CASE REPORT

You are what you eat: ophthalmological manifestations of severe B₁₂ deficiency

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SUMMARY

Severe B₁₂ vitamin deficiency due to diminished dietary intake is a known cause of severe pancytopenia with bleeding diathesis. The authors report a case with sudden-onset bilateral vision loss, severe pancytopenia and multiple organ failure secondary to B₁₂ vitamin deficiency in a patient with a strict vegetarian diet. On funduscopic examination the patient had multiple bilateral exuberant haemorrhages in all retinal layers. Five months after presentation, he had a complete visual recovery without ophthalmological intervention.

BACKGROUND

Vitamin B₁₂ derives predominantly from animal alimentary products, such as meat, fish, eggs and milk. Malabsorption is the most frequent cause of B₁₂ deficiency. In contrast, an inadequate dietary supply represents only a minority of the cases, with body reserves being usually enough for 3–4 years.¹ Strict vegetarians (vegans) are at higher risk of developing vitamin B₁₂ deficiency in comparison with non-vegetarians due to suboptimal intake.² Because of this, they are advised to consume vitamin B₁₂-fortified foods or supplements.³ In addition to numerous systemic manifestations (neurological, epithelial surfaces, etc), B₁₂ deficiency presents notably with megaloblastic anaemia and pancytopenia.

Severe anaemic hypoxia damages arteriolar endothelium and impairs its reparation, leading to capillary disruption and subsequent haemorrhage.⁴ The association with thrombocytopaenia seems to increase the likelihood of retinopathy.⁵ Fundus findings in these patients include retinal and preretinal haemorrhages, vitreous haemorrhage, Roth's spots, cotton wool spots and optic disc swelling.^{4,5}

This case report draws attention to the impact of the ocular manifestations of unusually severe anaemia and thrombocytopaenia secondary to vitamin B₁₂ deficiency.

CASE PRESENTATION

A 25-year-old Caucasian man was presented to the emergency room unconscious, hypothermic, hypotensive and with severe malnutrition. His body mass index (BMI) was 16.5 kg/m², and according to his parents he had been a strict vegan for the past 4 years and he had a recent history of fatigue and dizziness.

Advanced life support was given, with blood transfusions, intubation, dopaminergic support and heating. The patient was admitted to the intensive

care unit (ICU), where he stayed for 13 days. After clinical improvement of the respiratory, cardiovascular, haematological and hepatic failure, and after recovering consciousness, he was transferred to the internal medicine ward, when he first perceived bilateral vision loss.

On examination, visual acuity was 20/400 in both eyes with an unremarkable anterior segment examination. On funduscopy, there were multiple exuberant retinal haemorrhages of all layers, bilaterally. Numerous haemorrhages with white centred dots (Roth spots), flame-shaped, extensive retrolental haemorrhage and cotton wool spots were present, as shown in figures 1 and 2.

INVESTIGATIONS

On presentation, there were lactic acidosis and severe pancytopenia (haemoglobin: 2.1 g/dL; white cell count: 2.1×10⁹; platelets: 17×10⁹). Peripheral blood smear showed multinucleated erythroblasts, anisopoikilocytosis, macrocytic red cells and abnormal nuclear segmentation of neutrophils, compatible with B₁₂ or folate deficiency. There was severely low serum vitamin B₁₂ (54 pg/mL), slightly low folate (5.1 ng/mL), low iron with high ferritin level (serum iron 28 µg/dL, ferritin 281 ng/mL) and the international normalized ratio was 4. Head CT scan was normal. ECG, echocardiogram, blood cultures, chest X-ray and urinalysis were also unremarkable.

A diagnosis of malnourishment with B₁₂ vitamin deficiency was made.

DIFFERENTIAL DIAGNOSIS

All causes of pancytopenia may cause a similar haemorrhagic picture of the fundus. Acute leukaemia is the most frequent, followed by multiple myeloma, pernicious anaemia and less commonly iron deficiency anaemia.⁴

Bacterial endocarditis is another cause of retinal haemorrhages. In this case, however, echocardiogram, blood cultures, chest X-ray and urinalysis were normal.

Terson syndrome may have similar fundoscopic findings, but head CT was unremarkable.

