usually horizontal or rotary, but may sometimes be vertical. Vertical nystagmus in adults is most commonly due to intracranial pathology. Children however may demonstrate vertical nystagmus in the presence of normal neuroimaging, this nystagmus is invariably associated with poor visual acuity.[3-5] In most children where the sensory nystagmus persists, the nystagmus eventually becomes horizontal in direction.[4]

The child described above developed vertical, pendular sensory-type nystagmus following a shaking injury with documented intracranial and intraocular haemorrhages. Resolution of the nystagmus coincided with clearing of the intraocular haemorrhages. The ocular movements then reverted to conjugate, random movements characteristic of cortical visual impairment. We postulate that this child developed reversible sensory nystagmus as a result of the occlusive effect of the intraocular haemorrhages. Future reporting of similar cases may clarify whether sensory nystagmus is more likely to be vertical in the presence of diffuse brain injury from shaking or other causes.

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Sir,

Leukaemic infiltration of the optic nerve as the initial manifestation of leukaemic relapse

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Ocular problems in patients who have leukaemia are commonly observed by the ophthamologists.[1] Cases of leukaemic involvement of the central nervous system (CNS) are becoming more frequent because of the increased survival rate associated with more effective treatment including combination therapy of systemic chemotherapy, prophylactic irradiation, and intrathecal injection of cytotoxic drugs.[1–5] Direct invasion of the orbit with the neoplastic cells is common, but the involvement of the optic nerve, uveal tract, and retina is relatively rare.[2,3] The optic nerve is known to be one of the disease-relapse sites in a patient with systemic or meningeal leukaemia,[2,4] but it was rarely reported as the initial isolated presentation for the relapse in a patient with complete remission. Moreover, the optic nerve had been characterized to be a pharmacologic sanctuary, relatively unaffected by systemic chemotherapy.[3,5] Thus, a separate treatment modality, often radiotherapy, is required for the optic nerve involvement of leukaemia.[2,5,6] Here, we report three cases of leukaemia with the leukaemic infiltration of the optic nerve as the initial isolated presentation of disease relapse. Systemic remission was proved by bone marrow aspiration and peripheral blood studies at the time of presentation.

Case report

Patient 1

Acute myeloid leukaemia was diagnosed in the 36-year-old male on November 1987. He was treated with cytotoxic drugs including cytarabine, 6-mercaptopurine, and daunomycin. Systemic remission was achieved after three complete courses of chemotherapy.

He complained of pain and mild visual distortion in his left eye on February 1989. His best-corrected visual acuity was 6/6 in the right eye and 6/6.7 in the left eye. Ophthalmic examination of the anterior segment was unremarkable in both eyes. Ophthalmoscopy showed normal optic disc and retina in the right eye. In the left eye, the optic disc was markedly swelling. The retinal vessels were engorged with dot-shape haemorrhage. The vitreous was clear without cell.

After 2 weeks, visual acuity in the left eye decreased to 6/30. Computed tomography showed an enlargement of the left optic nerve (Figure 1). Then, he was admitted for evaluation and for another course of maintenance chemotherapy. Bone marrow aspiration revealed a state

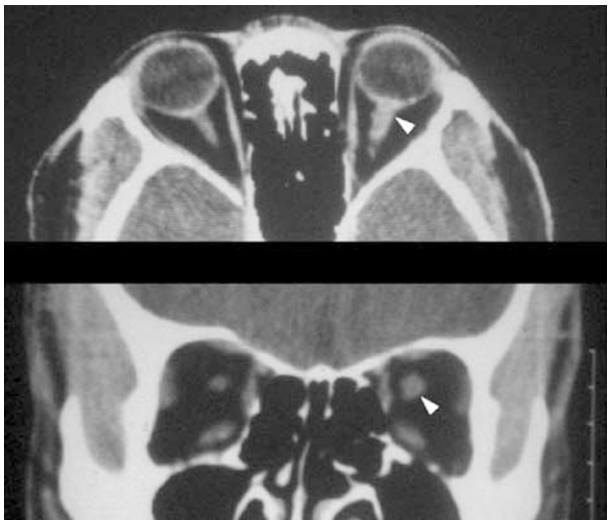

Figure 1 Case 1. Computed tomography showed an enlarged optic nerve of the left eye.

