CASE REPORT

Retinal haemorrhages: a clue to the underlying leukaemia

Mudit Tyagi, Komal Agarwal, Remya Maureen Paulose, Padmaja Kumari Rani

Smt Kanuri Santhamma Center for Vitreo Retinal Diseases, LV Prasad Eye Institute, Hyderabad, Telangana, India

Correspondence to
Dr Padmaja Kumari Rani,
rpk111@gmail.com

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SUMMARY

A 40-year-old man presented with a sudden onset of diminution of vision in his left eye for 2 days. Anterior segment of both eyes was within normal limits. Right eye retinal evaluation was normal. However, the left eye retinal evaluation showed isolated subinternal limiting membrane haemorrhage at the fovea along with a white-centred haemorrhage above the fovea. There was no antecedent history of trauma or valsalva. He was normotensive and his glycaemic status was also normal. His blood investigations along with peripheral smear were done, which helped to clinch the diagnosis of an underlying chronic myeloid leukaemia.

BACKGROUND

Ocular changes in leukaemia may be induced primarily by direct infiltration of leukemic cells in the eye such as iris, choroid, retina or optic nerve or may be secondary to vascular and haematological abnormalities such as anaemia, thrombocytopenia and hyperviscosity states affecting the retina.¹ Patients with chronic myeloid leukaemia (CML), if diagnosed and treated, have been reported to have a survival rate of 90 per cent. Therefore, it is important to diagnose the disease early. Ocular manifestations as a presenting sign of leukaemia, especially chronic, are rare. We are reporting an unusual case of subinternal limiting membrane (ILM) haemorrhage, which on investigations aided in the diagnosis of the underlying CML and hence acted as a pointer to unmask the underlying systemic condition.

CASE PRESENTATION

A 40-year-old healthy man presented with complaint of sudden onset central scotoma in the left eye for 2 days. He denied ocular pain or valsalva inducing activities. He had a history of laparoscopic removal of a gastrointestinal stromal tumour (GIST) 10 years ago, which was not followed by radiation or chemotherapy.

The best corrected visual acuity in the right eye was 20/20 and 20/50 in the left eye. The right eye fundus was normal. However, the posterior segment examination of the left eye showed a sub-ILM haemorrhage at the fovea, with a single pale-centred haemorrhage in the posterior pole and few superficial retinal haemorrhages in the inferotemporal arcade ([figure 1A](#)). There were no other signs suggesting any vascular cause. There were no significant vessel changes. Fundus fluorescein

angiography did not reveal any signs of ischaemia or neovascularisation ([figure 1B](#)). Amsler grid of the left eye showed a central scotoma.

Optical coherence tomography was done, which conformed the sub-ILM nature of the haemorrhage ([figure 2](#)).

INVESTIGATIONS

All patients with retinal haemorrhages or pale-centred haemorrhages should be investigated for any underlying systemic disease like diabetes, hypertension or any underlying haematological abnormality. A complete blood count along with a peripheral smear should be done in all such cases. Our patient did not have any antecedent history of trauma or valsalva, and there was no evidence of any systemic disease. He was normotensive and his glycaemic status was also normal. A haematological evaluation was ordered. It revealed a high total count with peripheral smear showing a shift to left. His total count was $139\,800/\text{mm}^3$ with normal red blood cell count and increased platelet count ($367 \times 10^9/\text{L}$). Peripheral blood smear showed marked myeloid hyperplasia, with mature neutrophils, myelocytes with presence of blast cells ([figure 3](#)). A physical examination also revealed the presence of palpable splenomegaly. Fluorescent in situ hybridisation (FISH) showed karyotype 46, XY, t(9;22), Philadelphia chromosome. These findings were consistent with the diagnosis of CML.

DIFFERENTIAL DIAGNOSIS

Sub-ILM haemorrhages are known to occur in Valsalva retinopathy, Tersons syndrome, blood dyscrasias or ocular trauma. However, there was no history of any such manoeuvre or any trauma in our patient. The patient was also normotensive, and there was no evidence of any hypertension.

