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Case Report

Ocular manifestations of acute myeloid leukaemia

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ABSTRACT

Aim: Each and every ocular tissue may be affected in leukemia and ocular involvement is a known entity since a long time . Prevalence of ocular involvement in leukemia ranges from 9% to 90% and can result from primary/direct infiltration of ocular tissues by leukemic cells or secondary/indirect involvement following systemic leukemic involvement.

Materials and Methods: We present a case of a 30 years old female presented to emergency opd with history of epistaxis, low grade fever and headache from last 1 month and blurring of vision bilaterally from last 3-4 days. Examination reveals pallor, pedal edema, raised jugular venous pressure and hepatosplenomegaly. Hematology shows Hb - 4.1gm%,platelet count- 9000/mm^3, total leucocyte count - 11,000/mm^3 ,international normalized ratio -2.02,elevated lymphocytes(82%) and deranged liver function tests. Peripheral smear shows microcytic hypochromic anaemia having metamyelocytes 3%, blast cells 71% with negative myeloperoxidase and periodic acid Schiff.

Results: Visual acuity was finger counting at one metres in both eyes. On slit lamp examination,there were bilateral diffuse subconjunctival hemorrhages, clear cornea, quite anterior chamber and anterior vitreous. Ocular movements were full and pupils were reactive bilaterally. Fundus examination in right eye shows dense intraretinal hemorrhages with central clearing in superior and inferior temporal arcade with macular hemorrhage and severe macular edema. In left eye, a large preretinal hemorrhage in superonasal and superotemporal arcade with vitreous hemorrhage was present along with multiple scattered intraretinal hemorrhages and severe macular hemorrhage with macular edema. Patient was diagnosed of having leukemic retinopathy with macular edema in a case of acute myeloid leukaemia.

Conclusions: All leukemia patients should have an ocular acessment and examination at diagnosis and at least every 6 months . Ophthalmologist may have a secondary role in the treatment of leukemias but proper recognition of the ocular manifestations is crucial in the management of a case of leukemia.

1. Introduction

Malignant proliferation of hematopoietic bone marrow stem cells and infiltration of the bone marrow by immature neoplastic leucocytes is called leukemia.There is also infiltration of tissues, organs and peripheral blood by immature leukocytes.[1] Each and every ocular tissue may be affected in leukemia and ocular involvement is a known entity since a long time. Prevalence of ocular involvement in leukemia ranges from 9% to 90%.[2,3]

They are classified into myeloid or lymphoid based on their origin and into acute and chronic depending on the clinical course. The chronic leukemias arise from the lymphocytic (chronic lymphocytic leukemia, CLL) or myeloid (chronic myelocytic leukemia, CML) precursor cells. They are different from acute leukemias in that the morphology of the cell lines show marked differentiation and are divided into acute lymphocytic leukemia (ALL) and acute myelocytic leukemia (AML). Leukemias may present with, or be associated with ocular disorders.[4]

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Leukemia can affect the ocular tissues during the course of the disease or can precede the diagnosis of leukemia.[5] And, there may be primary/direct or secondary/indirect ocular involvement following systemic disease.

Primary leukemic infiltration can present as anterior segment uveal infiltration; orbital infiltration including chloromas, spontaneous hyphema, orbital hemorrhages, and proptosis; and central nervous system involvement in the form of optic nerve infiltration, cranial nerve palsies, and papilledema.

The secondary changes may be sequel to therapy with steroids, chemotherapy, bone marrow transplantation (BMT) , total body irradiation or may be due to result of hematological abnormalities of leukemia such as anemia, thrombocytopenia , hyperviscosity, and also may be due to immunosuppression. Manifestations may be retinal or vitreous hemorrhage, infections, and vascular occlusions.[6–8]

Earlier, retinopathy was assumed to be of no prognostic significance[9] ,but now it has been proved that ocular involvement is associated with poor prognosis in acute childhood leukemia.[10] In both acute myelogenous leukemia (AML) and acute lymphocytic leukemia (ALL), the presence of specific orbital and ocular lesions was associated with a higher frequency of bone marrow relapses and CNS involvement, leading to a lower survival rate according to a study done by Russo et al.[11]

Leukemic infiltrates development in leukemia patients requires immediate systemic and neurological re-evaluation.[12] Therefore, it is important for all leukemic patients to have thorough ophthalmic evaluation.

