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Case Report

Bilateral Macula-Involving Subhyaloid and Peripapillary Haemorrhages in Severe Pancytopenia with Transient Visual Loss and Recovery on Observation: A Case Report

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Article Information:
Received: 13 July 2026 | Revised: 16 August 2026 | Accepted: 14 September 2026 | Published: October 12, 2026
Cite this article:
C R Asla Jahan, Aswathi Muraleedharan, Gopal S Pillai, Rehna Rasheed, Niveda G and Jasleen Ashish Chaudhari (2026). Bilateral Macula-Involving Subhyaloid and Peripapillary Haemorrhages in Severe Pancytopenia with Transient Visual Loss and Recovery on Observation: A Case Report. *Public Health Open Journal*. 11(2):27–33. 10.17140/PHOJ-11-27

Abstract

Background: Retinal haemorrhage is a recognised ocular manifestation of bone marrow failure, but bilateral macula-involving subhyaloid haemorrhage and its visual course are rarely documented with serial fundus photography.

Case presentation: A 37-year-old male presented with blurred vision in both eyes for 10 days. An outside hospital had found multiple retinal haemorrhages and pancytopenia, and he was admitted for evaluation of the pancytopenia. At presentation, visual acuity was 6/9 in the right eye and 6/6p in the left eye, near vision was N6 in both eyes, and intraocular pressures were 15 and 16 mmHg. Fundus examination showed bilateral boat-shaped macular subhyaloid haemorrhages, dense haemorrhages along the superotemporal arcade adjacent to the optic disc, and scattered intraretinal haemorrhages. Haemoglobin was 8.0 g/dL, platelet count 15 × 10^3/µL, white cell count 2.7 × 10^3/µL (calculated absolute neutrophil count ≈0.62 × 10^3/µL) and absolute reticulocyte count 15.6 × 10^3/µL, with erythropoietin 326.8 mIU/mL; PT/INR was normal. He was treated with eltrombopag, tranexamic acid and cyclosporin. Visual acuity then fell to 6/60 in the right eye and 6/24 in the left eye as the haemorrhage involved the fovea. Nd:YAG laser hyaloidotomy was considered, but because blood counts remained low he was observed closely. On serial examination the haemorrhages contracted progressively and cleared from the macula, and visual acuity recovered to 6/6 in both eyes.

Conclusion: Severe pancytopenia can produce bilateral macular subhyaloid haemorrhage with transient, marked visual loss when the fovea is involved. Even so, close observation without hyaloidotomy, while blood counts remained low, was followed by spontaneous resolution and full visual recovery. A dilated fundus examination should form part of the work-up of severe cytopenia, and retinal intervention should be approached conservatively while thrombocytopenia persists.

Keywords: pancytopenia; thrombocytopenia; aplastic anaemia; subhyaloid haemorrhage; eltrombopag

1. Introduction

Bone marrow failure states, including aplastic anaemia, myelodysplasia, leukaemia and drug- or immune-related cytopenias, may be complicated by a haemorrhagic retinopathy. Low platelet counts and anaemia act together on the retinal vasculature, and bleeding is more likely when both are present than when either occurs alone [1][2][3]. In published series of aplastic anaemia, retinopathy affects roughly one fifth to one quarter of patients, and retinal haemorrhage is its commonest sign [4]. The blood may lie within the retina, beneath the internal limiting membrane (sub-ILM), in the subhyaloid space or in the vitreous. Retinal haemorrhage was also found in about 29% of patients with severe thrombocytopenia due to haematological or oncological malignancy who underwent fundoscopy, which supports routine fundus examination in this group [5].

Severe aplastic anaemia is diagnosed when a hypocellular marrow is accompanied by at least two of the following: an absolute neutrophil count below 0.5 × 10^9/L, a platelet count below 20 × 10^9/L and a reticulocyte count below 20 × 10^9/L [6][7]. Treatment rests on immunosuppression with cyclosporin, with or without antithymocyte globulin, together with the thrombopoietin-receptor agonist eltrombopag, or on haematopoietic stem cell transplantation [7][8].

We report a patient with bilateral subhyaloid haemorrhages involving the macula in severe pancytopenia. Visual acuity fell to 6/60 and 6/24 when the fovea was involved and then recovered to 6/6 with close observation, and serial fundus photographs document the course. The case illustrates the dilemma between Nd:YAG hyaloidotomy and observation in a patient with persistent severe thrombocytopenia.

