Uveitis in a Child: Masquerade Syndrome Revisit

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Abstract

We present a case of relapsing acute lymphoblastic leukemia (ALL) in the anterior chamber, uveitis masquerade syndrome, which was confirmed by anterior chamber paracentesis and aqueous fluid cytology. Three months previously, the patient developed anterior uveitis without hematologic relapse. The uveitis responded well to topical steroid. After anterior chamber paracentesis, bone marrow relapse was detected. High doses of chemotherapy were prescribed. Ocular radiation was planned but the patient developed septicemia and expired. In our opinion, paracentesis should be performed without delay when uveitis develops in ALL, regardless of systemic relapse. Ocular manifestation may be the only sign of leukemic relapse or may present several months prior to systemic relapse.

Key word : Uveitits Masquerade Syndrome, Leukemia, Paracentesis

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Uveitis masquerade syndrome is an uncommon ocular inflammation occurring as a manifestation of underlying noninflammatory diseases. There are several conditions both malignant and non-malignant that can activate ocular inflammation or uveitis. Examples of non-malignant conditions include intraocular foreign body, multiple sclerosis, and retinal degeneration[1-3]. For malignancy, intraocular lymphoma and leukemia are the common conditions[4-6].

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Acute lymphoblastic leukemia (ALL) is associated with ocular manifestations more frequently than acute myeloid leukemia and chronic leukemia[7]. Either the anterior or posterior segment of the eye can be involved. The patient may present with anterior uveitis with or without hypopyon, hyphema, glaucoma, iris or retinal infiltrates, and optic nerve head infiltration[8].

We present a child who developed anterior uveitis with hypopyon during complete remission of ALL. We also demonstrate the laboratory investigation that helps confirm the diagnosis of leukemic relapse in the anterior chamber of the eye, the so called uveitis masquerade syndrome, and discuss the appropriate management of this condition.

CASE REPORT

A 9 year-old girl was referred to us for evaluation and management of her right eye. She was diagnosed with acute lymphoblastic leukemia twenty-four months prior and was treated with vincristine, prednisolone, adriamycin, and L-asparagenase in phase I induction. Phase II intensive treatment included prednisolone, 6-mercaptopurine, methotrexate, and cyclophosphamide. There was a history of 1800 cGy of cranial radiation and intrathecal methotrexate for phase III central nervous system prophylaxis. Phase IV maintenance chemotherapy was continued with 6-mercaptopurine, methotrexate, and cyclophosphamide. She was followed regularly and was in complete remission for fourteen months.

Three months previously, the parent noticed a white sediment in the anterior chamber of her right eye. The eye was slightly red. The patient did not report visual loss or eye pain. Visual acuity, measured with Snellen chart, was 6/6. The intraocular pressure, measured with Schiotz tonometer, was 25.8 mmHg. Slit lamp examination of the right eye revealed 1.4 mm level of white hypopyon in the anterior chamber. The pupil, iris, and fundus examination was normal. There was no abnormality detected in the left eye. General physical examination and bone marrow aspiration study were negative for systemic relapse of ALL.

The patient was diagnosed with hypopyon uveitis and secondary glaucoma in the right eye. Topical steroid (1% Prednisolone acetate eye drop) and anti-glaucoma medication (0.5% Timolol maleate eye drop) were prescribed for the eye condition. There was good response to treatment in which hypopyon disappeared within one week. Only minimal cells were detected in the anterior chamber.

Two weeks prior to hospitalization, the patient developed blurred vision in her right eye. Ocular examination revealed recurrent anterior uveitis with hypopyon. Best-corrected visual acuity was 6/12 and the intraocular pressure was 25.8 mmHg. Slit lamp examination demonstrated plasmoid aqueous and posterior synechiae with iris bombé. The pupil was 6 mm in diameter and did not react to light. White infiltrates were detected in the inferior retina. Anterior chamber paracentesis with aqueous fluid lavage was performed in order to confirm the diagnosis of uveitis and to wash out plasmoid aqueous.

Intraoperatively, both the anterior and posterior chamber (area beneath the iris) was filled with viscous aqueous fluid. There were numerous white-colored cells floating in the anterior chamber. The anterior and posterior chambers were irrigated with balanced salt solution and aqueous fluid was collected for cytopathologic study. There was no intraoperative complication. Post-operatively, best-corrected visual acuity had not improved, but the intraocular pressure was reduced to normal without medication. There was less plasmoid aqueous and cells in the anterior chamber.

Cytopathologic study of the aqueous fluid showed 92 per cent lymphoblastic cells with prominent nucleoli (Fig. 1). Systemic evaluation demonstrated bone marrow relapse of ALL. At this point, induction course of chemotherapy consisting of prednisolone, vincristine, L-asparagenase and intrathecal methotrexate were reintroduced. External beam radiotherapy to the right eye was planned. Unfortunately, the patient developed septicemia and expired.

DISCUSSION

Uveitis in children, although uncommon, is not a rare condition and might be associated with serious underlying diseases. There are four main presentations of uveitis: anterior uveitis, intermediate uveitis, posterior uveitis, and diffuse uveitis. According to Cunningham,[9] anterior uveitis accounts for 30-40 per cent, posterior uveitis for 40-50 per cent, intermediate uveitis for 10-20 per cent, and diffuse uveitis for 5-10 per cent of uveitis in children.