TREATMENT

In the acute phase, the patient was given advanced life support, including blood transfusions, intubation, dopaminergic support and heating. A diagnosis of vitamin B₁₂ deficiency was made and the patient was given two hydroxocobalamin 1 mg

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Figure 1 Colour fundus photograph of the right (A) and left eye (B) on presentation showing multiple haemorrhages and an extensive premacular retrohyaloidal haemorrhage with a blood-liquid gravitational level.

intramuscular injections. Because there was no gastrointestinal dysfunction, nutritional rehabilitation was started at the ICU with enteric nutrition (nasogastric) at a low rate, closely monitored to avoid 'refeeding syndrome'. After clinical improvement he was given normal oral diet, dietary advisement, regular folic acid and B₁₂ vitamin oral supplementation, and was referred to further psychiatric and ophthalmological evaluation.

OUTCOME AND FOLLOW-UP

Supplementation therapy with folic acid and B₁₂ vitamin and dietary change to a varied, unrestricted omnivorous diet resolved the pancytopenia. The patient recovered and was discharged. A timeline of the clinical case is displayed in [table 1](#).

On follow-up appointments there was further clinical and analytical improvement and retinal haemorrhages cleared progressively. Five months after presentation, his BMI had increased from 16.5 Kg/m² to 25 kg/m², and analytical parameters were unremarkable. Visual acuity had improved to 20/20 in both eyes and there were discrete macular pigmentary changes on funduscopy ([figure 3](#)).

DISCUSSION

A wide spectrum of diseases causing increased capillary fragility may present with retinal Roth spots. These include endocarditis, leukaemia, anaemia, diabetes, sickle cell disease, scurvy, shaken baby syndrome and connective tissue disorders.⁶ Roth spots have also been described in alcoholic patients with pancytopenia due to folate and less frequently to B₁₂ deficiency, with resolution after deficiency correction.^{4 6-8} Macauley and Nag⁹ also described Roth spots in patients with pernicious anaemia.

It is postulated that in patients with severe anaemia, retinal haemorrhages are due to the severe hypoxic damage of arteriolar endothelium and impaired reparation mechanisms. Capillary

Table 1 Timeline of the clinical case

Day 1	At the ER ► Multiorgan failure and severe malnutrition ► Advanced life support: transfusions, intubation, dopaminergic support and heating ► Hydroxocobalamin 1 mg intramuscularly Admitted to the ICU
Day 2	At the ICU ► Advanced life support ► Enteric nutrition ► Hydroxocobalamin 1 mg intramuscularly
Day 13	Transferred to the internal medicine infirmary ► Conscience recovery and complaints of bilateral vision loss ► Transition to oral diet ► Vitamin B ₁₂ oral supplementation
Day 30	Gradual recovery and discharge
5 Months after presentation	► Supplementation therapy and change to a varied, unrestricted omnivorous diet ► Progressive weight gain ► Gradual visual recovery and clearing of retinal haemorrhages

ER, emergency room; ICU, intensive care unit.

disruption leads to haemorrhage and leucocytes extravasation, haemostatic fibrin plug and Roth spots formation.⁴ A sudden increase of intravascular pressure caused by Valsalva manoeuvres may also lead to the leakage of blood into the retina. The ophthalmological changes seen in our patient were explained by the severe pancytopenia and the coagulation deficit.

Primary management of patients with retinal haemorrhages secondary to severe pancytopenia such as in this case should include transfusion of red blood cells and platelets, avoiding volume overload, as well as B₁₂ and folate supplementation.

As most of these haemorrhages resolve spontaneously, complete resolution without ophthalmological intervention may be achieved. Refractory cases of preretinal haemorrhages may require Nd:YAG laser posterior hyaloidotomy.¹⁰ Nd:YAG laser hyaloidotomy is an inexpensive, effective and apparently safe procedure for premacular subhyaloid haemorrhage, allowing rapid restoration of visual function and avoiding more invasive procedures.¹¹⁻¹³ It is not known whether this treatment is superior to watchful waiting in reducing the risk of long-term retinal changes.¹⁴ Despite the excellent final visual acuity and the fact that the patient was asymptomatic, he has not been tested for

Figure 2 Colour fundus photographs (A,B,C) showing bilateral white centred retinal haemorrhages — Roth spots.

Figure 3 Colour fundus photograph (A,B) and red-free fundus photograph (C,D) 5 months after presentation showing subtle macular pigmentary changes and complete resolution of the haemorrhages.

other subtler visual sequelae such as abnormal contrast sensitivity, colour vision or microperimetric changes.

Learning points

- ▶ Vegan populations are at a higher risk of vitamin B₁₂ deficiency.
- ▶ Roth spots are not pathognomonic for subacute bacterial endocarditis; they have also been described in many haematological and other conditions.
- ▶ Complete visual recovery may be achieved without ophthalmological intervention.
- ▶ Although this kind of haemorrhages are benign and usually improve spontaneously, blood presence in the retina may cause permanent macular changes.

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