1.1 Case Report

A 37-year-old male was admitted under Medical Oncology and Haematology for evaluation of pancytopenia. He had noticed blurring of vision in both eyes for 10 days and had consulted an outside hospital, where multiple retinal haemorrhages and pancytopenia were diagnosed, before being referred for further evaluation.

1.2 Clinical findings

Anterior segment examination was normal in both eyes. Visual acuity was 6/9 in the right eye and 6/6p in the left eye, and near vision was N6 in both eyes. Intraocular pressure was 15 mmHg in the right eye and 16 mmHg in the left eye. Fundus examination showed normal optic discs, with multiple intraretinal haemorrhages predominantly in the peripapillary area and a subhyaloid haemorrhage involving the macula in both eyes.

Colour fundus photographs at presentation (Figure 1) showed a well-demarcated, boat-shaped subhyaloid haemorrhage with a horizontal sedimentation level in the macular region of each eye. Dense, dark, dome-shaped haemorrhages lay along the superotemporal arcade adjacent to the optic disc, together with peripapillary haemorrhages and scattered dot-blot and flame-shaped intraretinal haemorrhages in the posterior pole. Optical coherence tomography (OCT) showed the haemorrhage to be subhyaloid in both eyes (Figure 1C and 1D).

1.3 Investigations

Laboratory results are summarised in Table 1. There was pancytopenia with severe thrombocytopenia (15 × 10^3/µL), anaemia (haemoglobin 8.0 g/dL; normocytic, MCV 97.2 fL; raised RDW 19.8%) and leucopenia with neutropenia (white cell count 2.7 × 10^3/µL; calculated absolute neutrophil count ≈0.62 × 10^3/µL). The reticulocyte count was inappropriately low (0.615%; absolute count 15.6 × 10^3/µL) despite a markedly raised erythropoietin level (326.8 mIU/mL). PT and INR were normal and the APTT was not prolonged, which argues against a coagulation factor defect. Renal and liver function, calcium, electrolytes and bilirubin were normal, and LDH was marginally raised (263 U/L). The peripheral smear was consistent with aplastic anaemia.

1.4 Treatment

Systemic management was directed by the haematology team. The patient received oral tranexamic acid 500 mg, eltrombopag 50 mg and cyclosporin capsules. Ophthalmic management consisted of close observation, as described below.

1.5 Follow-up and outcome

During follow-up the haemorrhage enlarged to involve the fovea in both eyes, and visual acuity fell to 6/60 in the right eye and 6/24 in the left eye. Because the haemorrhages were dense and central, Nd:YAG laser hyaloidotomy was considered. In view of the persistently low platelet and other blood counts and the bleeding risk of intervention, the decision was made to observe closely. Blood counts remained low during this period, and the patient was reviewed weekly. Fundus evaluation showed progressive contraction of the macular subhyaloid haemorrhages in both eyes (Figures 2 and 3). The sedimentation level was lost, and the peripapillary haemorrhages shrank and darkened. At the later visit (Figure 3), the right eye retained a small pigmented macular haemorrhage and a small haem-