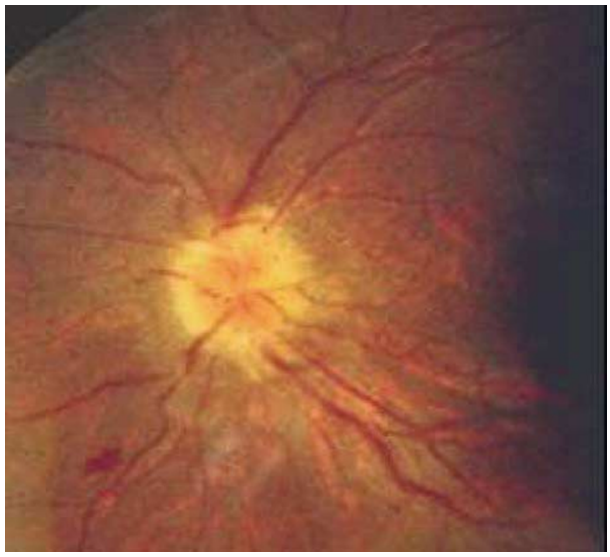

Figure 2 Case 2. The optic disc of the left eye was markedly swollen, and retinal venous engorgement with dot-shape haemorrhage was also noted.

of complete remission of leukaemia in this patient. Though the result of lumbar puncture showed no evidence of leukaemic cells in the cerebrospinal fluid (CSF), radiotherapy was performed over the left orbit area with 2100 cGy in seven fractions as a palliative therapy. Unfortunately, the patient died of leukaemia relapse and multiple organ failure 1 month later.

Patient 2

On April 1988, a 19-year-old male was diagnosed as having acute lymphoblastic leukaemia, L1, T-cell type when he presented with headache, generalized petechia, and gum bleeding. He received systemic chemotherapy including vincristine sulphate, L-asparaginase, daunomycin, and prednisolone for consolidation and further maintenance chemotherapy. Intrathecal methotraxate was administrated and radiotherapy with 2400 cGy in 12 fractions was performed for CNS prophylactic management. The bone marrow study revealed hypocellularity on October 1988.

He complained of mild blurred vision and ocular pain on the left eye on January 1989. His best-corrected visual acuity was 6/6 in both eyes. Impaired color vision with only seven Ishihara color plates identified was noted in the left eye. Ophthalmoscopic examination showed normal disc and retina in the right eye and oedematous disc with vascular tortuosity in the left eye (Figure 2). The fluorescein angiography showed fluorescence dye leakage from the disc in the left eye. On account of the suspected CNS involvement of leukaemia, intrathecal chemotherapy with methotraxate and cytarabine was administrated. CSF study did not find any definite leukaemia cell and the bone marrow analysis revealed no malignant cell then.

However, paracentral scotoma in the left visual field was noted on February 1989. The best corrected visual acuity was still 6/6 in both eyes, and the examination of the anterior segment was unremarkable in both eyes. Ophthalmoscopy showed peripapillary retinal oedema in the right eye and mild disc oedema in the left eye. Computed tomography revealed a swollen left optic nerve. The result of CSF study was negative for the leukaemic cell. Focal irradiation for the optic nerve involvement was scheduled, but was delayed because the patient's general condition deteriorated rapidly. After 2 weeks, blast cell was found in the bone marrow smear. The patient died of leukaemia relapse with CNS infection on March 1989.

Patient 3

A 40-year-old male found generalized ecchymosis over his body and gum bleeding for 2 weeks on February 2001. Studies of peripheral blood and bone-marrow smears showed leucocytosis and large lymphoblasts. The diagnosis of acute lymphoblastic leukaemia with Philadelphia chromosome was made on March 2001. Methotraxate, dexamethasone, and cytarabine were injected intrathecally for prophylactic therapy of CNS involvement. Complete remission was achieved after seven courses of cytotoxic chemotherapy with cyclophosphamide, vincristine sulphate, L-asparaginase, daunomycin, and dexamethasone.

