Caspian Journal of Pediatrics
Babol University of Medical Sciences
e-ISSN: 2383-3106

Isolated Ocular Relapse of Acute Lymphoblastic Leukemia in Down Syndrome: A Case Report and Literature Review

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Article Info.

Article type:
Case Report

Received: 27 Nov. 2023
Revised: 7 Jan. 2024
Accepted: 20 Feb. 2024
Published: 6 March 2024

Keywords:
Acute Lymphoblastic Leukemia,
Down Syndrome,
Ocular Relapse

ABSTRACT

Background and Objective: Relapse of acute lymphoblastic leukemia (ALL) usually occurs in the bone marrow, testes and brain, but the occurrence of relapse in the orbits seems to be rare. In this case, we present a relapse of ALL that occurred in the eyes.

Case Report: A 9-year-old girl with Down syndrome, a known case of ALL, was in remission after complete chemotherapy (Berlin-Frankfurt-Munich (BFM) protocol) and presented to Amirkola Children' Hospital with conjunctivitis and blurred vision. She had been in remission for one year (since 1991-1992). Paracentesis of the anterior chamber was performed to obtain a sample of the aqueous humor for cytology. The smear revealed involvement of the eye with leukemic cells. Hematologic examinations were performed. The bone marrow and central nervous system (CNS) were normal. While we continued chemotherapy for four months, the patient presented with headache and bone pain. A re-examination revealed that she had a relapse in the bone marrow and CNS. She died from leukemia, despite appropriate therapy.

Conclusion: Ocular paracentesis should be performed without delay when blurred vision develops in ALL, regardless of systemic signs and symptoms.

Cite this article: Galini Moghadam T, Mahmoodi Nesheli H. Isolated Ocular Relapse of Acute Lymphoblastic Leukemia in Down Syndrome: A Case Report and Literature Review. *Caspian J Pediatrs* March 2024; 10: e3.

[DOI: 10.22088/CJP.BUMS.10.0.3]

Introduction

Acute leukemia is the most common type of cancer in children and accounts for around 30 percent of all childhood malignancies [1]. The risk of developing acute lymphoblastic leukemia (ALL) is about 10 to 20 times higher in children with Down syndrome (DS) than in children without DS and accounts for 1 to 3 percent of all patients with ALL [2, 3].

Children with DS who develop ALL often respond to chemotherapy in a similar way to children without DS. Prior to the use of preventive central nervous system (CNS) therapy, up to 80 percent of children with ALL who were in complete bone marrow remission relapsed with "leukemic meningitis [4].

Craniospinal radiotherapy or cranial radiotherapy, once considered the standard of care, was effective in preventing CNS leukemia but was associated with significant toxicities such as cognitive impairment and altered white matter development [5]. In one report, eye abnormalities occurred in 38 percent of infants aged 2-12 months and 80 percent of children aged 5-12 years [6]. Involvement of the anterior chamber of the eye is uncommon in patients with ALL and has never been described in DS with ALL. After initial treatment, patients are routinely monitored to detect treatment-related complications and disease relapse. Ophthalmologic disorders requiring monitoring and intervention affect the majority of children with DS. The retina and vitreous may be affected in ocular recurrences. Leukemic infiltrates, glaucoma and opportunistic infections may occur in the anterior segment of the eye. Proptosis, conjunctival hemorrhage, choroidal infiltrate and cataract have been reported as recurrences [7, 8]. Isolated extramedullary ocular relapse of ALL can occur after peripheral blood stem cell transplantation [9]. Early diagnosis and treatment of ocular leukemia relapse probably offers the best chance of definitive cure in children [10]. Isolated ocular relapse can be successfully treated, especially if it occurs after discontinuation of therapy [11]. Treatment should be a combination of topical corticosteroids, chemotherapy and radiotherapy [12]. Ophthalmic relapse may be asymptomatic [13]. Bilateral exudative retinal detachment may be a sign of ALL in an otherwise healthy young adult. Clinicians should be aware of the possibility of leukemia in such patients [14]. Cure is possible in patients who have had leukemic ophthalmopathy in first complete remission and have been treated with chemotherapy and high-dose radiotherapy to the affected eye [7].

