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## Ocular involvement in Children with newly diagnosed leukemia

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### Abstract

**Background:** Knowledge of ocular involvement in leukemia is important because the eye is the only site where involvement of nerves and blood vessels can be directly observed and eye symptoms may be the initial mode of presentation of the systemic illness or the first manifestation of relapse after remission – inducing chemotherapy

**Objective:** To figure out the ophthalmologic complications of leukemia in a sample of children patients at a stage before the initiation of treatment.

**Methods:** A total sample of 102 patients (aged between 1 and 15 years) with leukemia was studied. The sample was taken from the Maternal and Child hospital. All the children diagnosed as leukemia and admitted during the period from March 2002 through November 2003 were pooled and included in the study. Eye complications were checked through a complete ophthalmic examination.

**Results:** Ocular lesion were seen in 50 (49 %) of patient with leukemia; 28 (27.4%) males and 22 (21.5%) females. . Eye changes were seen more in patients with acute lymphoid leukemia 43 (42.1%). Retinal changes were the most common pathology.

**Conclusion:** Retinal lesions are the most common eye changes in leukemia especially in the acute lymphocytic type.

**Keywords :** Leukemic retinopathy ,acute lymphocytic leukemia ,acute myelogenous leukemia,chronic myelogenous leukemia

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### Introduction

The leukemias are malignant neo-plasma of the haematopoietic stem cells, characterized by diffuse replacement of the bone marrow by neoplastic cells<sup>[1]</sup>.

It is classified according to the duration and mode of presentation as acute or chronic based on the predominant cells involved, both types are further classified as myelogenous or lymphocytic forms .Thus, the diagnosis of leukemia will be either acute myelogenous leukemia (AML), acute lymphocytic leukemia (ALL), chronic myelogenous leukemia (CML) or chronic lymphocytic leukemia (CLL)<sup>[2, 3]</sup>. Ophthalmic involvement can be classified into two major categories

1-Primary or direct leukemia infiltration.

2-Secondary or indirect involvement.

The direct leukemia infiltration can show three patterns: anterior segment uveal infiltration, orbital infiltration and neuro-ophthalmic signs of central nervous system. leukemia that include optic nerve infiltration , cranial nerve palsies and papilloedema. The secondary changes are the result of haematological abnormalities of leukemia such as anemia, thrombocytopenia, hyperviscosity and immunosuppression. These can manifest as retinal or vitreous haemorrhage infection and as vascular occlusions, in some cases the ocular involvement may be asymptomatic<sup>[4, 5]</sup>.

Retinopathy is relatively common: the findings may be similar to those of anemia with flame-shaped haemorrhages, Roth spots and cotton –wool

spots, and peripheral retinal neovascularization which is an occasional feature of chronic myeloid leukemia, rarely leukemia pigment epitheliopathy secondary to choroidal infiltration characterized by a (leopard spot retinal)<sup>[6]</sup>, or vascular abnormalities affecting the retina: intraretinal hemorrhages, white-centered retinal hemorrhages, cotton–wool spots, macular hemorrhage, subhyaloid hemorrhage, vitreous hemorrhage, or neuro-ophthalmic sign and central nervous system disease may lead to papilloedema secondary to raised intracranial pressure and isolated cranial nerve palsies<sup>[7,8,9]</sup>.

The aim of this study is to determine the eye changes in the newly diagnosed patients with Leukemia.

### Patients & Methods

#### Settings:

The study was conducted in the oncology unit of Basra Maternal and Child hospital during the period from March 2002 through November 2003.

#### Design:

A cross sectional study was designed as a cohort one.

#### Sampling:

A total of 102 newly diagnosed leukemia patients admitted to Basrah maternal and child hospital was studied. The sampling technique was a non random consecutive sample by pooling all the patients with

Leukemia that were admitted to this hospital in the defined period of the study.

**Methods:**

The diagnosis of leukemia was based on the history, clinical features, examination of blood film and bone marrow aspiration ,lumbar puncture examinations and chest x – ray and computed tomography (CT) scan of the brain and orbit was useful in differentiating between optic nerve infiltrate and papilledema then Subdivision of leukemia into myelogenous and lymphocytic was made by using cytomorphology and cytochemistry which were available in our center and subdivision of acute lymphocytic leukemia to standard or high risk depend on these investigations because there is no facility for cytogenetic study .The age of the patients in that sample was ranging between 1-15 years. Regarding the gender; there were 68 males and 34 females. All the patients were examined by the same expert ophthalmologist to determine the degree of the ocular involvement during the initial diagnosis. Eye examination was done within 3 days of diagnosis before starting the course of chemotherapy.

