Case Report:

Subhyaloid haemorrhage in a patient with vitamin B_{12} deficiency: a unique presentation

Z.A. Wadood Khan,[1] Sudha Vidyasagar,[1] Ragini Bekur,[1] Sushma Belurkars,[2] S. Shailaja[3]

Departments of [1]Medicine, [2]Pathology, [3]Ophthalmology, Kasturba Medical College, Manipal

ABSTRACT

Vitamin B_{12} deficiency causes pancytopenia and also is also assocciated with platelet dysfunction. We report the case of a 17-year-old girl, who presented with fatigue and sudden painless, non-progressive loss of vision in the left eye. An ophthalmologic evaluation revealed bilateral subhyaloid haemorrhage, with macular involvement on the left eye. Earlier Bone marrow aspiration and biopsy were suggestive of partially treated vitamin B_{12} deficiency with pancytopenia. The patient had received four doses of vitamin B_{12} injections. She was given a complete course of vitamin B_{12} injections. Both the pancytopenia and subhyaloid haemorrhage improved completely with restoration of normal vision. This case documents the rare occurrence of subhyaloid haemorrhage in vitamin B_{12} deficiency.

Key words: *Retinal haemorrhage, Megaloblastic anaemia, Pure vegans, Vitamin B_{12} deficiency*

Wadood Khan ZA, Vidyasagar S, Bekur R, Belurkars S, Shailaja S. Subhyaloid haemorrhage in a patient with vitamin B12 deficiency: A unique presentation. J Clin Sci Res 2013;2:161-4.

INTRODUCTION

Vitamin B_{12} deficiency causes megaloblastic anaemia and pancytopenia when severe, due to defect in deoxyribonucleic acid (DNA) synthesis.[1] Vitamin B_{12} deficiency is also associated with platelet dysfunction.[2] Megaloblastic anaemia can be associated with bleeding manifestations due to thrombocytopenia. Various haemorrhagic manifestations have been described due to vitamin B_{12} deficiency.[3,4]

The common causes of retinal haemorrhage include diabetic and hypertensive retinopathy, physical trauma, bleeding diathesis and increased intracranial pressure.[5] Depending on the location of haemorrhage within retinal layers, ophthalmic appearance vary. Retinal bleeding due to severe anaemia with or without thrombocytopenia secondary to pernicious anaemia, aplastic anaemia and leukemias has been reported.[6] Retinopathy due to megaloblastic anaemia has been reported from Africa.[7] Only one case report of bilateral retinal haemorrhage due to megaloblastic anaemia due to combined deficiency of folate and vitamin B_{12} in an alcoholic patient has been reported.[8] PUBMED search did not reveal any case reports of subhyaloid bleeding due to vitamin B_{12} deficiency in adults from India where majority of people are vegetarians. We present a rare case of subhyaloid bleeding due to vitamin B_{12} deficiency in a young patient.

CASE REPORT

A 17-year-old girl, who was a pure vegan who did not consume milk or dairy products came to the hospital with fatigue, feverishness and sudden onset of non-progressive painless loss of vision in the left eye since 5 days. Investigations done outside showed Haemoglobin of 3.6 g/dL (normal 12-15g/dL), platelet 39,000/mm^3 (normal,150000-350000/mm^3), total leucocyte count 2800/mm^3 (normal, 4000-10000/mm^3) with history of taking four doses of parenteral vitamin B_{12}. She did not have any history of bleeding from other sites or menorrhagia. Petechiae, ecchymoses or organomegaly were not evident. General physical examination revealed severe pallor, systemic examination was unremarkable. Fever was not documented during the period of in-hospital stay. An ophthalmologic evaluation revealed bilateral

Received: 20 April, 2013.

Corresponding Author: Dr Ragini Bekur, Associate Professor, Department of Medicine, Kasturba Medical College, Manipal, India. **e-mail:** raginibekur@gmail.com

