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OCULAR INVOLVEMENT IN CHILDHOOD LEUKEMIAS*

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SUMMARY: Soylu M, Tanyeli A, Özdemir N, Eroğlu A, Ersöz TR. (Departments of Ophthalmology and Pediatrics, Çukurova University Faculty of Medicine, Adana, Turkey). Ocular involvement in childhood leukemias. Turk J Pediatr 1994; 36: 35-41.

Ocular involvement was detected in 36 of 84 children suffering from acute leukemia. The major manifestation of leukemic ophthalmopathy was retinal hemorrhage. Neither platelet counts nor hematocrit values correlated with the occurrence of hemorrhages. As the eye is a pharmacologic sanctuary, it is emphasized that full ophthalmologic evaluation of leukemic patients is a critical part of their follow-up and will guide the choice of therapeutic regimen. *Key words: childhood leukemias, ocular involvement, retinal hemorrhages, optic nerve involvement, local radiotherapy.*

Leukemias are a heterogenous group of neoplasms characterized by malignant transformation of hemopoietic cells. Ophthalmopathy is commonly seen in leukemic patients. Ocular involvement such as retinal hemorrhages, exudation and / or papilledema may not require specific treatment. However, direct leukemic infiltration does require specific therapy[1-5].

Ocular involvement in leukemias is relatively constant. The incidence of leukemic ophthalmopathy was found to be 23-80 percent in autopsy series, and 9-62 percent in clinical studies[1,2,6,7].

In the present study, ophthalmoscopic examinations were performed in children with leukemia to evaluate the factors affecting leukemic ophthalmopathy, and the findings were recorded and analyzed retrospectively.

Material and Methods

The study group consisted of 84 patients with leukemia who were followed in the Pediatric Hematology and Ophthalmology Clinics at Çukurova University Medical Faculty between 1987 and 1992. There were 54 (64.3%) boys and 30 (35.7%) girls between the ages of 6 months and 15 years (mean age 8.36 ± 3.84 years).

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The patients were followed for one month to five years. Seventy-three (87%) of the patients were diagnosed with acute lymphoblastic leukemia (ALL), and 11 (13%) with acute myeloblastic leukemia (AML).

In all patients, visual acuity testing, and biomicroscopic, direct and indirect ophthalmoscopic evaluations were done. Fundus photographs were taken if the patients were cooperative. The type of leukemia, date of initial diagnosis, hematological and systemic manifestations were recorded, and a statistical analysis was done using Fisher's exact test.

Results

Ocular involvement occurred in 36 patients (43%). Thirty-three (45.2%) cases with ALL and three (27.2%) with AML showed leukemic ophthalmopathy.

Anterior segment involvement in one of the patients with AML, a mass was detected on the upper eyelid, and another patient had a subconjunctival hemorrhage. In the ALL group, there were subconjunctival and / or subcutaneous hemorrhage in three, mixed ciliary injection and tyndallization in one, and posterior subcapsular catarct[5] in two cases. The catarcts developed three and 36 months after initial diagnoses (Table I).

Table I: Types of Ocular Involvement in Leukemic Children

Type of Ocular Involvement	Type of Leukemia	
	ALL (n)	AML (n)
Anterior segment involvement		
infiltration	–	1
hemorrhages	3	1
keratitis	2	–
uveitis	1	–
cataract	2	–
Posterior segment involvement		
infiltration	6	2
hemorrhages	16	3
exudate	4	1
vascular dilatation	4	1

Table II: Relationship Between Some Hematological Parameters and Retinal Hemorrhages

Hematological Parameter	Retinal Hemorrhages	
	n	%
Thrombocyte count (/ mm^3)		
< 30.000	8	42.1
30.000-100.000	4	21
> 100.000	7	36.8
Hematocrit (%)		
< 30	15	79
30-35	3	15.8
> 35	1	5.2

Table III: Nerve Involvement

Type of Leukemia	Papilledema	Optic Atrophy	Cranial Palsy
ALL	9	10	3 Facial, 1 Abducent
AML	1	–	–

Table IV: Relationship Between Ocular Involvement and Duration of Leukemia

Type of Lesions n (%)	0-2 Months	3-10 Months	11 Months-4 Years
Retinal hemorrhages	13 (68.5%)	4 (21%)	2 (10.0%)
Papilledema	3 (30%)	4 (40%)	3 (3%)
Optic atrophy	3 (37%)	4 (50%)	1 (13%)
Retinal exudate	–	–	1

* Figures in paranthesis indicate percentages.