After taking the history; visual acuity was recorded using snellen charts where possible,

eyelids, conjunctive, cornea, anterior chamber, iris, pupil and lens were examined with a torch light and slit lamp. Fundus examination was done with a direct and indirect ophthalmoscope after dilating pupils with 1% tropicamide eye drops in the dark examination room, children who were very young and not cooperative were sedated before fundus examination. The results were entered into a database and analyzed using SPSS computer program.

**Results**

Out of 102 leukemia patients that were examined 34 were females (33.3%) and 68 (66.6%) were males, The mean age of patients was 5.4 years with a range between one year and 15 years

Eighty patients (78.4%) had acute lymphoid leukemia, 16 (15.6%) had acute myeloid leukemia and 6 (5.9%) had chronic myeloid leukemia (table 1).

Ocular lesions were seen in 49% (50 out of 102) of leukemia patients (28 males and 22 females, eye changes was seen more often (42.1%) in patients with acute lymphoid leukemia, 4.9% in acute myeloid leukemia and 1.9% in chronic myeloid leukemia (table 2).

**Table 1: distribution of cases according to age, sex and type of Leukemia**

Type	Male n : 68 (66.6%)			Femal n :34 (33.%)			Total 102	
	< 2 years	2-5	> 5	< 2 years	2-5	>5	No.	%
<b>ALL</b>	5	20	25	2	18	10	80	78.4%
<b>AML</b>	-	4	9	-	-	3	16	15.6%
<b>CML</b>	-	1	4	-	-	1	6	5.9 %
<b>TOTAL</b>	5	25	38	2	18	14	102	

**Table 2: ocular involvement according to age, sex and type of Leukemia**

Type	Male			Female			Total	
	< 2 years	2-5	>5	< 2 years	2-5	> 5	No.	%
<b>ALL</b>	2	10	11	-	15	5	43	42%
<b>AML</b>	-	-	3	-	-	2	5	5 %
<b>CML</b>	-	2	-	-	-	-	2	2 %
<b>TOTAL</b>	2	12	14	-	15	7	50	

Table (3) shows the type of eye changes as retinal changes in 24 patients of acute lymphoid leukemia, 2 in AML and 2 in CML, while infiltration of ocular tissues was seen in 5 patients with ALL and 2 with AML but was not seen in patients with CML. Neuro–ophthalmic sign was seen more in ALL (14 patient), in one patient with AML but was not observed in CML.

Table (4) shows various eye changes in acute lymphocytic leukemia and this table show some

patients present with more than one sign and symptom so there is overlap; retinal changes (dilated tortuous vein) in 22 patients (21.5%), Neuro-ophthalmic changes (papilledema) in 11(10.8%) ,6<sup>th</sup> nerve palsy in 4 patients (3.9) and infiltration of ocular tissues (proptosis) in 4 patients (3.9%) while choroidal infiltration in one patient who was dignosed clinically

**Table (3): Pathological changes in different types of leukemia**

Eye changes	ALL (80)		AML (16)		CML (6)		Total 102)	
	No.	%	No.	%	No.	%	No.	%
<b>Retinal changes</b>	24	23.5	2	1.9	2	1.9	28	27.4
<b>Ocular tissue infiltration</b>	5	4.9	2	1.9	-	-	7	6.8
<b>Neuro- ophthalmic sign</b>	14	13.7	1	0.9	-	-	15	4.7
<b>Total</b>	43	42.1	5	4.9	2	1.9	50	49

Table 4: numbers and percentages of various eye changes in acute lymphocytic leukemia

Type of eye change	n	%
<b>Retinal change</b>		
- intraretinal hemorrhage	3	2.9
- white centered hg.	2	1.9
- Dilated tortuous veins	22	21.5
- Cotton – wool spot	5	4.9
- Macular hemorrhage	1	0.9
- Sub-hyaloid hemorrhage	-	-
- Vitreous hemorrhage	-	-
- Central retinal vein occlusion	2	1.9
<b>Infiltration of ocular tissue</b>		
- orbital infiltration (proptosis)	4	3.9 %
- optic nerve infiltration	-	-
- choroidal infiltration	1	0.9
<b>Neuro – ophthalmic sign</b>		
- Papilledema	11	10.8
- Cortical blindness	-	-
(6 th nerve palsy )	4	3.9
<b>Other . sub-conjunctival hemorrhages</b>	12	11.8

#### Discussion:

Knowledge of ocular involvement in leukemia is important because the eye is the only site where the leukemia involvement of nerves and blood vessels can be directly observed for the eye symptoms may be the initial mode of presentation of the systemic illness or the first manifestation of relapse after remission – inducing chemotherapy [7].

