Leukaemic retinopathy: An uncommon initial presentation of chronic myeloid leukaemia in a paediatric patient

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SUMMARY

An 11-year-old girl presented with unilateral eye redness and blurred vision, accompanied by a one-month history of abdominal distension. Ocular examination revealed reduced visual acuity, bilateral optic disc swelling, dilated and tortuous retinal vessels, multiple retinal haemorrhages, and yellowish retinal deposits suggestive of leukaemic retinopathy. Systemic examination and haematologic investigations confirmed the diagnosis of chronic myeloid leukaemia. The patient was commenced on chemotherapy, after which her ocular findings and visual acuity progressively improved. This case emphasises the importance of recognising ocular signs such as disc swelling, haemorrhages, and retinal deposits as potential early indicators of underlying systemic malignancies, particularly in paediatric patients. Prompt ophthalmic evaluation and timely referral can facilitate early diagnosis and significantly improve both visual and systemic outcomes.

INTRODUCTION

Ocular manifestations of CML are relatively uncommon but can serve as early and sometimes critical indicators of the disease.[1] In some cases, ophthalmologists may be the first to detect underlying haematologic malignancy during routine eye examinations, where ocular signs are either incidental or the primary complaint. These ocular findings may occur at initial diagnosis or signal disease relapse.[1]

CML is a clonal myeloproliferative neoplasm arising from haematopoietic stem cells, characterised by the presence of the Philadelphia chromosome and the BCR-ABL1 fusion gene.[2] While it predominantly affects older adults with a median age of diagnosis around 64 years, paediatric and adolescent cases are rare. CML accounts for approximately 2% of all leukaemia in children under 15 years and 9% in adolescents aged 15–19 years.[3] The annual incidence in these age groups is estimated at 1 per million and 2.2 per million, respectively.[3]

A hallmark laboratory feature of CML is hyperleukocytosis, which can lead to leukostasis, a condition marked by impaired microcirculation due to excessive, bulky, and adhesive leukocytes. In the eye, this can manifest as leukostasis retinopathy, a rare but vision-threatening complication of CML.[4] This condition results from microvascular occlusion and ischaemia, leading to a variety of retinal findings such as haemorrhages, venous dilation, cotton wool spots, and optic disc swelling.[4] This case report describes a rare ocular presentation as the initial clinical manifestation of CML in an 11-year-old girl. It underscores the diagnostic challenges posed by atypical presentations in paediatric patients and highlights the vital role of ophthalmic evaluation in the early detection of systemic malignancies.

CASE PRESENTATION

An 11-year-old girl presented with redness and blurred vision in her right eye, which had been occurring for one week. The onset of redness was sudden and followed several bouts of coughing. Additionally, she had experienced abdominal distention for a month prior to this. Initially, her parents sought medical attention from a private ophthalmologist for her eye complaints, who then referred them to our centre.

Upon examination, her best corrected visual acuity (BCVA) was 6/45 in the right eye and 6/15 in the left eye. There was no relative afferent pupillary defect. Examination of the right eye showed periorbital ecchymosis with generalised conjunctival chemosis and subconjunctival haemorrhage, while the left eye appeared normal. Fundus examinations of both eyes revealed generalised optic disc swelling, dilated and tortuous veins, multiple yellowish retinal deposits on the fovea, and multiple retinal haemorrhages (Figs. 1a and 1b). No signs of neovascularisation or retinal ischaemia were observed. Optical coherence tomography (OCT) shows retinal deposits overlying the fovea in both eyes (Figs. 2a and 2b).