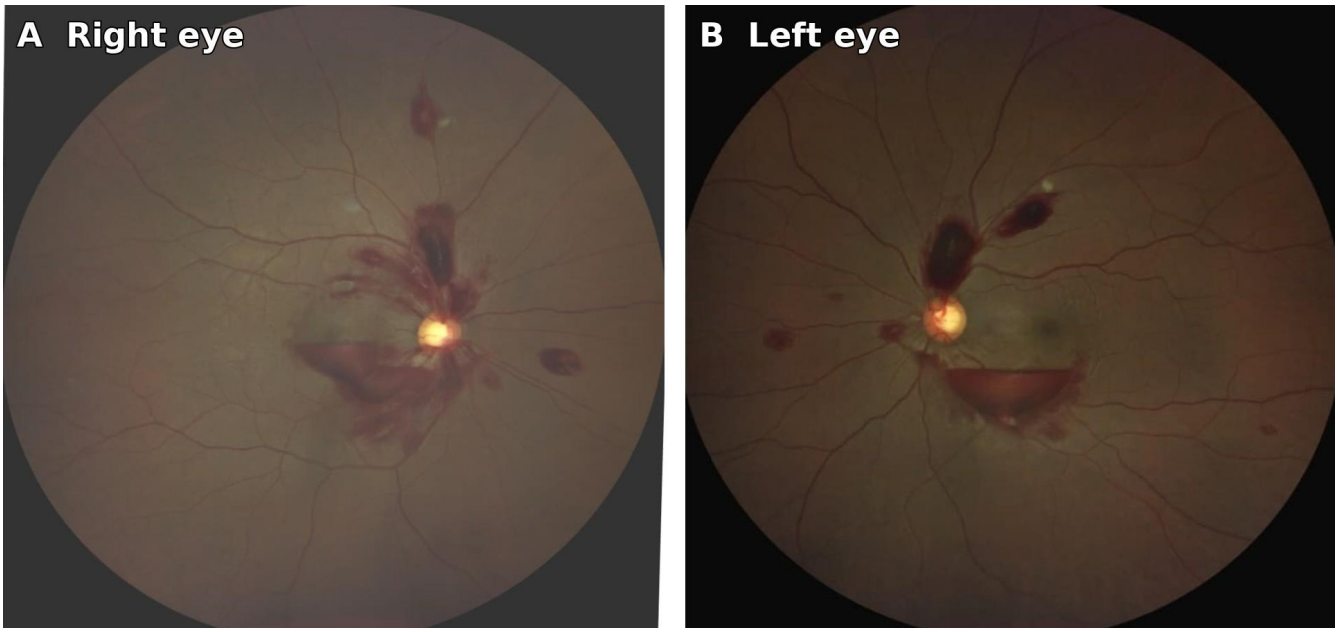


Figure 1. Baseline colour fundus photographs of the right eye (A) and left eye (B), showing boat-shaped macular subhyaloid haemorrhages with a sedimentation level, dense peripapillary haemorrhages along the superotemporal arcade and scattered intraretinal haemorrhages. OCT images of the right eye (C) and left eye (D) correspond to the subhyaloid haemorrhage.

Table 1. Laboratory results at presentation

Parameter	Result	Reference range
Haemoglobin	8.0 g/dL	13.0–17.0
Haematocrit	24.3%	40.0–50.0
RBC count	2.50×10^6/µL	4.5–5.5
MCV / MCH / MCHC	97.2 fL / 32.0 pg / 32.9 g/dL	83–101 / 27–32 / 31.5–34.5
RDW	19.8%	11.6–14.8
Platelet count	15×10^3/µL	150–400
Mean platelet volume	9.89 fL	6.8–10
White cell count	2.7×10^3/µL	4.0–10.0
Neutrophils / lymphocytes	22.9% / 70.1%	60–80 / 20–40
Absolute neutrophil count (calculated)		–
Reticulocytes (% / absolute)	0.615% / 15.6×10^3/µL	0.5–1.0 / 26–126
Erythropoietin	326.8 mIU/mL	3.22–31.9
PT / INR	14.4 s / 0.98	12.8–16.6 s
APTT	26.8 s	28.1–33.9 s
LDH	263 U/L	0–248
Creatinine / urea	0.90 / 33.6 mg/dL	0.7–1.2 / 19–44
AST / ALT / ALP	19.9 / 25.5 / 64.5 IU/L	0–50 / 0–40 / 0–130
Total bilirubin	0.49 mg/dL	0–1.1
Sodium / potassium	139.1 / 3.9 mmol/L	136–145 / 3.5–5.1
HIV-1/2 (p24 Ag and Ab)	Non-reactive (index 0.07)	–
Blood group	A Rh D positive	–