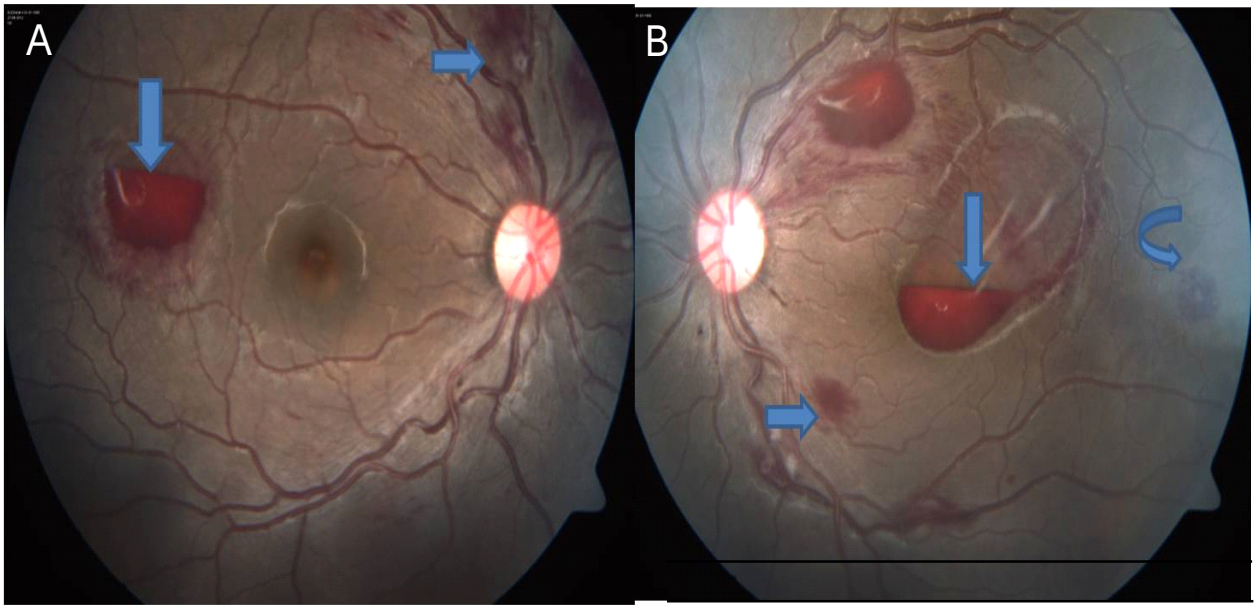

Figure 1: Fundus photograph of the right (A) and left (B) retina showing bilateral subhyaloid haemorrhage (arrows) with involvement of centre of fovea on left side