Laboratory tests revealed hyperleukocytosis, a total white blood cell count of 670 × 10^9/L (4.5–11.0 × 10^9), anaemia with haemoglobin level of 7.3 g/dL (12.0-16.0 g/dL), and thrombocytosis with platelet count of 930 × 10^9 (150-400 x 10^9/L). A full blood picture indicated the presence of blast cells, suggestive of CML in the late chronic or early accelerated phase. A contrast-enhanced computed tomography (CECT) scan of the brain was normal. However, CECT of the neck, thorax, and abdomen revealed gross hepatosplenomegaly, peribroncho-vascular nodules, ground-glass opacities in the basal segments of the left lower lobe, and small hilar nodes, indicating a possibility of

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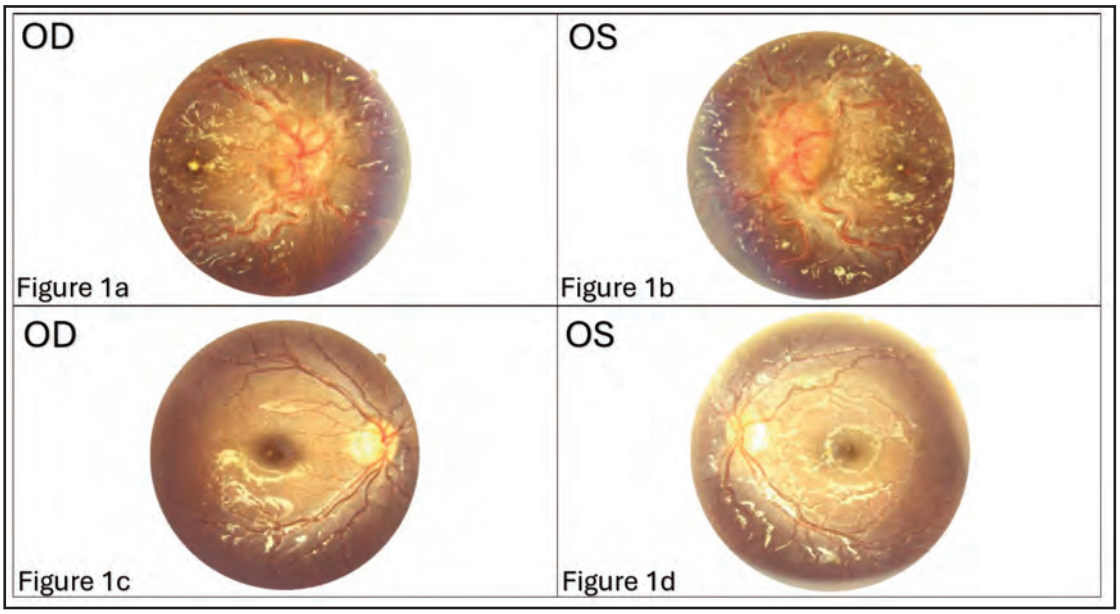

Fig. 1: 1a and 1b show both eyes' optic disc swelling with dilated and tortuous vessels and multiple retinal haemorrhages with leukaemic retinal deposits before treatment, and 1c and 1d show resolution of optic disc swelling and resolution of both eyes' dilated and tortuous vessels 6 months after treatment.