In the current study, a number of patients with different types of leukemia were examined for the presence of ocular lesions, ocular involvement was observed in 50 (49%) of the patients, similar results were observed by S.C. Reddy [2].

A higher prevalence of eye changes was seen in patients with acute lymphocytic leukemia this result was in agreement with T.Sharm-et al studied that the eye is involved directly or indirectly far more often in the acute leukemia than in chronic cases, while a study was done by Dwivedi [10] revealed a higher prevalence of eye changes in chronic leukemia . In our study ocular lesions were observed in young and old children with no sex

difference; similar results were observed by Davis JL Parke [11].

Retinal changes was the most common ocular lesion observed in acute lymphocytic leukemia (23.5%) as shown in other studies [1] and the possible explanation is that the retina is involved in leukemia more often than any other ocular tissue, it is estimated that up to 69% of all patients with leukemia show fundus changes at some point in the course of their disease although no effective treatments were present [12] and various ocular complications in leukemia are due to direct invasion by leukemic cells or haematological abnormalities associated with leukemia for example anemia ,thrombocytopenia and hyperviscosity states ,these complications usually occur when the disease is clinically and haematologically active [13]

Dilated tortuous veins were the most common retinal changes seen (21.5%), similar result was observed by Allen [14]. This is attributed to the

hyperviscosity and perivascular sheathing as a result of collection of leukemic cells<sup>[15]</sup>.

Retinal hemorrhages were also observed in patients with acute lymphocytic leukemia and were commonly seen at the posterior pole and have been described as dots or blots. Flame-shaped and cotton-wool spots in the retina are due to nerve fiber layer infarcts or a localized collection of leukemia cells, the same result was observed by Allen<sup>[14]</sup>.

Orbital infiltration in leukemia presents with proptosis, lid edema and chemosis this may appear before, after or concurrently with hematological manifestations<sup>[2]</sup>, in the present study orbital infiltration was observed in acute leukemia more than in chronic leukemia and occurred more commonly in lymphocytic leukemia (4.9%) compared to myeloid leukemia (1.9%) the same observation was seen by other study<sup>[16,17]</sup>. Orbital involvement could be also present as orbital abscess due to infection of periorcular tissues secondary to neoplastic infiltration or immuno-suppression<sup>[18]</sup>.

Choroidal infiltration by leukemia cells is usually seen on histological examination. Clinically choroidal involvement may present as serous retinal detachment<sup>[19]</sup> that have been reported in CCL,ALL, CML and AML<sup>[1]</sup>.

In this study choroidal infiltration was seen in one patient with acute lymphocytic leukemia but without any retinal detachment. A similar finding was observed by S.C Reddy et al<sup>[2]</sup>. The involvement of choroid by leukemic cells tend to be perivascular and may be patchy or diffuse and is the most common ocular tissue to be involved in leukemia (85%) as shown in other study<sup>[1, 20]</sup>, the choroid may be thickened to many times normal at the posterior pole, the overlying retinal pigment epithelium may show secondary alteration including atrophy and hypertrophy may lead to secondary photoreceptor cell loss, serous detachment<sup>[1, 21]</sup>.

Eye symptoms and signs in CNS leukemia include blurring of vision, diplopia, and extra ocular muscle palsy due to involvement of cranial nerves<sup>22, 23</sup>. CNS leukaemia may also present as an asymptomatic papilloedema<sup>[24]</sup>, optic nerve involvement may be an extension of CNS leukemia by direct infiltration of the nerve head in which case the intracranial pressure may be normal or be passive swelling because of retrolaminar leukemia invasion or by passive swelling secondary to the increased intracranial pressure. Massive direct infiltration of the optic nerve head by leukemic cells can give rise to a clinical picture identical to that of papilloedema<sup>[25]</sup>. In our study neuro-ophthalmic changes were observed most in acute lymphocytic leukemia (13.2%) and papilloedema was the most common presentation that occurred in about (10.8%) of patients with leukemia Similar results were observed by S.C Ready<sup>[2]</sup>.

Other eye changes were observed subconjunctival hemorrhages especially in patients with acute lymphocytic leukemia; this was also registered by Duke-Elder<sup>[26]</sup>.

It can be concluded from this study that retinal lesions are the most common eye changes in leukemia especially in acute lymphocytic (ALL), so collaboration among physicians, oncologists, and ophthalmogists is strongly recommended to discover these lesions as early as possible to prevent the irreversible damage that may occur to the eye. Beside, ophthalmic examination should be included as a part of the routine evaluation at the time of diagnosis of leukemia before starting the course of chemotherapy with prompt ophthalmic assessment of patients with or without eye manifestations because ocular lesions were detected in many patients who had no eye symptoms.