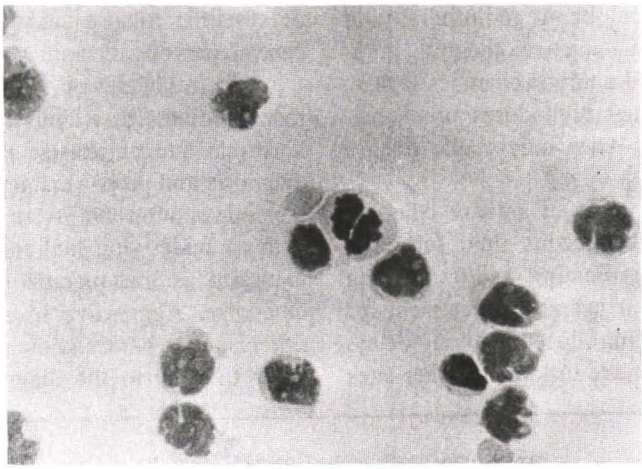

Fig. 1. Photomicrograph reveals aggregate of large, heterogeneous-sized lymphoblasts, with irregular and indented nuclei and variable nuclear/cytoplasmic ratio. Nucleoli are prominent. (Wright's stain, magnification x 400).

Among several complications associated with uveitis, complicated cataract and band keratopathy are common and might result in significant visual impairment[10]. Management of cataract can be very difficult in an eye with uveitis due to severe intraocular inflammation postoperatively. Other complications associated with uveitis include glaucoma, cystoid macular edema, and ocular neovascularization[11].

Juvenile idiopathic arthritis and toxoplasmic retinochoroiditis are the most common causes of anterior and posterior uveitis respectively. Both of them are inflammatory diseases in nature. In some children, however, uveitis occurs as a manifestation of underlying noninflammatory diseases. This is called "uveitis masquerade syndrome". Reported conditions associated with uveitis masquerade syndrome involve both malignant and non-malignant diseases such as retinitis pigmentosa, intraocular foreign body, multiple sclerosis, retinoblastoma, and hematologic malignancies especially lymphoma and leukemia. In case of uveitis developing prior to the diagnosis of primary disease, definite treatment might be delayed and cause devastating results.

Ocular manifestations of leukemia can occur primarily at the diagnosis of leukemia or during the remission phase of the disease. Retina, choroid, and optic nerve are the common sites of involvement. Anterior chamber and iris infiltrates are less common manifestations. In our patient, the first episode of uveitis developed after 11 months of complete remission of ALL. The interval between initial diagnosis of ALL and the first ocular relapse was 21 months. This duration is within the range previously reported (12 to 74 months)[12].

It is controversial whether anterior chamber paracentesis should be routinely performed to diagnose uveitis masquerade syndrome, since it may cause surgical complications such as iris prolapse and cataract formation. Badeeb et al attempted to differentiate leukemic infiltrates from nonspecific uveitis by clinical manifestation alone without laboratory support[13]. They concluded that the following clinical clues suggest leukemic infiltrates in the eye: normal sized pupil, segmental swelling of iris, hypopyon, hyphema, absence of posterior synechiae, and increased intraocular pressure.

Three months prior to hospitalization, our patient developed uveitis and only topical steroid was prescribed for intraocular inflammation. Retrospectively, we should have performed anterior chamber paracentesis to document ocular relapse of ALL without delay. Although the eye condition responded well to topical medication and hematologic relapse was not demonstrated, we could not exclude leukemic relapse in the eye.

Because the anterior segment part of the eye is a sanctuary for tumor cells, we could not depend on systemic chemotherapy alone to eradicate ocular relapse. Recommended treatment

methods include external beam radiotherapy or radioactive plaque,[14] local chemotherapy, intrathecal chemotherapy, and anterior chamber lavage. It is controversial whether high doses of chemotherapy should be added when only ocular relapse is evident[15].

The main advantages of anterior chamber lavage include providing aqueous fluid for cytopathologic study and eradicating and/or diluting tumor cells in the anterior chamber. Treatment for ocular relapse must be introduced without delay. Attempt should also be made to identify other sites of systemic relapse such as bone marrow or the central nervous system.

In conclusion, we present uveitis masquerade syndrome in a child with acute lymphoblastic leukemia and emphasize the importance of early diagnosis and proper management of this condition. It is our opinion that uveitis developing in children with an underlying malignant condition should be managed as masquerade syndrome until proven otherwise. Aggressive investigation such as anterior chamber paracentesis should be performed in order to confirm the diagnosis.

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ภาวะม่านตาอักเสบในเด็กจากโรคมะเร็งเม็ดเลือดขาว

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ผู้ป่วย Acute lymphoblastic leukemia (ALL) 1 ราย ได้รับการวินิจฉัยภาวะกำเริบของ ALL ในช่องหน้าลูกตาด้วยการตรวจน้ำจากช่องหน้าลูกตาด้วยกล้องจุลทรรศน์ ผู้ป่วยเคยมีประวัติช่องหน้าลูกตาอักเสบ ซึ่งตอบสนองดีต่อยาหยอดตาสเตียรอยด์ เมื่อ 3 เดือนก่อน ภายหลังการตรวจน้ำจากช่องหน้าลูกตา แพทย์ตรวจพบการกำเริบของ ALL ในไขกระดูกด้วย จึงได้ให้การรักษาด้วยยาเคมีบำบัด และเตรียมฉายรังสีบริเวณลูกตา แต่ผู้ป่วยเกิดภาวะติดเชื้อในเลือดและเสียชีวิตเสียก่อน ผู้รายงานมีความเห็นว่า ผู้ป่วย ALL ที่มีการอักเสบของช่องหน้าลูกตา ควรได้รับการเจาะตรวจน้ำจากช่องหน้าลูกตา เพราะอาจเป็นอาการนำ หรือเป็นเพียงอาการเดียวที่บ่งถึงการกำเริบของโรค

คำสำคัญ : Uveitits Masquerade Syndrome, Leukemia, Paracentesis

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