Ocular Manifestations in Adult Leukemia

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Abstract

Purpose: To evaluate the prevalence and types of ocular manifestations in adult leukemia.

Setting: Mashhad University of Medical Science; Imam Reza Hospital.

Patients and Methods: Thirty-two adult (more than 12 years old) leukemic patients hospitalized from year 1998 to 1999 in the hematology department of Imam Reza Hospital.

Results: Thirty-two patients (male: 19, female: 13) diagnosed to have leukemia by peripheral blood film, bone marrow aspiration and biopsy were examined. These cases included 15 patients (47%) with acute lymphocytic leukemia, 15 patients with (47%) acute myeloid leukemia and 2 patients with (6%) chronic myeloid leukemia. Six patients (18.7%) presented with eye symptoms. Ocular changes were found in 11 patients (34.4%) including: retinal hemorrhage in 10 patients (31.2), Roth’s spot in 5 (15.6), cotton wool spot in four (12.5), subconjunctival hemorrhage in 2 (6.2%) and one case with vitreous haemorrhage. There was significant relationship between the presence of retinal hemorrhage and thrombocytopenia less than 50000/mm³ (P<0.02) but no significant relationship existed between the presence of retinal hemorrhage and anemia.

Conclusion: In our study, the overall prevalence of ocular manifestations in adult leukemia was 34.4%. The most common ocular manifestation was intraretinal hemorrhage. In view of the high prevalence of asymptomatic ocular lesions in adult leukemia, routine ophthalmic examination should be included as a part of the evaluation at the time of diagnosis.

Key words: Ocular Manifestations, Adult Leukemia, Thrombocytopenia, Anemia.

Introduction

There have been several published series and review articles concerning the ophthalmic complications of the leukemias. However, depending on the type of leukemia and the study design, the estimated prevalence of ocular disease varies from 30% to 90%. 1 Ocular involvement can be the presenting complaint. Clinically evident ocular involvement is common in patients with acute leukemia and has been described in up to half of patients at the time of diagnosis. 2,3 Acute leukemias affect the eye four times more than the chronic types. 4 Ocular involvement have been seen more often in adults (49.1%) than in children (16.5%), and in myeloid leukemia (41.0%) than in lymphoid leukemia (29.2%). 5 Ocular involvement in chronic lymphocytic leukemia is rare. [6] Of all leukemic patients, about 5% have been reported to develop visual loss attributable to the underlying condition. 2

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Ocular involvement in leukemia can either be direct via leukemic infiltrate or indirect as a consequence of compromised immune function, hyperviscosity, thrombocytopenia, anaemia, leukostasis, which can lead to retinal hemorrhages and ischemia. Immunosuppression, both from leukemic neutropenia or secondary to treatment with antineoplastic agents, increases susceptibility to a variety of opportunistic infections of the eye. Schachat et al. had reported primary ophthalmic leukemia infiltrate in 3% and secondary ophthalmic findings in 39% and ocular changes unrelated to leukemia in 20% of their patients.  

On the basis of histologic evidence, leukemic infiltrates most often involve the choroid and have been reported in 50% to 82% of patients but this is rarely visible clinically. Clinically the retina is the most common ocular site to be involved by leukemia. Leukemic retinopathy can be observed in both the acute and chronic form of leukemia. The most frequent findings of leukemic retinopathy are sheathing of retinal vessels, intraretinal hemorrhages (either round or flame-shaped and white-centered hemorrhages; “Roth spots”), and cotton-wool exudates. Retinal ischemia and neovascularization has been described in chronic myeloid leukemia due to increased blood viscosity caused by the marked leukocytosis, although there have been few reports of such cases.  

The optic nerve is affected in 34% of the cases and the iris and anterior segments are affected in 0.5% to 2.6% during the course of the disease. Secondary glaucoma, ocular nerve palsy, orbital and lid involvement, and opportunistic eye infections have all been reported to complicate leukemia.

We planned to determine the nature and extent of ocular complications in newly diagnosed leukemic patient and see if routine screening of leukemic patients for ocular disease is justified.

Patients and Methods

In a prospective study, between 1998 and 1999, all newly diagnosed (less than 2 weeks after diagnosis) leukemic patients hospitalized in hematology department of Imam Reza Hospital undergone a complete eye examination, which included clinical examination of the ocular adnexae and slit-lamp examination, tonometry, direct and indirect ophthalmoscopy. Ocular abnormalities were classified as follows:

- Primary (direct) ocular complications likely to result from leukemic infiltration
- Secondary ocular complications likely to result from systemic haematological disturbance such as anaemia or thrombocytopenia
- Opportunistic infection due to immune deficiency

A literature search was also performed to identify relevant case reports, series, or review articles.