### References

- 1-T sharma, J Grewal , S Gupta ophthalmic manifeststions of acute leukaemia the ophthalmologists role- Eye 2004;18:663-672
- 2-S.c Reddy, N.Jackson .B.s. Menon. Ocular involvement in leukemia –Astudy of 288 cases. Ophthalmologica 2003; 217:441-445
- 3-Murtha TJ: Haematologic diseases, leukaemia dysporteinemia and anaemia. Principles and practice of ophthalmology. Philadlphia , saunders 1994 Vol5; P-2986 -3004
- 4-curto Mlo, Zingone A, Aquaviva A et al.leukaemie infiltration of the eye results of therapy in a retrospective multicentric study. Med pediater oncol 1989; 17: 134 -139
- 5-ohkoshi K, Tsiaras WG. Prognostic importance of ophthalmic manifestation in childhood leukaemia. Br J ophthalmol 1992; 76: 651-655.
- 6-Jack J. Kanski. Clinical ophthalmology Asystematic Aapproach. Oxford Auckland Boston . Jonannesbury melbourne new alelitt. Fourth Edition ;1999,P510-511.
- 7-Kincaid Mc, Green WR : Ocular and orbital involvement in leukemia. Surv ophthalmol 1983, 27: 211-232
- 8-Rosenthal AR : ocular manifestations of leukaemia :A review ophthalmology 1983;90 : 899-905.
- 9-Schachat AP : The leukaemia and lymphomas in inherited retinal Diseases. St louis, Mosby, 1994; P 873-890.
- 10-Dwivedi PC, Raizzada JK, saini VK, singh G: study of retinal changes in leukaemia J indian Med Assoc 1986; 84:35-37 .
- 11-Davis JL. Parke : Granulocytic sarcoma of the orbit. Aclinicopathologic study ophthalmology. 1985;92:1758-1762
- 12-Alemayehu W, shamebo M, Bedri A, Mengistu Z. Ocular manifestations of leukaemia in Ethiopians. Ethiop Med J 1996;34: 217-224

- 13- Kazuaki Miyamoto :Serous retinal detachment caused by leukemic choroidal infiltration during complete remission.Br J Ophthalmol 2000;84:1318
- 14-Allen RA, Straatsman BR: ocular involvement in leukaemia and allied disorders. Arch ophthalmol 1961;66:490-508.
- 15-Bailantyne AJ, Michaelson K. : Textbook of the fundus of the Eye. Baltimore, Williams and Wilkins. 1970; pp: 290-292
- 16-schachat AP, Markowitz. JA , Guyer DR, et al ophthalmic manifestations of leukaemia. Arch ophthalmol 1989;107-697.
- 17-Jakobiec FA, Jonesls, lymphomatous plasmacytic, histiocytic, haematopoietic tumours. In: Jones Jakobiec FA(eds) Diseases of the orbit. ttagerstown Md. Harper and Row 1979; P309
- 18- Esmaeli B, Medeiros LJ , Myers J, Champlin R, Singh S, Ginsberg L. Orbital mass secondary to precursor T- cell acute lymphoblastic leukaemia as a retro-orbital mass (review ) TPNJ clin Hematol 1999; 40:1193-1197 .
- 19- Tang RA, Aguirre vita- coro A, Walls, Frankel Ls: Acute leukaemia presenting as a retinal pigment epithelium detachment. Arch ophthalmol 1998; 106: 21-22
- 20-Williams G.Ocular manifestations of hematologic and oncologic disease .Curr Opinion Ophthalmol 1990;1:181-6
- 21- Burns CA, Blodi PC, Williamson BK. Acute lymphocytic leukaemia and central serous retinopathy. Trans AM Acad ophthalmol otolaryngol 1965 ; 69 : 307-309.
- 22- Dawson DM, Rosen thal DS, Moloney WC: neurologic complications of acute leukaemia in adult. Ann intern Med 1973; 79: 541-544 .
- 23- Kensei Tobinai. Toshiki watanabe : Adult. T cell leukaemia – lymphoma.Clinical oncology 2004 . 3<sup>rd</sup> edition Martin D. Abeloff et al P3115 .
- 24- Brown GC, Shields JA, Augsburger ...etc at: leukaemia optic neuropathy in ophthalmol 1981; 3: 111-116.
- 25- Kincaid MC, Green WR. Ocular and orbital involvement in leukaemia. Surv ophthalmol 1983; 27: 211-233
- 26- Duke – Elder S. System of ophthalmology. Cornea and conjunctiva, vol 8. CV Mosby : st louis, 1965; 119-195.
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