Discussion

Ophthalmopathy is commonly seen in leukemias, usually when the disease is clinically and hematologically active. In our study, no significant difference in ocular involvement was found in patients with ALL and AML. The incidence of leukemic ophthalmopathy is known to be higher in acute leukemias than in

chronic leukemias, but no data are available regarding the differences among the types of acute leukemias[3].

Infiltration of the anterior segment by leukemic cells is uncommon. Involvement of the orbit and adnexa, nodular infiltration in the limbus, conjunctival and corneal infiltration, hyphema, uveitis, glaucoma and cataracts can all be seen in leukemias[2,3,8,9]. In our study, no significant difference was found between anterior segment involvement and the type of leukemia ($p = 0.849$). Anterior uveitis was detected in one of our patients with ALL. In clinicopathologic studies, it was found that in uveitis, the cells in the anterior chamber are leukemic cells[2]. Posterior subcapsular cataracts were detected in two cases with ALL. Although the mechanism of cataract development is not well known, it is postulated that lens opacities result from the toxic effect of various therapeutic agents on the lens[8].

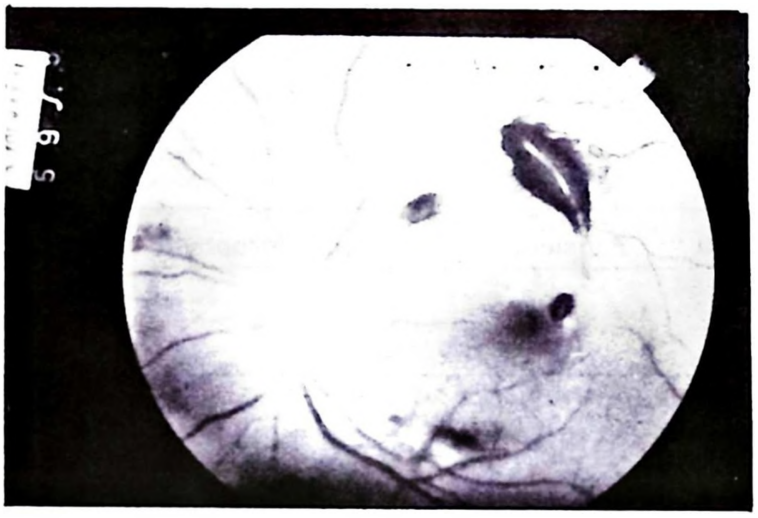

Fig. 1: Intraretinal and white centered hemorrhages in a patient with ALL.

Fig. 2: Papilledema and retinal hemorrhages in a patient with ALL who had CNS involvement.

No statistically significant difference in retinal involvement was found between patients with ALL and those with AML ($p = 0.366$). Retinal hemorrhages are significant features of leukemic ophthalmopathy. Although they have been attributed to anemia and thrombocytopenia the exact mechanism of hemorrhages is not well known. No significant correlation has been found between hematologic status and hemorrhages. In our study group, neither platelet counts nor hematocrit values were correlated with retinal hemorrhages.

There are at least three mechanisms by which the optic nerve and retina may be involved in leukemia. There may be: 1. papilledema secondary to increased intracranial pressure; 2. direct infiltration of the retina by leukemic cells; or 3. the presence of neoplastic cells in the optic nerve without retinal involvement[2,4]. Papilledema, usually bilateral, is a common sign of increased intracranial pressure in patients in whom malignant cells have proliferated in the subarachnoid space. These cells produce mechanical or ischemic effects on the optic nerve, axoplasmic transport is obstructed, and as a result papilledema occurs[1,2]. Except in one case, all cases with papilledema in our study group exhibited central nervous system (CNS) involvement, and intrathecal chemotherapy and radiotherapy were started.