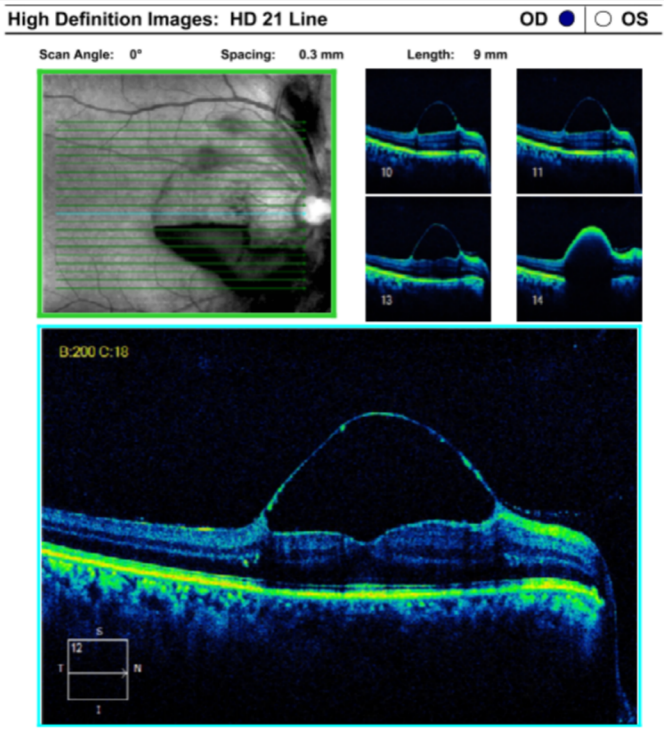
Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; INR, international normalised ratio; LDH, lactate dehydrogenase; MCH/MCHC/MCV, mean corpuscular haemoglobin/haemoglobin concentration/volume; PT, prothrombin time; RDW, red cell distribution width.

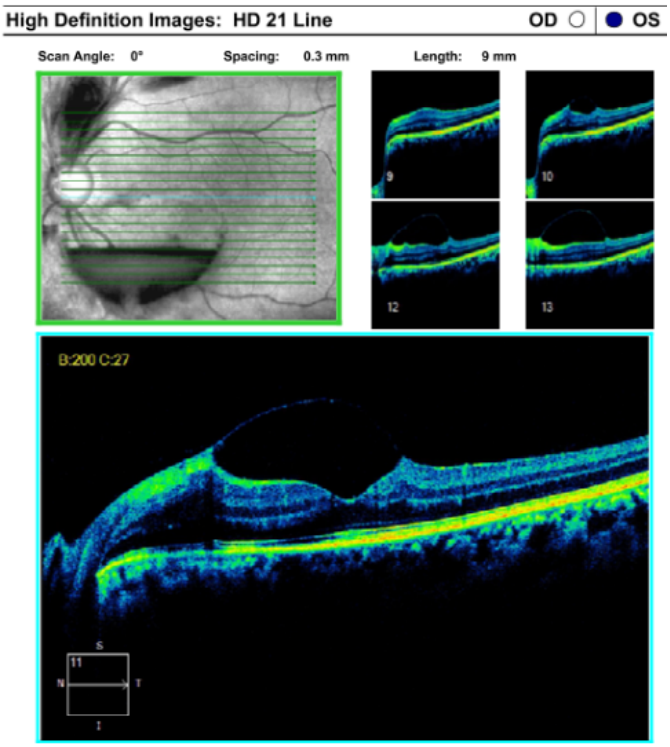
orrhage adjacent to the disc, and the left eye a small residual dark haemorrhage at the macula. The final photographs (Figure 4) show clearance of the haemorrhages in both eyes, and visual acuity recovered to 6/6 although the blood counts remained low throughout the course.

2. Discussion

This patient had extensive bilateral haemorrhages in the premacular and peripapillary regions during evaluation for pancytopenia. The main clinical point is the link between a serious underlying haematological disorder and haemorrhagic retinal change, which here caused a marked but reversible fall in vision.

Bleeding into the retina in cytopenic states results from





fragile capillaries and defective primary haemostasis when platelets are low, and anaemic hypoxia aggravates this by increasing vessel permeability. Thrombocytopenia and anaemia act together [1], and white-centred haemorrhages are seen in many haematological conditions [2]. Our patient had a platelet count of 15×10^3/μL together with haemoglobin of 8.0 g/dL, and the normal PT/INR and non-prolonged APTT argue against a coagulopathy. In a large aplastic anaemia series, bilateral haemorrhage predominated among the retinal findings and the mean platelet count of affected patients was low, close to the value seen here [4]. A Valsalva-type rise in venous pressure can also provoke sub-ILM bleeding in a thrombocytopenic eye [9], so the history should be explored for coughing, vomiting or straining.