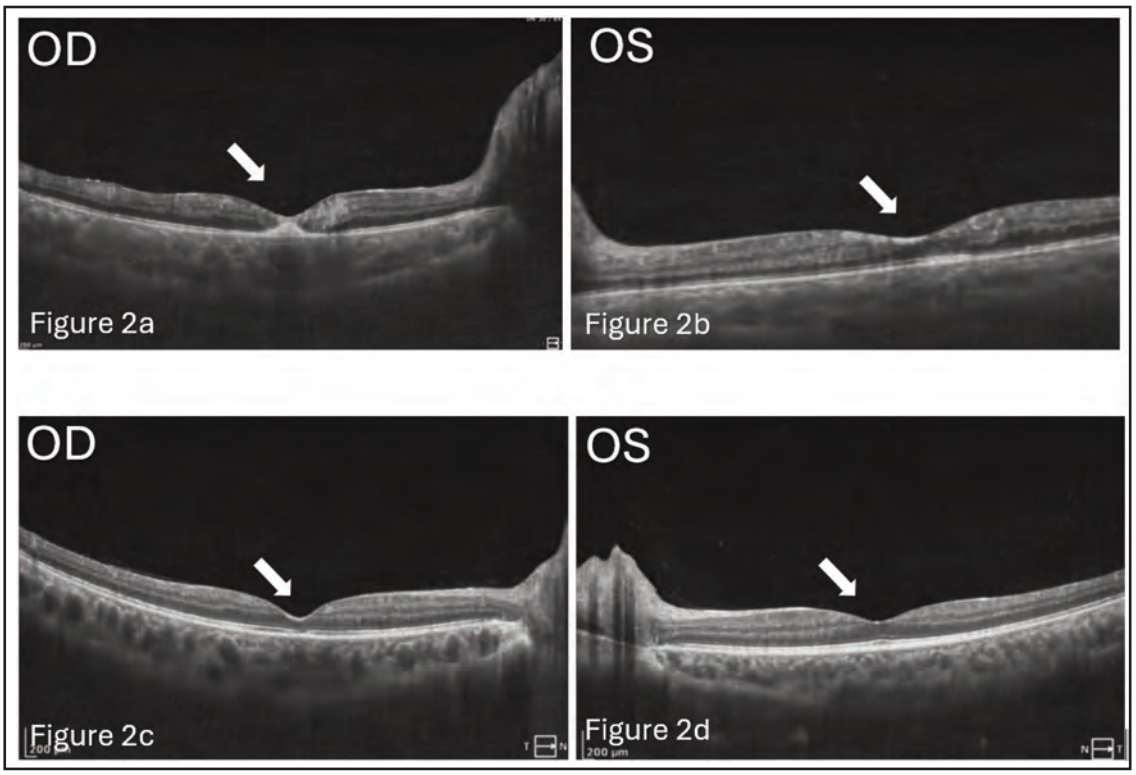

Fig. 2: Pre-treatment OCT shows leukaemic retinal deposits overlying the fovea in both eyes (Figure 2a and Figure 2b), and post-treatment OCT shows reduction of the leukaemic infiltrate in both eyes (Figure 2c and Figure 2d).

haematogenous malignancy with lymphangitic carcinomatosis. A paediatrician was consulted, and the child was diagnosed with hyperleukocytosis and anaemia secondary to CML. A bone marrow aspiration trephine biopsy was later performed, confirming the diagnosis of chronic myeloid leukaemia in the chronic phase.

The patient was started on a chemotherapy regimen that included intravenous Cytarabine 200mg/m^2 of her total body surface area for one week, followed by oral Imatinib 400mg daily and oral Hydroxyurea 1g daily. During her ophthalmology follow-up one month later, the subconjunctival haemorrhage had subsided, and her BCVA

improved to 6/36 for the right eye and 6/10 for the left eye. Fundus examination showed resolution of retinal haemorrhages, reduced tortuosity of vessels, and a less swollen but pale optic disc. There were retinal deposits in both foveae, more prominently in the right eye, which contributed to her poorer visual acuity in that eye. Her total white blood cell count improved to 5.8×10^9/L.

After seven months on Imatinib, the child became refractory to treatment, as evidenced by an increasing trend in total white blood cell counts. This necessitated a change from Imatinib 400mg daily to Nilotinib 200mg twice daily. Despite this change, the child's visual acuity continued to improve, reaching 6/12 for the right eye and 6/7.5 for the left eye. Fundus examination showed improvement in optic disc swelling, retinal vessel tortuosity, and a decrease in the retinal deposits (Figs. 1c and 1d). The OCT of the macula also revealed a reduction in retinal deposits, which contributed to improved visual acuity (Figs. 2c and 2d).

DISCUSSION

CML is a rare but significant haematological malignancy in the paediatric population, accounting for only 2-3% of childhood leukaemia.[5] Understanding the ocular manifestations of leukaemia is crucial, as the eye provides a clear window to observe the disease's effects on nerves and blood vessels. In 3.6% of cases, ocular symptoms can even be the first indication of leukaemia.[6] Ocular complications arise from direct infiltration of structures like the orbit, iris, choroid, and optic nerve or vascular abnormalities in the retina. Signs of leukaemic retinopathy can vary. It can present as multiple preretinal and intraretinal haemorrhages, Roth's spot, cotton wool spots, exudates, retinal venous tortuosity, perivascular sheathing, and neovascularisation.[7]

Ocular manifestations as the initial presentation in CML, although uncommon, can serve as a critical diagnostic clue. In the present case, an 11-year-old girl presented with sudden-onset unilateral periorbital ecchymosis with subconjunctival haemorrhages and blurred vision, with ophthalmic examination revealing optic disc swelling, dilated tortuous vessels, multiple retinal haemorrhages, and multiple retinal deposits later identified as secondary to hyperleukocytosis from underlying CML in the chronic phase. Retinal deposits are aggregates of malignant white blood cells (blasts or mature myeloid cells in the case of CML) that infiltrate the retinal layers, particularly the perivascular areas or subretinal space.[1,8] On OCT, these infiltrates appear as hyperreflective lesions. The concurrence of ocular signs, hepatosplenomegaly, and abnormal blood counts reinforced the systemic nature of her disease.