Results

During one year period, 32 patients (19 males and 13 females) were recruited. The average age was 24 years (range 12-56 years). No patient had received treatment for leukemia. Fifteen (47%) patients had acute lymphoblastic leukemia (ALL), 15 (47%) had acute myeloid leukemia (AML) and two patients (6%) had chronic myeloid leukemia (CML) [Figure 1].

No patient had primary direct leukemic complications. Eleven patients (34.4%) had secondary ocular involvements: intraretinal hemorrhage in eight patients (25%), Roth’s spot in five (15.6), cotton wool spot in 4 patients (12.5%) , subconjunctival hemorrhage in 2 (6.2%), two cases of splinter hemorrhage (6.2%) and one case of vitreous hemorrhage (Figure 2). In addition three patients had cranial nerve involvement. Women had more ocular involvement than men (46.1% vs 26.3%) , older patient were also more affected (Figure 3, 4). Thirty three percent of patients with ALL, 33% of patients with AML and 50% of patients with CML had ocular involvement (Figure 5). Ocular involvements in different types of leukemia are listed in (Table 1).
**Figure 1.** Prevalence of different type of leukemia in 32 patients

**Figure 2.** Prevalence of different ocular manifestation in 32 patients

**Figure 3.** Sex distribution of ocular involvement in 32 patients.

**Figure 4.** Age distribution of ocular involvement in 32 patients

**Figure 5.** Prevalence of ocular involvement in different type of leukemia in 32 patients

**Table 1.** Ocular manifestation according to the type of leukemia

<table>
<thead>
<tr>
<th>Type of Leukaemia</th>
<th>ALL</th>
<th>AML</th>
<th>CML</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraretinal hemorrhage</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Splinter hemorrhage</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Vitreous hemorrhage</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Roth's spot</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Cotton-wool spot</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Subconjunctival hemorrhage</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

No iris, anterior segment, optic nerve and orbital involvement were found. In addition three patients had six-nerve palsy due to rise of intracranial pressure, presenting with papilledema.
Average of platelet count in patients with retinal haemorrhage was 21000/mm³ and 65100/mm³ in patients without retinal haemorrhage. There was significant relationship between the presence of retinal hemorrhage and thrombocytopenia less than 50000/mm³ (P<0.02).

Although in patient without retinal haemorrhage hematocrit is higher than patients with retinal haemorrhage (29ml/dl vs 25ml/dl) but the difference was not statistically significant.

No opportunistic ocular infection due to immune deficiency was found in our study.

**Discussion**

This study showed that 11 (34.4%) of the 32 leukemic patients had ocular abnormalities related to leukemia. In spite of the small number of reported cases, common leukemic eye manifestations were seen. Ocular manifestations could be related to direct infiltration of the eye by leukemic cells, or secondary to anemia, hyperviscosity, increased intracranial pressure, pancytopenia and treatment with irradiation or chemotherapy. In addition immunosuppression, either due to neutropenia or secondary to treatment with antineoplastic agents, increases susceptibility to a variety of opportunistic infections that may involve the eye.

As previously reported most ocular changes occurred in the acute forms of leukemia. Probably because the acute forms of leukemia are the more common and involve the CNS more frequently than do the chronic forms.

In this study, we examined newly diagnosed patients and only six patients (18.7%) presented with eye symptoms. In spite of a high incidence of involvement of choroid at autopsy, only one of the 120 patients in the Schachat study and none of our patients had clinical involvement. Retina is the most common ocular tissue to be involved in leukemia, clinically. Duke-Elder suggests that up to 90% of patients will develop retinopathy at some stage of their disease. Retina was involved in 11 of our patients, as secondary form of leukemic ophthalmopathy. Finding were: intraretinal hemorrhage in eight patients (25%), Roth's spot in five (15.6), cotton wool spot in 4 patients (12.5%), subconjunctival hemorrhage in 2 (6.2%), two cases of splinter hemorrhage (6.2%) and one case of vitreous hemorrhage. There was significant relationship between the presence of retinal hemorrhage and thrombocytopenia less than 50000/mm³ (P<0.02) but no relationship was found between the presence of retinal hemorrhage and anemia.