The macular lesions were boat-shaped with a horizontal level, reflecting layering of red cells under gravity in the subhyaloid space. OCT helps to separate subhyaloid from sub-ILM haemorrhage: sub-ILM blood lies under a thin, taut, hyper-reflective membrane, whereas subhyaloid blood lies beneath a detached posterior hyaloid. The distinction affects management, because Nd:YAG hyaloidotomy releases the blood into the vitreous cavity and has given good visual results in dense premacular haemorrhage [10][11], but it carries risks that include macular hole, retinal detachment and persistent vitreous opacity [10]. The choice of treatment depends on the initial acuity, the size and location of the haemorrhage and the patient's general health [12]. In our patient the indication was debatable. Vision had fallen to 6/60 and 6/24 with foveal involvement, which would usually favour early hyaloidotomy to shorten the period of visual loss and limit toxicity of blood on the macula. However, both eyes were affected, platelet and other counts remained low, and any laser-induced bleeding or vitreous haemorrhage would have been difficult to manage. We therefore observed closely, and the haemorrhages cleared spontaneously. One series reserved laser for haemorrhages that had not resolved on their own [11], and conservative management has been chosen for a patient on anticoagulant therapy [12]. Our outcome supports observation as a reasonable first approach in selected thrombocytopenic patients, provided follow-up is close and intervention remains available if the haemorrhage persists or clot organisation threatens the fovea.

The combination of severe thrombocytopenia, neutropenia below 1.0×10^9/L, an inadequate reticulocyte response and a markedly raised erythropoietin level points to hypoproliferative marrow failure, and treatment with cyclosporin and eltrombopag follows standard practice for aplastic anaemia [7][8]. Spontaneous resolution of aplastic anaemia retinopathy has been described, with near-complete clearing and visual improvement over about 16 weeks after stem cell transplantation [13], and ocular lesions have been reported to evolve in step with systemic improvement [14]. Retinal haemorrhages have likewise regressed as platelet counts rose in immune thrombocytopenia [15]. In our patient the haemorrhages cleared while blood counts