Paediatric CML is rare compared to adult CML and accounts for approximately 2-3% of cases of newly diagnosed paediatric leukaemia. According to the United States-based Surveillance, Epidemiology, and End Results cancer registry, the age-adjusted incidence rate from 2010 to 2014 was 1.4 per 1,000,000 for the 0-14 years age group and 2.1 per 1,000,000 for those aged 0-19 years.[5] Subconjunctival haemorrhage, although uncommon, can sometimes be an initial clinical sign of an underlying haematologic disorder, including CML.[1,4,8] This case emphasises the importance of thorough evaluation and consideration of haematologic malignancies in paediatric patients with unusual bleeding episodes.

CML is characterised by the uncontrolled proliferation of myeloid cells. It is typically marked by the presence of the Philadelphia chromosome (Ph chromosome), resulting from a translocation between chromosomes 9 and 22 [t(9;22)(q34;q11)].[2] While CML is more commonly diagnosed in adults, it can rarely occur in children, comprising less than 3% of paediatric leukaemia.[5] The diagnosis of CML in paediatric patients requires a high index of suspicion and a comprehensive diagnostic workup. Clinical manifestations can be diverse and often non-specific. Systemic signs may include fatigue, malaise, pallor, unexplained weight loss, easy bruising, recurrent infections, abdominal distension due to hepatosplenomegaly, and, in some cases, splenic infarction.[5] Spontaneous bleeding episodes, such as subconjunctival haemorrhage, may also be an early clue to an underlying haematological disorder.[1]

Ocular presentations, although less common, can be the initial manifestation of CML and include blurred vision, floaters, periorbital ecchymosis, optic disc swelling, retinal haemorrhages, Roth's spots, venous tortuosity, and leukaemic retinal infiltrates. These findings often reflect underlying hyperleukocytosis and leukostasis, which can compromise retinal and optic nerve perfusion.[1,7] Laboratory investigations, including complete blood count with peripheral blood smear, bone marrow aspiration, biopsy, and cytogenetic analysis, are essential for accurate diagnosis and risk stratification.

Management of paediatric CML often involves a combination of tyrosine kinase inhibitors (TKIs), such as Imatinib, Dasatinib, or Nilotinib, and occasionally stem cell transplantation in high-risk cases.[5] Despite the initial favourable response to Imatinib, the patient later became refractory, as evidenced by a rising white blood cell count. The transition to Nilotinib, a second-generation TKI, was a critical therapeutic pivot. Studies indicate that Nilotinib and Dasatinib are effective in paediatric patients resistant to Imatinib, with improved molecular response rates.[5] Visual improvement paralleled systemic haematologic remission. OCT demonstrated a reduction in retinal deposits and resolution of optic disc swelling, which correlated with BCVA improvement to 6/12 in the right eye. Nevertheless, persistent subfoveal deposits in the right eye explained the incomplete recovery, consistent with reported cases of residual structural damage post-infiltration.[8]

Given the rarity of paediatric CML and its diverse clinical presentations, collaboration among paediatric haematologists, oncologists, and other specialists is crucial for timely diagnosis and optimal management. Additionally, long-term follow-up is necessary to monitor treatment response, disease progression, and potential late effects of therapy in this population.

CONCLUSIONS

A child presenting with eye redness and poor vision should not be taken lightly. A holistic approach and thorough examination are paramount to a correct diagnosis. Co-management with a paediatrician is important to deliver the optimum treatment care. Timely identification of leukostasis retinopathy associated with CML is essential, and prompt initiation of treatment can potentially save lives and preserve vision.

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