Clinical & Experimental Ophthalmology

Hung and Kuo, J Clin Exp Ophthalmol 2014, 5:5
http://dx.doi.org/10.4172/2155-9570.1000359

Case Report Open Access

Unilateral Optic Nerve Leukemic Infiltration and Exudative Retinal Detachment as Initial Manifestations of Central Nervous System Relapse in Acute Lymphoblastic Leukemia of Children

Kuo-Chi Hung[1] **and Hsi-Kung Kuo**[1*]

[1]*Department of Ophthalmology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan*

[*]**Corresponding author:** Hsi-Kung Kuo MD; Department of Ophthalmology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan 2F, No.123, Dapi Rd, Niaosong Dist, Kaohsiung City 83301, Taiwan (R.O.C.), Tel: +886-7-731-7123; Fax: +886-7-735-2775; E-mail: hsikung@cgmh.org.tw

Received date: Jul 07, 2014, **Accepted date:** Sep 28, 2014, **Published date:** Sep 30, 2014

Abstract

Acute lymphoblastic Leukemia (ALL) is a malignant neoplasm caused by the proliferation of poorly differentiated precursors of the lymphoid cells, which are known as blast cells. It is primarily the most common type of childhood Leukemia. Although 70-80% with ALL is cured with modern chemotherapy, 20-30% still have to endure relapse, particularly in the central nervous system (CNS) after attainment of remission. Treatment to prevent recurrence is based on cranial irradiation and intrathecal chemotherapy after conventional induction chemotherapy and the achievement of complete remission. However, the orbital cavity and optic nerve are relatively unaffected by being shielded during brain irradiation and serve as sanctuaries of ALL. Here, we describe a 12-year-old boy with ALL for one year who achieved complete remission after induction chemotherapy. He developed sudden loss of ipsilateral vision prior to CNS relapse twice. His initial ocular presentations noted on ophthalmic examination are unilateral optic nerve Leukemic infiltration and exudative retinal detachment (RD) respectively.

Keywords: Optic nerve infiltration; Retinal detachment; Leukemia

Case Report

In February 2010, a 12 year old boy presented with intermittent postprandial vomiting, constipation, abdominal dull pain, high grade fever, and progressive lethargy for one week. He did not have any congenital or systemic diseases before. The complete blood count revealed a hemoglobin level of 11.3 g/dL, a leukocyte count of 268,400/μL (91% blasts, 6% neutrophils), and a platelet count of 43,000/μL. His blood urea nitrogen and serum creatinine are 36 mg/dL and 5.8 mg/dL respectively. Hepatosplenomegaly and petechiae over anterior chest wall were also discovered. Bone marrow (BM) examination was suggestive of ALL of T-cell lineage with L1 morphology. Based on the National Cancer Institute risk group classification [1], he is a high risk case with poor prognosis due to leukocytosis greater than 50,000/μL and diagnosed age older than 10 years. Very high risk induction chemotherapy with conventional protocol (TPOG-ALL-2002 VHR) comprising of vincristine 1.5 mg/m^2, idarubicin 8 mg/m^2, prednisone 40 mg/m^2, asparaginase 5,000 U/m^2, cyclophosphamide 1000 mg/m^2, cytarabine 75 mg/m^2, and mercaptopurine 60 mg/m^2 was instituted for ten weeks. Complete remission was achieved in 43rd day after induction chemotherapy based on his subsequent peripheral blood smears and examination of his BM documents. Then consolidation chemotherapy with oral mercaptopurine 25 mg/m^2 and 24-hour infusion of methotrexate 5 g/m^2 were given to the child for eight weeks, following by re-induction chemotherapy. His cerebrospinal fluid (CSF) examination was done prior to every drug instillation and thereafter showed no evidence of CNS disease.

In November 2010, the child complained of dimness of vision in his left eye. His best corrected visual acuity (BCVA) in right eye was 20/20 and in left eye was 20/40. His color vision with SPP 2 test was abnormal in left eye, and relative afferent pupillary defect also appeared. Temporal restricted visual field was noted in left eye. On ophthalmoscopy, left sided optic disc edema, edematous peripapillary nerve fiber layer with exudates, and tortuous veins were detected (Figure 1).

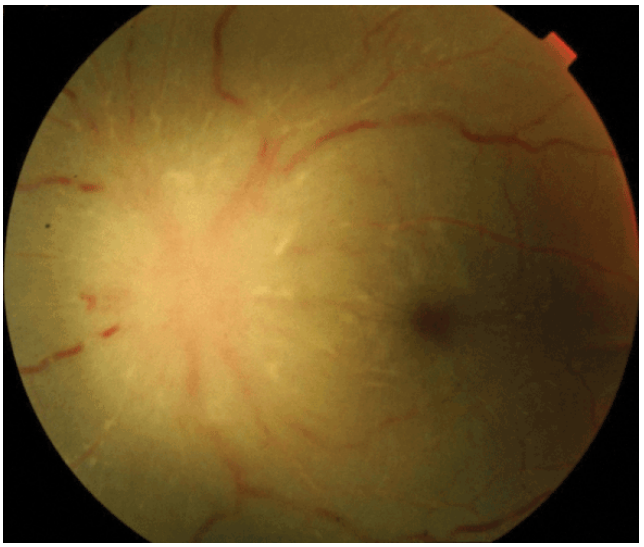

Figure 1: Ophthalmoscopy demonstrated optic disc edema in left eye.