Case presentation

A nine -year -old girl, with Down syndrome, a known case of ALL, was treated according to the current UKALL protocol, which did not include cranial irradiation. She was in remission from 1991 to 1992 and presented with conjunctival hemorrhages and poor vision in the left and right eye that persisted for two weeks. After three years of treatment, the patient was in remission for one year. She was routinely monitored to detect treatment-related complications and disease relapse.

Eye examinations were performed; anterior chamber paracentesis with aqueous humor cytology confirmed the diagnosis of ocular involvement by lymphoblasts. Hematology tests were performed and the blood film was normal. Further investigations revealed that she had no bone marrow and central nervous system relapse. Lumbar puncture revealed normal central nervous system fluid .

Local irradiation of both orbits with a maximum dose of 800 cGy followed by re-induction chemotherapy and craniospinal irradiation was performed for ocular recurrence. Patient treated with Vincristine, peg asparjinase, ciclophosphamide and adriamycine for CNS relaos prophilaxia intratecal chemotherapy was done. While we continued the chemotherapy for four months, the patient presented with headaches and bone pain .

Further investigations indicated that she also had a recurrence in the bone marrow and central nervous system. This is the report of a child who had no recurrence of hematologic leukemia for one year after three years of chemotherapy, but developed CNS leukemia after remission. Unfortunately, the patient died 11 months after the ocular relapse.

[DOI: 10.22088/CJP.BUMS.10.0.3]

Fig 1. Presentation of conjunctivitis in leukemia involvement

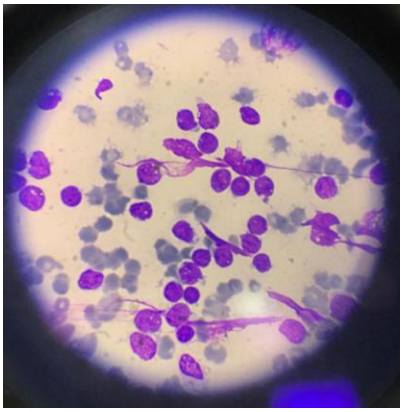

Fig 2. Leukemia bone marrow relapse: lymphoblastic cells

Discussion

Our patient had developed conjunctival hemorrhage, photophobia and blurred vision without symptoms of leukemia relapse. Ophthalmic examination showed infiltration of the anterior chamber of the eye. Although this phenomenon is rare, it is very important. Early diagnosis of relapse in any part of the body leads to a better prognosis than delaying the diagnosis of relapse.

Other studies reported that the only sign of relapse was bilateral anterior uveitis, bilateral leukemic optic nerve infiltration, conjunctival mass, pseudohypopyon refractory to topical and systemic corticosteroids, and unilateral hypopyon as the first manifestation of extra-medullary relapse [7, 8, 15-17]. Our patient died despite radiation and systemic chemotherapy. In the event of a recurrence of ALL in the anterior chamber, aggressive follow-up treatment appears to be warranted [18]. We should consider a serious event if any point of the body was affected. Although the bone marrow was initially intact, it was affected despite chemotherapy. This is a reason for paying attention to consanguinities such as testis, brain, eyes and so on.

If ocular involvement is suspected in ALL, an ocular puncture should be performed as soon as possible.

Conclusions

Although involvement of the anterior chamber of the eye is uncommon in patients with ALL and has never been described as a primary relapse in a DS with ALL, it should be noted as a site of leukemic cell infiltration. An ophthalmic assessment is essential in patients with hematologic malignancies to make an early diagnosis of ocular involvement. In our opinion, if anterior chamber infiltration is suspected in ALL, paracentesis should be performed immediately regardless of systemic relapse.

Acknowledgments

The authors would like to thank the Clinical Research Development Department of Amirkola Children's Hospital for the necessary coopration.

Funding

This study was self-funded.

Ethical approval

This study was approved by the Ethics Committee of Babol University of Medical Sciences (Ethical code: IR.MUBABOL.REC.1402.043).

Conflict of interest

There was no conflict of interest.

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[DOI: 10.22088/CJP.BUMS.10.0.3]