On September 2001, he suffered from progressive visual loss in his both eyes. His visual acuity was no-light perception in the right eye and 1/60 in the left eye. The examination of anterior segment revealed mid-dilated pupil with sluggish light reflex in both eyes. Ophthalmoscopy showed severe disc oedema and retinal venous engorgement in both eyes. After 2 days, visual acuity of the left eye deteriorated to hand movement only. Fluorescence angiography disclosed late-phase staining and leakage of dye around the disc in both eyes. Magnetic resonance imaging of the orbits showed evidence of enhanced soft tissue component wrapping around the optic nerve bilaterally, with extension to the prechiasmal segment, compatible with leukaemic infiltration (Figure 3). Radiotherapy of the whole brain including both orbits was preformed with 2000 cGy in 10 fractions. His best-corrected visual acuity was 6/6.7 in both eyes on December 2001. Ophthalmoscopy showed mild swelling of the disc in both eyes (Figure 4). Follow-up computer tomography revealed no definite lesion over the optic nerve (Figure 3). He received scheduled peripheral blood stem cell transplantation (PBSCT) and the acute lymphoblastic leukaemia was in remission to date.

Discussion

Ocular manifestation of leukaemia can present over the orbit, eyelid, the retina, uveal tract, and the optic nerve.[2,5] Direct invasion to the orbit may cause severe proptosis, which could result from massive soft tissue infiltration or retrobulbar haemorrhage.[2,5] Leukaemic retinopathy is more commonly found in the acute form of leukaemia. Tortuous dilated retinal veins, cotton–wool patches, intraretinal haemorrhages, and sheathing vessels are classic features of the retinopathy.[2,5] The choroidal infiltration with leukaemic cells are common, especially in the case of acute lymphocytic leukaemias. Leopard-spot pattern of the retinal pigment epithelium and serous retinal detachment can be associated with diffuse infiltration of choroids.[5] Leukaemic infiltration of the optic nerve is relatively rare and is considered to be one of the significant clinical findings of central nervous system leukaemia.[4,7] Active bone marrow disease is usually present at the stage with optic disc involvement.[5,7] Isolated optic nerve involvement is relatively rare as an initial presentation of disease recurrence.[4–8] Primack *et al*[9] reported a case of acute lymphocytic leukaemia in prolonged remission, who had the extramedullary relapse presented with total retinal detachment and optic nerve involvement in one eye. Schwarts *et al*[10] described patients with acute lymphoblastic leukaemia, who had the optic nerve involvement as the isolated site of initial relapse with complete systemic remission. There was no evidence of cellular infiltration in the subarachnoid space surrounding the optic nerve, nor was there evidence of an intracerebral or meningeal leukaemic infiltration in these cases.

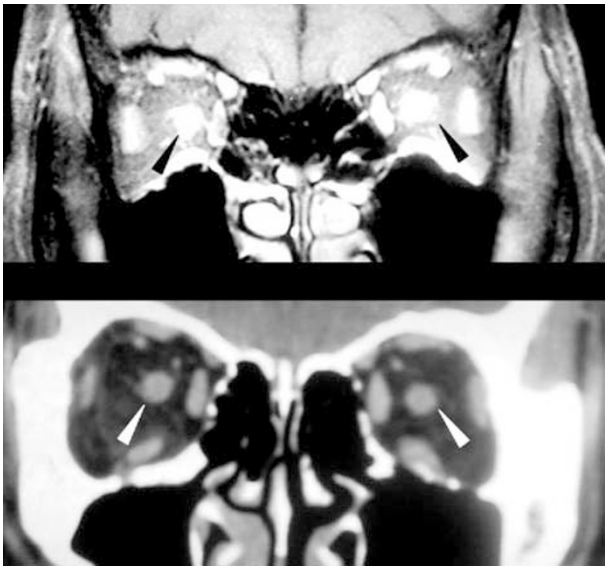

Figure 3 Case 3. Up: MRI showed soft-tissue component wrapping around the optic nerve bilaterally, compatible with leukaemic infiltration. Down: CT scan after radiotherapy showed no definite lesion around optic nerve after radiotherapy.