There was no peripapillary retinal hemorrhage. Vitreous, macula and retinal vessels were normal. His right eye was normal. Cytological

examination of CSF performed one week earlier did not reveal any Leukemic cells. Further investigations including his post-contrast fat-suppressed T1-weighted images on orbital magnetic resonance imaging (MRI) demonstrated no active optic perineuritis. One week later, his BCVA in left eye decreased to counting fingers at 15 cm and we initiated intravenous megadose steroids therapy (methylprednisolone 500 mg every six hours for four days), then changed to oral form (prednisolone 30 mg twice in a day). Blood tests including hemogram, viral survey, and inflammatory indices were all within normal limits. His fundus revealed gradual decrease in disc edema with residual fibrotic membrane and temporal retinal pigment epithelium degeneration (Figure 2).

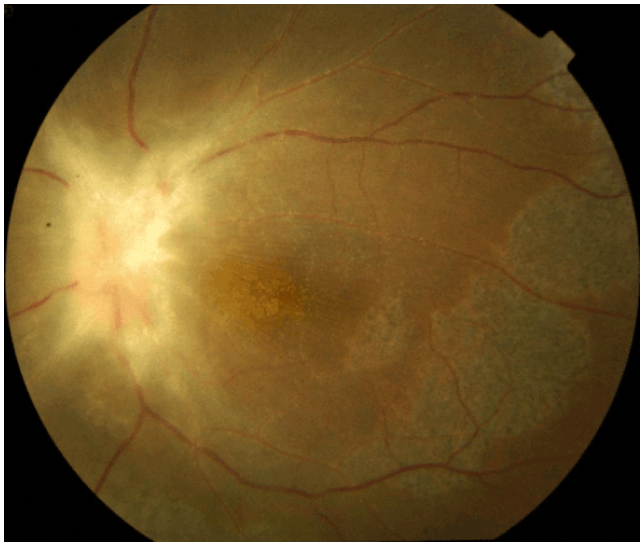

Figure 2: Ophthalmoscopy showed optic disc edema with residual fibrotic membrane in left eye.

Edema of macular or peripapillary region improved as well. There were no retinal folds or choroidal mass on ophthalmoscopy. He also felt subjective visual improvement in left eye and his BCVA in left eye returned to 20/50. His CSF study showed no Leukemic cells. We then continued to follow his scheduled chemotherapy of TPOG-ALL-2002 VHR. However, a repeated lumbar puncture three months later in February 2011 revealed that his CSF is infiltrated with moderate mononuclear white cells. Meanwhile, the BM remained cytologically and immunophenotypically negative for Leukemic involvement. CNS Leukemia is suspected and intrathecal continuation chemotherapy with methotrexate 12 mg/m^2 was reinstituted. Follow-up cytologic studies of the CSF revealed no residual Leukemic cells.

Unfortunately, about one year later in November 2011, he noticed a progressive enlarged black spot over his temporal visual field in left eye and his BCVA decreased to hand motion at 15 cm. Subretinal infiltrates and severe exudative RD in left eye was noted (Figure 3).

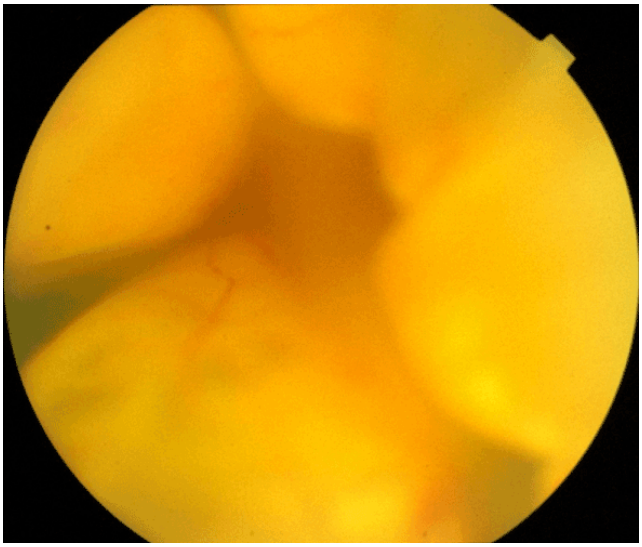

Figure 3: Ophthalmoscopy revealed prepapillary membrane with exudative retinal detachment.