2. Case Report

A 30 years old female presented to the DR.RPGMC tanda in the emergency medicine opd with history of epistaxis from last 4-5 days, undocumented low grade fever with chills and rigor from last 2-3 weeks, history of headache from last 1 month and blurring of vision in both eyes from last 3-4 days.On physical examination,patient was having pallor, bilateral pedal oedoma,raised jugular venous pressure and hepatosplenomegaly. On further hematological investigations in the form of complete blood count, Hb was 4.1gm%,platelet count was 9000/mm^3,total leucocyte count was 11,000/mm^3, red blood count was 1.23 million/microlitres, prothrombin time was 27.2 seconds, international normalized ratio was 2.02,elevated lymphocytes(82%) in differential white blood cell count, deranged liver function tests in the form of elevated aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase. Peripheral blood smear picture showed microcytic hypochromic anaemia with metamyelocytes 3%, blast cells 71% with negative myeloperoxidase and periodic acid Schiff. Considering all hematological investigations patient was diagnosed of having acute myeloid leukaemia. She was referred to ophthalmology department for complaints of blurring of vision in her both eyes.

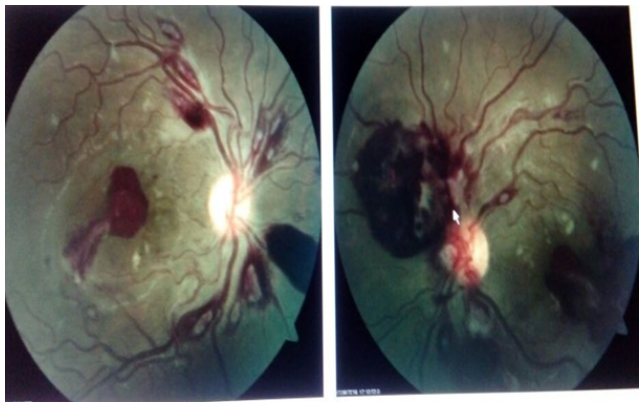

Fig. 1: Fundus photograph showing bilateral extensive retinal hemorrhages with roth's spots

Visual acuity of the patient was finger counting at one and half metres in both eyes. Pupillary reactions, intraocular pressure and ocular movements were within normal limits. Patient was having bilateral diffuse subconjunctival hemorrhage. On fundus examination, right eye was having dense intraretinal hemorrhages with central clearing in superior and inferior temporal arcade with macular hemorrhage and severe macular edema. Optovue OCT macula picture of 6x 6 mm zone shows the severe macular edema with central macular thickness of 776 um.

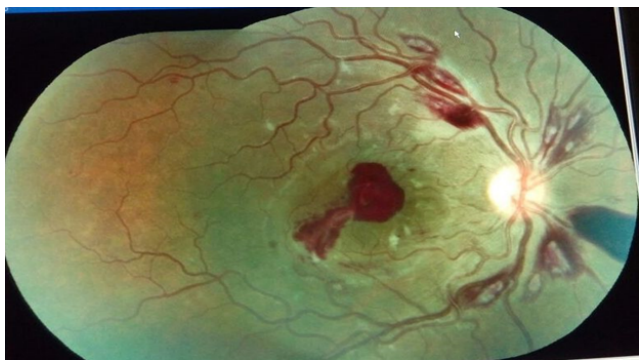

Fig. 2: Fundus photograph OD

On fundus examination of left eye, a large preretinal hemorrhage with vitreous hemorrhage in superonasal and inferotemporal arcade was present along with multiple scattered intraretinal hemorrhages and severe macular hemorrhage with macular edema .SD-OCT picture (Optovue) OS shows macular edema in 6x6 mm macular zone with central macular thickness of 477um.An ocular diagnosis of leukemic retinopathy with macular edema was kept.

Patient was given 1 unit of whole blood transfusion and 3 units of platelats were transfused. Injectable piperaillin and tazobactam 4.5 gms, vitamin k 10mg daily for 3 days