With more effective chemotherapy, the patients with leukaemia survived longer. More cases with frequent CNS relapses (such as optic nerve) reported.[2–5,9,10] Disease relapse is presumed to be due to an inadequate penetration of the antileukaemic therapy to the relapsing site. Previous reports suggested that intrathecal chemotherapy may not penetrate to the retrobulbar optic nerve in adequate amount to treat overt leukaemia.[3,5,11] Nikaido *et al*[5] reported five cases of relapsing optic nerve infiltration in patients with acute leukaemia, though complete remission was once achieved after intrathecal chemotherapy in these patients. Nevertheless, intrathecal chemotherapy might be not enough to eradicate all the leukaemic cells in paraneural space of the optic nerve. Thus, optic nerve is one of the relapsing sites that the disease recurs even following intrathecal chemotherapy.

The presentation of optic nerve involvement in leukaemia represents a visual emergency. Early diagnosis with treatment should be initiated before the irreversible neuronal damage occurs. Two of our patients (patient 2 and 3) received intrathecal chemotherapy for prophylaxis of CNS involvement, and two of them (patient 1 and 3) received focal radiotherapy. None of our patients had overt CNS leukaemia at the time of ocular manifestation, by the definition which requires >5 mononuclear leukaemic cell/mm^3 of CSF. The optic nerve is considered

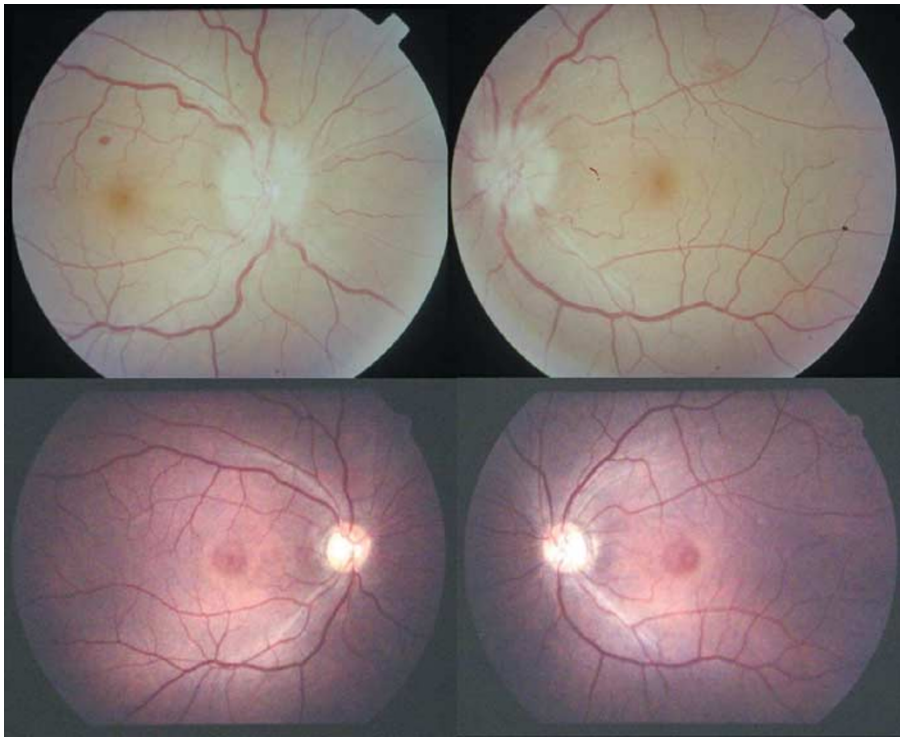

Figure 4 Case 3. Up: Severe optic disc oedema with retinal vessels engorgement was noted in both eyes. Down: The same optic nerve 4 weeks following local irradiation. Clear disc margin was noted.

a pharmacologic sanctuary from leukaemia therapy.[5,11] Nikaido *et al*[5] propose that there could be a barrier between the optic nerve lesions and the remainder of the CNS in the patients with leukaemic infiltration of the optic nerve. The barrier interrupts the smooth flow of CSF, so the cytotoxic drugs cannot reach the affected areas of the optic nerve. Focal irradiation is dramatically effective by reducing the leukaemic cell in the optic canal and this allows the cytotoxic drugs in the CSF to attack the neoplastic cells. Curto *et al*[12] suggested that high-dose radiotherapy to the eye (no less than 30 Gy) is needed for eradicating leukaemic cells. One of our patients had total recovery of his vision after intrathecal chemotherapy and focal irradiation with a total dose of only 2000 cGy given in 10 fractions. The other two patients died of systemic relapse of leukaemia after the initial leukaemic infiltration of the optic nerve. Thus, early administration of focal radiotherapy to reduce the leukaemic cell load is important for both visual recovery and possibly for prolonging survival.