Anterior segment of the eye was not involved in our patients (can be due to the small number of patients or because we studied newly diagnosed patients) but anterior segment involvement was previously reported in several studies. It was suggested that all anterior segment leukemic infiltration cases be treated by irradiation, even though they respond initially to chemotherapy, to eradicate the leukemic cells and prevent further relapses. The optic nerve was involved in none of our leukemic patients. It occurs most commonly when the patients are in CNS relapse. Leukemic infiltration of the optic nerve, in contrast to papilledema, is often unilateral. When it occurs bilaterally, it may be difficult to differentiate clinically from papilledema. CT scan is very helpful in this respect. In papilledema secondary to increased intracranial pressure due to CNS leukemic infiltration, dilatation of the brain ventricles, swollen sheath of optic nerves and engorged orbital vessels may be present. Orbital CT scan was found to be useful in confirming retrobulbar optic nerve infiltration. Although leukemic infiltration of optic nerve doesn't have good visual prognosis but the poor visual outcome in most of patients is due to delay in referral time and in receiving radiotherapy. This emphasizes the point that all leukemia patients should be reviewed by an ophthalmologist on presentation. Rosenthal suggested that radiotherapy be given urgently to all patients with optic nerve infiltrate to restore their vision.

Ophthalmological examination is helpful for determine prognosis of leukemic patient. The 5 year survival rate of patients with ophthalmic manifestations was 21.4%. This survival rate was significantly lower than that of those who lacked ophthalmic manifestations (45.7%, P<0.05).
Conclusion
Thé present study shows that direct invasion of the eye by leukemia is rare in newly diagnosed patient but retinal involvements are common and indicate the need for early ophthalmological examination. Therefore, leukemic patients should have an examination at presentation and regular follow-ups thereafter. Leukemia must be consider in the differential diagnosis of any patient with the common ocular leukemic manifestations as these ocular sign may be first presentation of the disease.

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References
توجهات جشمی در لوسیمی بالینی

دکتر میرنی موسوی ۱، دکتر مجید ابریشمی ۲، دکتر تونا تایی ۳، دکتر سمیک زارعی ۴

چکیده

هدف: بررسی شیوع انواع تظاهرات جشمی لوسیمی در بالینی.

مکان: دانشگاه علوم پزشکی مشهد، بیمارستان امام رضا (ع).

بیماران: ۲۳ بیمار بالای (سن بیشتر از ۱۲ سال) مبتلا به لوسیمی که در بخش خون شناسی بیمارستان امام رضا (ع) از سال ۱۳۷۷ تا ۱۳۷۸ بستری شده بودند.

پایش‌ها: ۲۳ بیمار (۱۹ مرد، ۴ زن) که تشخیص لوسیمی با توجه به اسیر خون محیطی، آسیراپسیون و یا بهبود منگ استخوان در آنها قطعی شده بود. مورد بررسی قرار گرفتند. ۱۵ نفر از بیماران (۶۴٪) لوسیمی حاد لنوسیتی، ۱۵ بیمار دیگر لوسیمی حاد میلیود و دو بیمار نیز لوسیمی مزمن میلیود داشتند. ۶ بیمار (۲۶٪) چهار مشکلات جشمی علامتی داشتند. در ممانات انجام شده، تظاهرات جشمی در ۱۱ بیمار (۴۸٪) وجود داشت. خودروبری شیبکه در ۱۰ بیمار (۴۳٪) راس در چهار بیمار، خودروبری زیر ملمتمه در دو بیمار (۸٪) و خودروبری زجاجی در یک بیمار مشاهده شد. ارتباط معنی‌داری بین خودروبری شیبکه و پلاکت کمتر از ۵۰۰۰ در میلی لتر مربع وجود داشت (۲٪) ولی ارتباط بین خودروبری شیبکه و کم خونی بستند نیامد.

نتیجه‌گیری: در مطالعه انجام شده، شیوع کلی تظاهرات جشمی در بیماران ۴/۲٪ بود. شایعترین نتایج تظاهرات خودروبری شیبکه بود. با توجه به اینکه نیاز بیماران بدون علامت بودن، انجام ممانات جشمی فضایی در هنگام تشخیص لوسیمی منظمی به نظر می‌رسد.

کلمات کلیدی: تظاهرات جشمی، لوسیمی بالینی، کاهش پلاکت، کم خونی.

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