White-centred or pale-centred haemorrhages are believed to represent accumulation of leukaemic cells or platelet fibrin aggregates. Blood dyscrasias such as anaemias, leukaemia, multiple myeloma and other platelet disorders may present with similar features. A physical examination revealed the presence of a palpable splenomegaly, and this reiterates the fact that when ophthalmological finding suggests a systemic disease, one should do a general physical examination to obtain more clinical clues. A subsequent haematological evaluation was done, which revealed a high total count with peripheral smear showing a shift to left, an elevated total count of $139\,800/\text{mm}^3$ with normal red blood cell count

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Figure 1 (A) Colour fundus photographs of the left eye showing sub-ILM haemorrhage (arrow) with a white-centred haemorrhage superior to it. (B) Fundus fluorescein angiography picture showing blocked fluorescence (arrow) due to the sub-ILM haemorrhage. ILM, internal limiting membrane.

and increased platelet count ($367 \times 10^9/L$). The peripheral blood smear findings of myeloid hyperplasia, myelocytes with presence of blast cell and FISH showing karyotype 46, XY, t(9;22), Philadelphia chromosome helped confirm the final diagnosis of CML.

TREATMENT

The patient was referred to an oncologist, and Imatinib (Glivec, Novartis Pharma) therapy was started for CML.

OUTCOME AND FOLLOW-UP

The sub-ILM haemorrhage gradually resolved over a period of 1 month, and the patient's visual acuity also improved to 20/20 in his left eye. The sub-ILM haemorrhages and pale-centred haemorrhages seen in blood dyscrasia are known to resolve spontaneously after starting treatment for the underlying condition and once the haematological status of the patient improves.

DISCUSSION

Ocular signs such as retinal haemorrhages are usually secondary to haematological abnormalities of leukaemia such as anaemia, thrombocytopenia, hyperviscosity and immunosuppression.¹ Retinal haemorrhages are one of the most striking findings in leukaemia, and since these can be directly observed, they provide a subtle but important clue towards an otherwise asymptomatic disease. These ocular signs may be the initial mode of presentation of the underlying haematological disturbance or can be an indicator of a later relapse.²

Figure 2 Optical coherence tomography picture of left macula showing a sub-ILM hyper-reflectivity indicating the presence of a sub-ILM haemorrhage. ILM, internal limiting membrane.

Figure 3 Peripheral smear photomicrograph (40x magnification) showing band cells (arrow) and myeloblasts (arrowhead).

Various studies have reported the incidence of retinal haemorrhages and ocular signs as ranging from 40 to 69 per cent in the course of the disease.^{3,4} Retinal haemorrhages are usually seen at the posterior pole and can occur at all levels of the retina but especially in the inner layers and may extend into subretinal space or vitreous.⁵ Leukemias are usually reported to have bilateral multiple flame-shaped dot blot or pale-centred haemorrhages.⁶⁻⁹ Our patient who was apparently healthy had visual disturbance as the only symptom and had only a single sub-ILM haemorrhage and one pale-centred haemorrhage in the retina. The ILM usually acts as an effective barrier to leukemic cell infiltration, and therefore, while a sub-ILM haemorrhage may be a result of changes in pressure within retinal veins, rarely, it can also be a manifestation of an underlying blood dyscrasia.¹⁰

Being one of the common manifestations of the disease, even a single retinal haemorrhage or a white-centred haemorrhage, as observed in our case, warrants a suspicion of an underlying blood dyscrasia and should also lead to a complete physical examination. Our patient had a palpable splenomegaly, which also helped in suspecting an underlying blood dyscrasia.

In addition, our patient also had a history of a GIST removal 10 years before the presentation. There was no ultrasonographic evidence of recurrence of the gastric tumour when the patient was evaluated for CML. There has been an isolated report on the concurrent occurrence of GIST and CML.¹¹ The authors had proposed that an error in the DNA repair mechanisms, which failed to repair the mutations, could have led to the simultaneous occurrence of GIST and CML.

Since the advent of tyrosine kinase inhibitors like Imatinib, the 5-year leukaemia-related survival rates in CML have increased to more than 90 per cent.¹² Therefore, it is important to diagnose

Learning points

- ▶ Retinal pale-centred haemorrhages can be an initial indicator of the underlying blood dyscrasia in a systemically asymptomatic patient.
- ▶ A complete hemogram and a peripheral smear should be warranted in all retinal haemorrhages to rule out underlying systemic condition before an alternative diagnosis is made.
- ▶ Chronic myeloid leukaemia if diagnosed early and treated promptly has a good survival rate.

the disease early since a prompt recognition of the ocular manifestations can help in initiating appropriate therapy. We speculate that atypical unexplained multilayered retinal haemorrhages or even a single white-centred haemorrhage should arise suspicion and needs to be held as a predictor of an underlying haematological disturbance and should be investigated accordingly.

Contributors MT and RMP diagnosed and clinically managed the case. MT, KA and PKR did the research for the manuscript and a literature review. RMP wrote the manuscript along with doing a literature review for the manuscript. MT and PKR did the future corrections and revisions of the manuscript.

Competing interests None declared.

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