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Sir,

Poland anomaly associated with ipsilateral combined hamartoma of retina and retinal pigment epithelium

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Poland anomaly appears with an incidence of about 1 in 30 000 live births and is three times more common in male than in female subjects. The syndrome was first described in 1841 by Alfred Poland, a British ophthalmologist, and typically comprises the combination of unilateral aplasia of the sternocostal head of the *pectoralis major* and an ipsilateral symbrachydactyly with a higher prevalence on the right side.[1] However, Poland anomaly is often associated with other abnormalities, such as hypoplasia or neoplasia of the breast, reduced axillar hair, anomalies of the bony thorax, dextrocardia, renal malformation, neuroblastoma, or leukemia/lymphoma. Most cases of Poland anomaly occur sporadically, but several familial cases have been reported, suggesting a postzygotic mutation of heterozygous individuals. Anomalies of the eye are rare and occur only in combination with Möbius syndrome; these comprise facial nerve palsy with eyelid paralysis or abduction inability.

Case report

We report on a 37-year-old Caucasian male who presented at our clinic with blurred vision in the right eye that had been present for more than 5 years. Medical history revealed that the man suffered from classical right-side Poland anomaly with ipsilateral symbrachydactyly that was surgically reconstructed and ipsilateral renal malformation and malrotation (Figure 1). Visual acuity in the right eye was 20/20, with a defined paracentral scotoma and metamorphopsia in the Amsler chart. The right eye fundus showed a slightly elevated grey lesion in the macular area involving the optic disc and adjacent retina. The lesion comprised a thickened retina with reduced transparency. The retinal vessels in

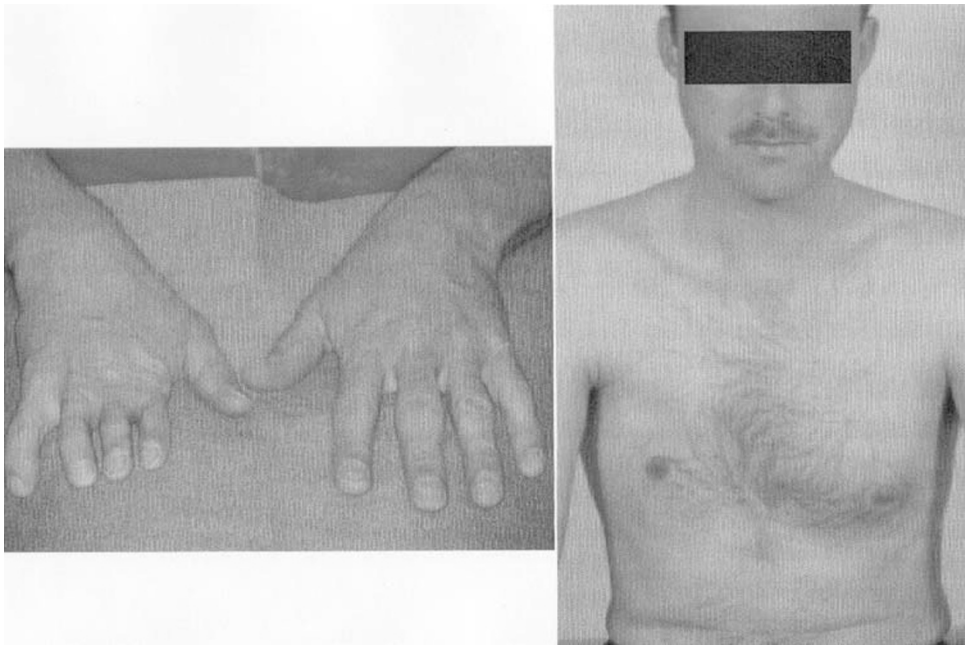

Figure 1 Our patient presenting typical right-sided Poland anomaly with hypotrophy of the *pectoralis major* and partially reconstructed symbrachydactyly.