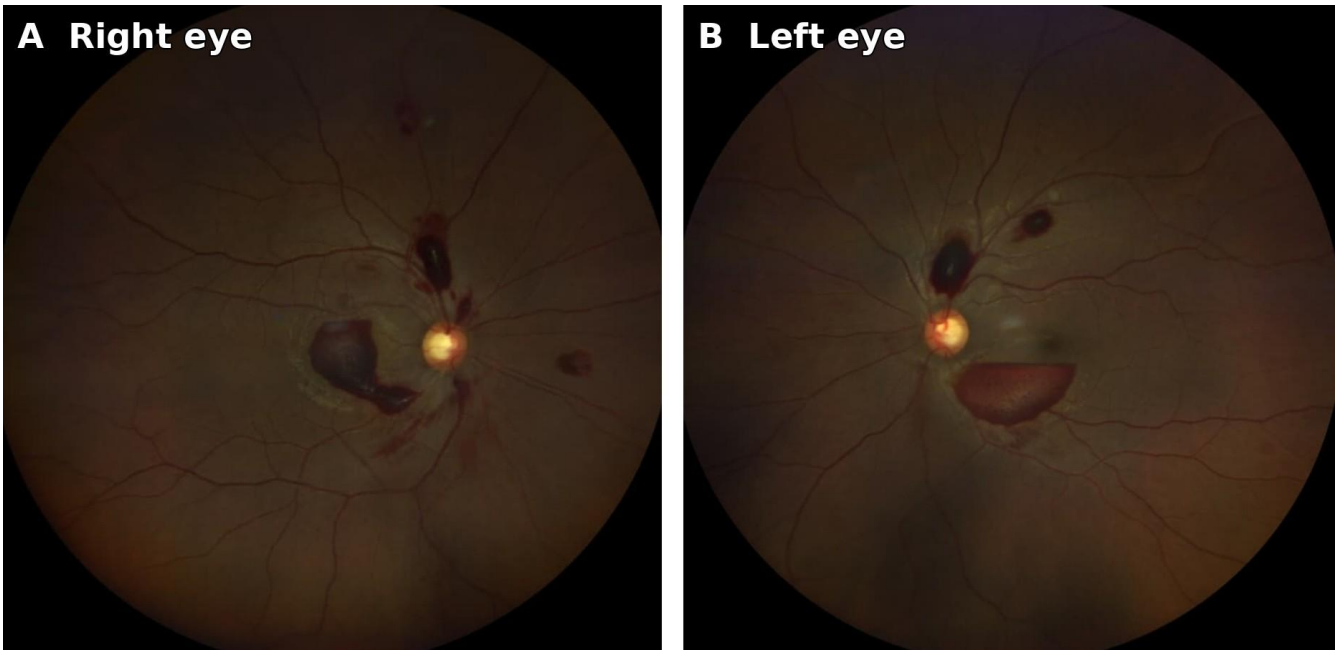


Figure 2. Early follow-up photographs of the right eye (A) and left eye (B), showing contraction of the macular haemorrhages, which are more compact and darker in the right eye; a sedimentation level persists in the left eye.

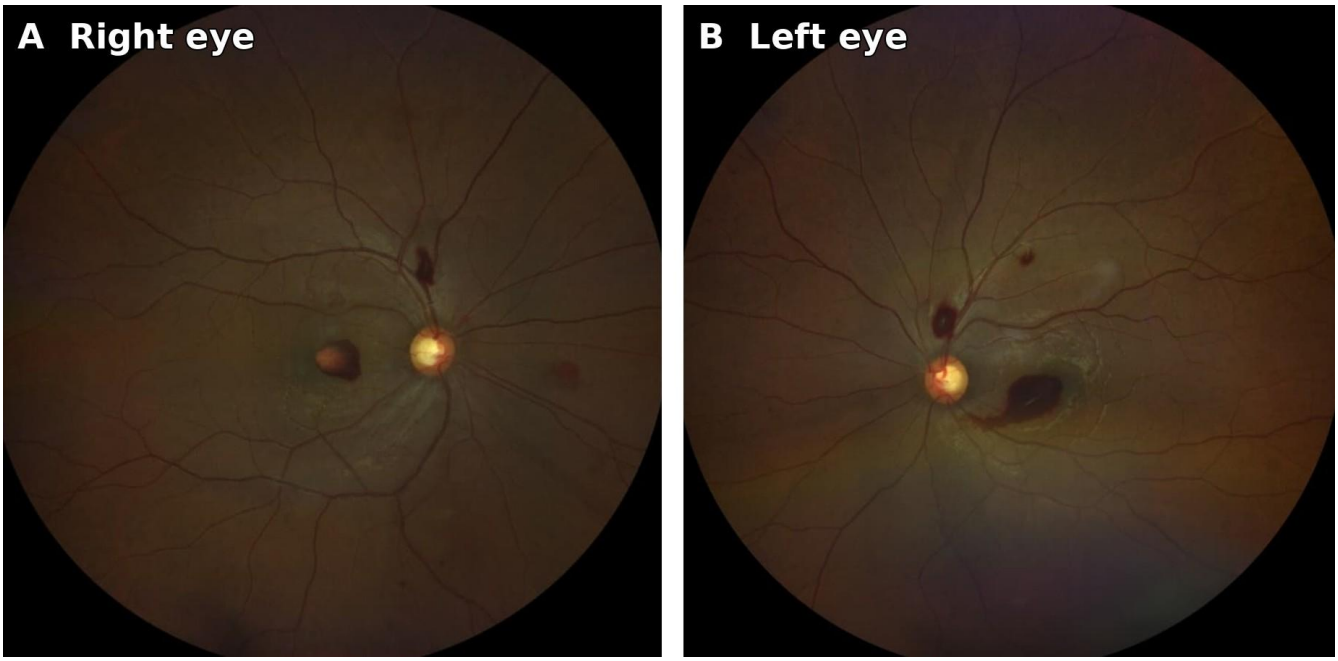


Figure 3. Intermediate follow-up photographs of the right eye (A) and left eye (B), showing a small residual pigmented/dark macular haemorrhage and shrinking peripapillary haemorrhages.

remained low, so full haematological recovery may not be a prerequisite for resolution, although a single case cannot establish this. The contribution of haematological treatment relative to natural resolution also cannot be separated. Ophthalmic surveillance is reasonable during long-term eltrombopag, and blood pressure should be monitored during cyclosporin therapy.