His cytological examination of the CSF revealed infiltration by several blasts, which was suggestive of CNS Leukemia. We continued to perform intrathecal continuation chemotherapy and regressed exudative RD and neovascular glaucoma with high intraocular pressure of 33 mmHg were found in his left eye during his follow-up. He finally received left orbital irradiation with a total of 3060 cGy in 17 fractions delivered to the whole brain including the retrobulbar area. His exudative RD partially regressed with residual subretinal infiltrates (Figure 4) but loss his visual acuity (negative light perception) in left eye.

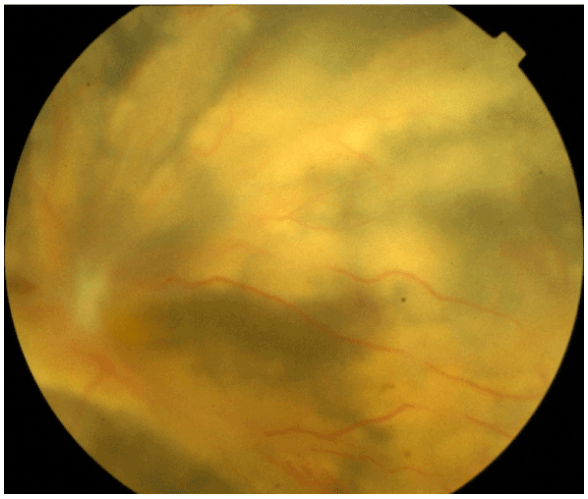

Figure 4: Exudative retinal detachment partially regressed with residual subretinal infiltrates on ophthalmoscopy.

Citation: Hung K, Kuo H (2014) Unilateral Optic Nerve Leukemic Infiltration and Exudative Retinal Detachment as Initial Manifestations of Central Nervous System Relapse in Acute Lymphoblastic Leukemia of Children. J Clin Exp Ophthalmol 5: 359. doi: 10.4172/2155-9570.1000359

Discussion

CNS involvement is becoming more frequent with more diagnostic and therapeutic treatments have allowed an improvement of the survival of patients suffering from ALL. Leukemic infiltration of the optic nerve is relatively rare and is considered to be one of the significant clinical findings of CNS Leukemia [2]. In our case, the patient is a 12-year-old boy with remission of his ALL, who presented with sudden onset of visual dimness in his left eye. Prior to his first episode of CNS relapse, optic disc edema was noted on ophthalmic examination. His CSF study revealed blasts and relapse of CNS Leukemia is impressed. We performed intrathecal chemotherapy on him and the CNS Leukemia was quiet down. Optic disc edema is the most frequent sign of optic nerve involvement. It could be due to direct infiltration of the nerve head in which case the intracranial pressure may be normal; or by passive swelling because of retrolaminar Leukemic invasion; or by passive swelling secondary to increased intracranial pressure [3].

Less commonly, RD has been reported in only a few cases of ALL worldwide, especially as a presenting sign of the disease or the first sign of relapse [4]. Following previous episode, the ophthalmic examination of our case remained stable for almost one year until we found exudative RD with subretinal infiltrates on ophthalmic examination. Neovascular glaucoma was impressed later owing to persistent RD. CSF study showed relapse of CNS Leukemia once again. His exudative RD regressed after brain and orbital irradiation but he lost his vision in left eye. Primack et al reported a case of ALL in prolonged remission, who had the extramedullary relapse presented with total RD and optic nerve involvement in one eye [5]. In our case, RD was found before the second CNS relapse in his course. We presumed that RD may develop due to choroidal involvement by Leukemic cells. The manifestation responded well to irradiation, suggesting Leukemic cell infiltration as the underlying pathology. Impairment of visual acuity might be the final result of ocular involvement by Leukemic cells.

In conclusion, optic neuropathy and RD are of paramount importance to early diagnosis of CNS relapse in Leukemia. Ophthalmologists should be aware of these possible manifestations and etiologies in childhood ALL even though they have already achieved remission. With timely and aggressive administrations, the possible cure may be achieved.

References

1. Smith M, Arthur D, Camitta B, Carroll AJ, Crist W, et al. (1996) Uniform approach to risk classification and treatment assignment for children with acute lymphoblastic leukemia. J Clin Oncol 14: 18-24.
2. Ellis W, Little HL (1973) Leukemic infiltration of the optic nerve head. Am J Ophthalmol 75: 867-871.
3. Bhatt UK, Gregory ME, Madi MS, Fraser M, Woodruff GH (2008) Sequential leukemic infiltration and human herpesvirus optic neuropathy in acute lymphoblastic leukemia. JAAPOS 12: 200-202.
4. Kim J, Chang W, Sagong M (2010) Bilateral serous retinal detachment as a presenting sign of acute lymphoblastic leukemia. Korean J Ophthalmol 24: 245-248.
5. Primack JD, Smith ME, Tychsen L (1995) Retinal detachment in a child as the first sign of leukemic relapse: histopathology, MRI findings, treatment, and tumor-free follow up. Journal of pediatric ophthalmology and strabismus 32: 253-256.