of the aqueous, vitreous or iris tissue. From a literature review³ it appears that patients with ocular leukaemia usually are treated with radiotherapy of the affected eye. The best treatment however remains largely undefined and the outlook for children with ocular relapse remains poor despite intensive local and systemic treatment.

Case Report

A six-year-old boy was diagnosed to have acute lymphoblastic leukaemia in September 1991. He was

in remission since then and was on maintenance chemotherapy with:

- 1) I/V vincristine 1.5mg/m² monthly.
- 2) Prednisolone 60mg/m² daily (5 days pulses with I/V vincristine).
- 3) six mercaptopurine 70mg/m² daily.
- 4) Methotrexate 20mg/m² weekly.

He presented with a history of acute pain and redness of the left eye for three days duration in June 1993. It was associated with reduced vision, severe headache and vomiting. His parent noted a white reflex in the left pupil.

The vision was 6/6 in the right eye and perception of light in the left eye. There was leukocoria in the left eye, the cornea was clear but the anterior chamber was very shallow and full of flare and cells. A hypopyon was also present (Fig. 1). Multiple fine vessels (rubeosis iridis) were seen on the left iris but there was no heterochromia.

CASE REPORT

The intraocular pressure was 40mm.Hg. in the left eye compared to a normal 16mm.Hg. in the right eye. Binocular indirect ophthalmoscopy examination of the left eye revealed nearly 3/4 of the fundus was filled up with an exudative retinal detachment with underlying choroidal detachment. White scattered retinal masses and vitreous opacities were also present (Fig. 2). The right fundus showed presence of multiple hypopigmented chorioretinal scars.

One week after admission he bled from the rubeotic vessels and developed diffuse hyphaema in his left eye.

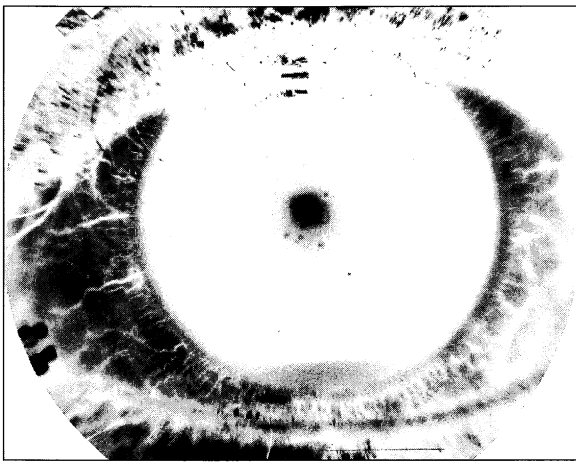


Fig. 1: Anterior segment showing level of hypopyon



Fig. 2: Funduscopy of the left eye showing white patches indicating direct retinal infiltration and subretinal haemorrhage

Anterior chamber paracentesis and vitreous biopsy were done on July 17, 1993. The specimens were sent for cytospin and cytology examination. The vitreous tap smear showed blast cells, with some degeneration and necrosis. Examination of the aqueous showed occasional degenerative cells. Bone marrow and lumbar puncture were carried out and the result also revealed abundant blast cells confirming the diagnosis of ocular, bone marrow and CNS relapse. CT scan of orbits and brain showed thickened left optic nerve with dilated ventricles. No pathogenic organisms were isolated on culturing the specimen.

He was induced with intensive chemotherapy with I/V methotrexate 1gm/m² followed by induction with UKALL X protocol with vincristine, daunorubicin, asparaginase and prednisolone. Intrathecal methotrexate was also given. Initially the left eye was given full antiglaucoma treatment with G. timolol 0.5% b.d., syrup Diamox 250mg. qid. and I/V mannitol. Oral glycerol together with topical corticosteroid drops. After the paracentesis, the intraocular pressure in the left eye was markedly reduced. However, radiotherapy of 4000 cGy had to be given to the left eye later as the intraocular pressure started to rise despite putting him back on full antiglaucoma therapy.

During the course of the treatment, unfortunately, the patient passed away. No post mortem was done as his parents did not give consent.

Discussion

Leukaemic infiltration of the eye tissues during the course of acute leukaemia seems to be a rather rare event. However, recently, it has been recognised more frequently. The incidence of ocular involvement in leukaemic patients varies in different postmortem studies. Analysis of 135 autopsy eyes for ocular involvement in leukaemia by Leonardy *et al* revealed that the overall incidence of ocular leukaemic cell infiltrations in the 135 patients with leukaemia was 31.1%¹. A multicentric retrospective study on leukaemic ophthalmopathy by Curis *et al* reported the incidence of isolated leukaemic infiltration of the eye as the first relapse to be 30%³.

Leukaemic infiltrates may be found in almost any

location in the eye. Anterior segment changes may be the first manifestation of leukaemia or may reflect the ocular toxicity of antileukaemic therapy. The anterior segment is an uncommon site of extramedullary relapse, accounting for between 0.5% and 2.6% of all the relapses in large published series and is most frequently seen in acute lymphoblastic leukaemia. The clinical findings in the anterior segment varied with iritis and hypopyon being the most common presentations. Other presenting symptoms of anterior segment relapse include redness, epiphora, photophobia and changes in the shape and reaction of the pupil or in the colour and appearance of the iris.

Our patient's left eye showed intense activity with plenty of flare and cells, hypopyon, hyphaema and rubeosis. The diagnosis of leukaemic uveitis is suggested by iris thickening, either nodular or diffuse, iris masses, iris colour changes, loss of iris crypts and rubeosis². The mechanism of anterior segment relapse is not clear. Migration of leukaemic lymphoblast along the posterior ciliary vessels in the subarachnoid space surrounding the optic nerve had been proposed as a mechanism linking the central nervous system and the anterior segment³. The hypopyon consists of leukaemic cells, necrotic tissue and proteinaceous exudate³.

Our patient also developed raised intraocular pressure with a shallow anterior chamber. Patients with glaucoma have histological evidence of leukaemic obstruction of the outflow channels, including the episcleral vessels but there is no specific pattern of vascular involvement in the anterior segment. Pathological studies also showed tumour infiltration of the iris and trabecular meshwork². Anterior chamber paracentesis was done for this patient and cytological study confirmed the presence of blast cells in the

aspirate. Another diagnostic procedure that can be done to obtain a histological specimen is iris biopsy.

This patient also presented with a rare manifestation of posterior segment involvement. Nearly 3/4 of the retina and choroid was detached and the remaining was filled up with white masses and the vitreous was hazy. Other retinal lesions found during the course of the leukaemic process include haemorrhages, cotton wool spots, retinal neovascularisation and microaneurysms. Retinal pigment epithelial changes such as atrophy, hypertrophy and hyperplasia have been reported¹. Oedema of the optic disc may accompany diffuse leukaemic involvement of the central nervous system or leukaemic infiltration of the optic nerve head.

Tumour regression and lowering of intraocular pressure had been the aims of ocular therapy. Topical corticosteroids have had variable success in reducing the severity of the iritis or arresting the tumour infiltration. Irradiation yields more reliable results and is effective in most forms of anterior segment leukaemia both in inducing clinical tumour regression and in controlling the secondary glaucoma.

From a literature review it appears that patients with ocular leukaemia usually are treated with aggressive systemic chemotherapy and often with radiotherapy of the affected eye. Low dose radiotherapy of the affected eye is needed to obtain long standing ocular remission and to avoid secondary ocular relapse. The known complication of radiotherapy is cataract formation.

The prognosis remains poor despite aggressive local and systemic treatment because of a substantial risk of subsequent bone marrow or CNS relapse.

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