Clinical implications: (1) Patients admitted with severe cytopenia should undergo a dilated fundus examination, since retinal haemorrhage is common in this setting and may go unnoticed or present late [4,5]. (2) Colour photography and OCT document morphology and monitor resolution. (3) Hyaloidotomy should be balanced against bleeding risk; where counts remain low, close observation can be effective, with laser reserved for non-resolving collections and ideally performed with platelet support. (4) The retinal findings reinforce the importance of correcting thrombocytopenia.

Limitations: This is a single case. The natural history of such haemorrhages is generally favourable, so the role of observation in the recovery cannot be separated

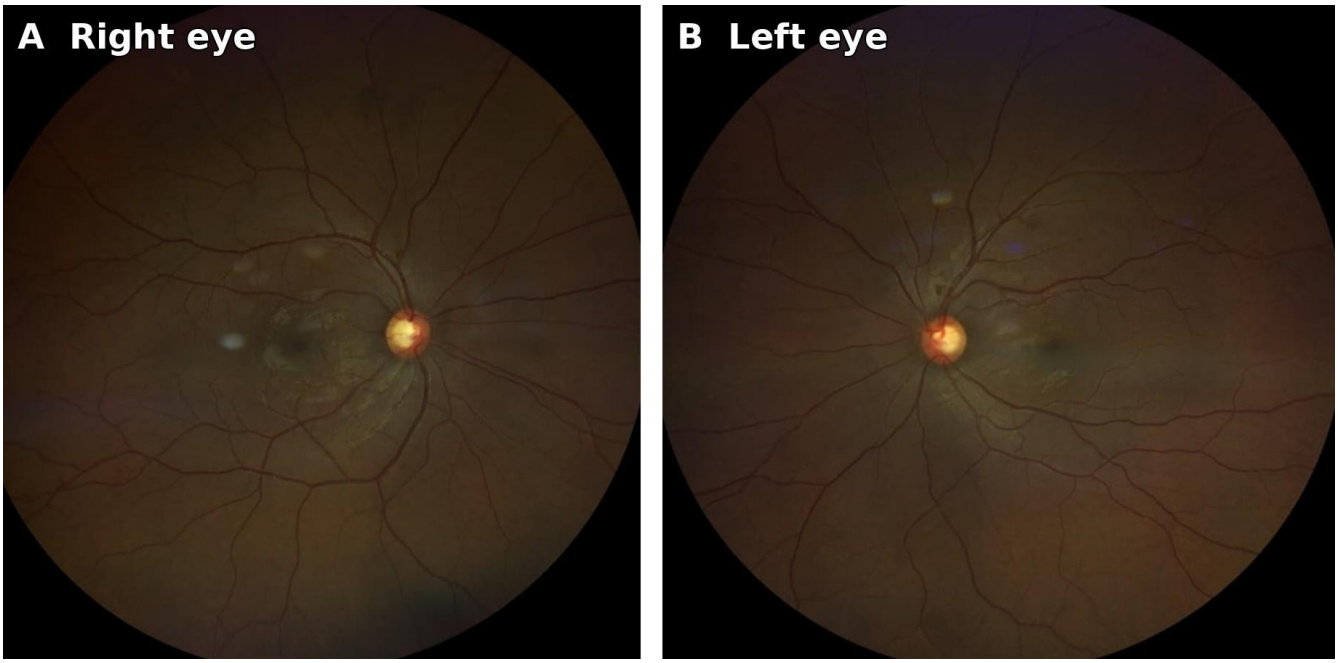


Figure 4. Final follow-up photographs of the right eye (A) and left eye (B), showing resolution of the subhyaloid and peripapillary haemorrhages.

from that of haematological treatment, and we cannot compare our outcome with that of hyaloidotomy.

3. Conclusion

Bilateral macula-involving subhyaloid haemorrhage in severe pancytopenia can reduce vision to 6/60 and 6/24 yet resolve with close observation, with recovery to 6/6, even while blood counts remain low. Early dilated fundus examination, multimodal imaging and close collaboration between retina and haematology services are central to protecting vision, and decisions about hyaloidotomy should be individualised to platelet status and bleeding risk.

4. Declarations

Ethical approval

The case was managed in accordance with the principles of the Declaration of Helsinki. Written informed consent for publication of the clinical details and images was obtained from the patient.

5. Conflicts of interest:

Nil

6. Financial support:

Nil

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