Although most descriptions of leukemic infiltration of the retina and optic nerve are based on appearances at necropsy, the diagnosis may be made during life, as the ophthalmoscopic appearance of leukemic involvement of the optic nerve is characteristic. Typically there are areas of opaque swelling, and these may develop asymmetrically and involve one eye before the other[4]. Also, magnetic resonance imaging (MRI) facilitates early recognition of optic nerve involvement[11]. In one of our cases with ALL, there was typical optic nerve involvement (Fig. 3). In this patient's other eye, there was optic atrophy. After the patient was treated with intrathecal chemotherapy and local radiotherapy, optic

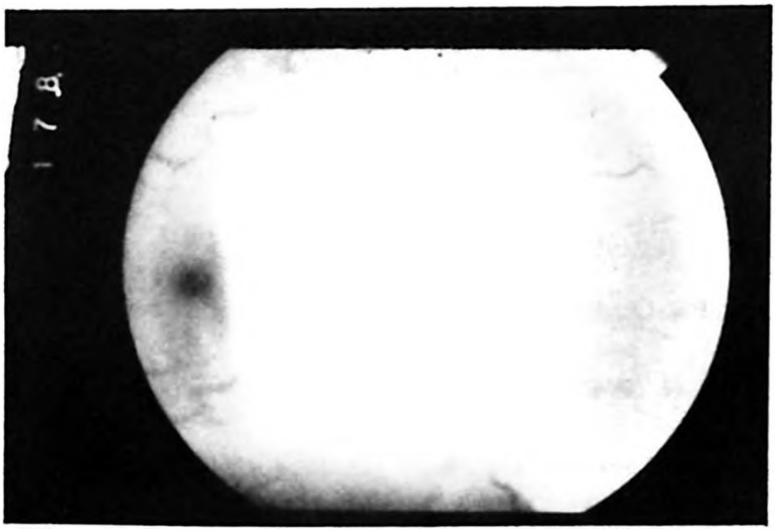

Fig. 3: Optic nerve involvement before treatment.

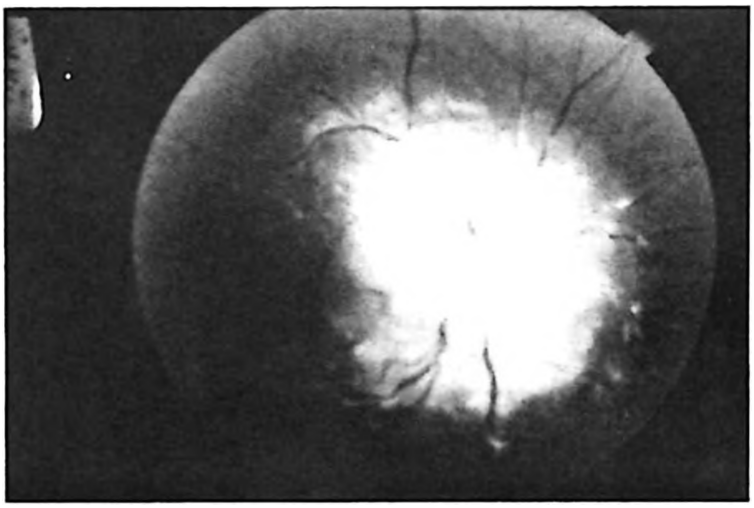

Fig. 4: After local radiotherapy, optic atrophy developed.

nerve involvement regressed and optic atrophy developed (Fig. 4). Although meningeal leukemia is sometimes treated with intrathecal cytotoxic drugs and cranial radiotherapy, such an approach to leukemic ophthalmopathy is not effective because the subarachnoid space ends just posterior to the globe. Thus, patients with optic nerve involvement need to be treated with local radiotherapy[4].

In our study group hemorrhages were detected mostly in the first months of diagnosis. Hemorrhages occur when the disease is active. It can be postulated that in time, chemotherapy leads to remission and hemorrhages dissappear[1,2].

It can be postulated that although leukemic ophthalmopathy is not an indicator for prognosis and mortality of leukemia, ophthalmoscopic evaluation should be performed in all patients. Ophthalmoscopic features play an important role, especially for the diagnosis of CNS and optic nerve involvement. Leukemic ophthalmopathy should be treated locally, as the eye is a pharmacologic sanctuary for leukemic cells. As a result, combined use of intrathecal cytotoxic drugs with local radiotherapy seems to provide the best chance of controlling or curing leukemic involvement of the eye.

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