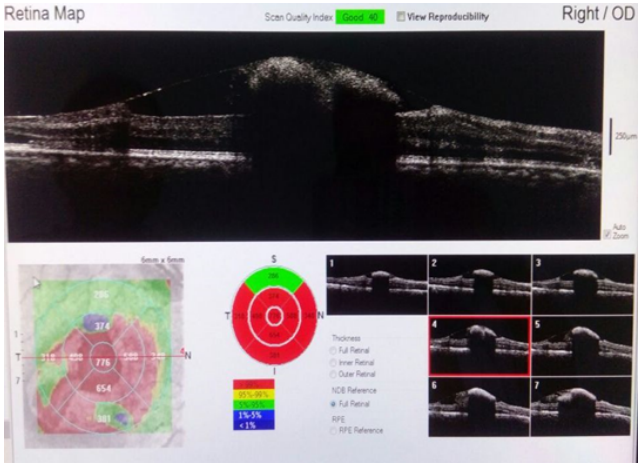

Fig. 3: OCT picture OD

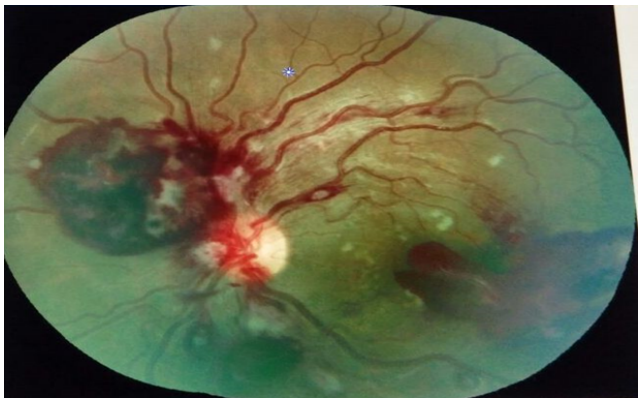

Fig. 4: Fundus photograph OS

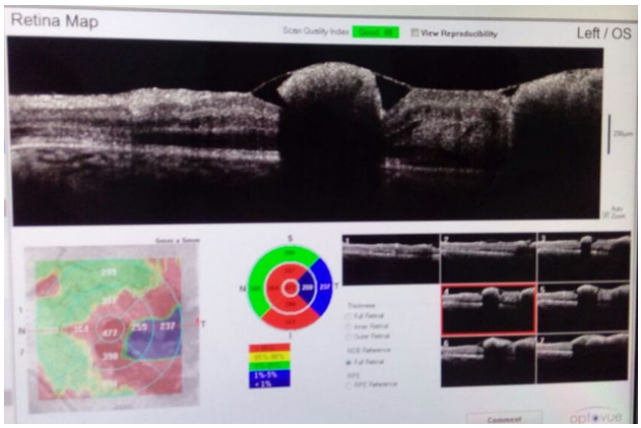

Fig. 5: OCT picture OS

was given. Patient was adviced regular follow up and later vitreoretinal consultation was sought at some other centre (due to non-availibility of vitreretinal services at our set up).Patient lost to follow up after some time.

3. Discussion

Eye is the only site where the leukemic involvement of nerves and blood vessels can be directly observed and eye symptoms may be the initial mode of presentation of the systemic illness making ocular examination utmost important in every case of leukemia[2].

Recently,many studies have been done showing ocular manifestations in cases of leukemia.[7,8,13,14]Leukemic ophthalmopathy is more common in acute and myeloid cases and less common in chronic and lymphoid subtypes. It is predominantly due to secondary rheological changes.[15]

Ocular involvement is seen in almost half of the patients of acute leukemia. Acute leukemia is more common in males and ophthalmic manifestations related to this disease are more prevalent in newly diagnosed patients with AML as compared to ALL. As a majority of the patients with ocular signs have no ocular symptoms, it is recommended to conduct a mandatory ophthalmic examination in all leukemic patients, at the time of diagnosis, to detect ocular complications at an early stage.[16]

Orbital and ocular lesions have been reported to be the third most frequent extramedullary location of acute leukemias, 1st and 2nd being meninges and testicles.[17] It is important to observe sites of extramedullary leukemic infiltration because of their local morbidity and also these sites may act as a reservoir for proliferation of leukemic cells, resulting in systemic relapse.[18]

The retina is commonly involved than other ocular tissue in case of leukaemia. Fundus changes are present in up to 90% of all persons with leukaemia at some point of time. Tortuous dilated retinal vessels due to development of hyperviscous state, perivascular sheathing and cotton wool spots due to collections of leukemic cells and haemorrhages in the posterior pole at any level of the retina have been reported in leukaemic patients. Numerous retinal hemorrhages depicts anemia and thrombocytopenia.

The haemorrhages may be rounded or irregular (in the deeper layers), striate or flame shaped (in the nerve fibre layer), preretinal or subhyaloid (between the surface of retina and vitreous).Sometimes the haemorrhage may break through into the vitreous cavity resulting in vitreous haemorrhage. Some of the haemorrhages may have a white center which may be due to accumulation of leukemic cells.[19] According to Robb et al, no correlation was found between retinal haemorrhage and blood profile in acute leukaemia, but it was found that an increased white cell level predisposed to leukaemic retinal infiltration.[20]

Retinochoroidal Manifestations of Leukaemia[5]

Table 1:

Retina	Microaneurysms, cotton wool spots, peripheral neovascularisation, retinal detachments, Haemorrhages at all levels, perivascular infiltrates, retinitis, vitreous haemorrhage, drusen, vascular occlusion, retinitis secondary to opportunistic infections
Choroid	Thickened with associated serous retinal detachment

Although in our patient ocular symptoms were not initial mode of presentation and secondary/indirect ocular involvement following systemic leukemic changes were present.

4. Conclusion

Ocular involvement is more often seen in acute leukemias and myeloid leukemias. The ophthalmologist has a secondary role in the treatment of leukemias, but, proper recognition of the ocular signs is important because of the poorer prognosis associated with ocular involvement. Ophthalmic assessment of all leukemia patients should be done at diagnosis and at least every 6 months. Many patients have no symptoms despite ophthalmic involvement which could be an early sign of CNS disease or relapse.

5. Source of funding

None.

6. Conflict of interest

None.

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