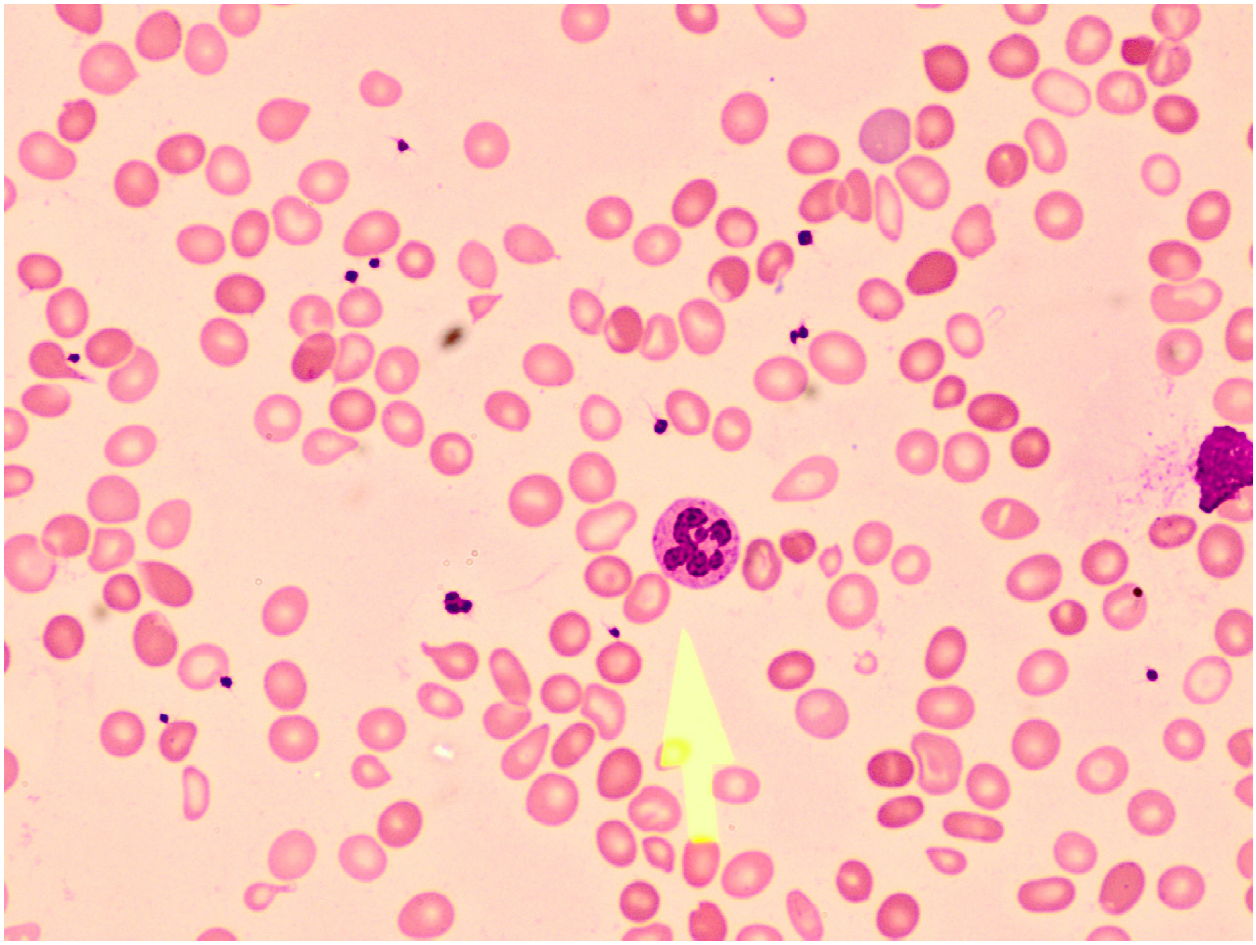

Figure 2: Photomicrograph of peripheral blood smear showing macrocytes with hypersegmented neutrophils (arrow) (Leishman's stain, × 400)

subhyaloid haemorrhage with the centre of the fovea involved on the left eye, accounting for predominant left eye vision loss (Figures 1A and 1B).

Laboratory investigations revealed Haemoglobin 5.9 g/dL, platelet count 81,000/mm^3 and total leucocyte count 3,800/mm^3 suggestive of pancytopenia. Mean corpuscular volume (MCV) was 108.1 fL (normal, 83-101 fL). Serum vitamin B_{12} levels were 1413 pg/mL (normal 330-1025pg/mL). Serum folate level was 9 ng/mL (normal, 3-12 ng/mL), and iron studies revealed serum iron 87 µg/dL(normal 45-170 µg/dL), serum ferritin was 163.3 ng/mL (normal,11-307ng/mL) Peripheral smear was suggestive of pancytopenia with macrocytic blood picture, hypersegmented neutrophils (Figure 2). Bone marrow biopsy and aspiration was done which confirmed megaloblastic anaemia with pancytopenia. She was treated with intravenous vitamin B_{12} injection 1000 µg daily for 5 days, then every week intramuscularly for 1 month, then was advised to take injections once every 3 months for 2-3 years. Her haematological parameters improved. At 6 weeks follow-up the laboratory parameters were as follows; haemoglobin 11 g/dL, total leucocyte count 5800/mm^3, platelet count 122,000/mm^3. The subhyaloid haemorrhage resolved completely and vision returned to normal.

DISCUSSION

The only source of vitamin B_{12} for humans is food of animal origin i.e., egg, fish and dairy products. Vegetables and fruits are free of cobalamine. Vitamin B_{12} body stores are normally in the range of 2-3 mg, sufficient for 3-4 years even if supplies are completely cut off.[1] Thus deficiency manifests with longer duration of cobalamine free food, hence is usually seen in pure vegans.

Vitamin B_{12} is involved in an important and complex interaction with folic acid in the production of purine and pyramidine synthesis which in turn are necessary for DNA and ribonucleic acid (RNA) replication, which accounts for the macrocytic red blood cells seen in both cobalamine and folate deficiency. Severe vitamin B_{12} deficiency has been found to be associated with pancytopenia, with associated qualitative defect in platelets. Thrombocytopenia is due to impaired DNA synthesis leading to ineffective thrombopoiesis.[1] It has been found that platelet response to agonists like adenosine diphosphate (ADP), restocetin and epinephrine is considerably decreased in vitamin B_{12} deficiency indicating defect in platelet aggregation, which improves on vitamin replacement.[2] Megaloblastic anaemia can be associated with haemorrhagic manifestations. Study done on children with megaloblastic anaemia from Chandigarh and Delhi documented bleeding from skin, subcutaneous tissue, epistaxis and few children presented with life threatening haemorrage from gut as well as intracerebral bleed, requiring emergency blood transfusion.[3,4] There was excellent response to parenteral vitamin B_{12} injections with haemostasis achieved as early as 12-24 hour in them. Severe anaemia, (haemoglobin < 8 g/dL), can cause retinal haemorrhage. Bleeding manifestations were seen in patients with severe anaemia and thrombocytopenia, especially in those with combined deficiency.[3,4,6] In Africa, retinopathy due to megaloblastic anaemia due to nutritional deficiency has been reported.[7] Occurence of bilateral retinal haemorrhages including subhyaloid haemorrhage due to megaloblastic anaemia with thrombocytopenia has been reported in a 33-year-old chronic alcoholic patient with both vitamin B_{12} and folate deficiency.[8]

Subhyaloid haemorrhage, is located between the posterior vitreous base and the internal limiting membrane of the retina. The causes include neovascularization in diabetes mellitus, bleeding dyscrasias, trauma, raised intracranial pressure, Terson's syndrome subhyaloid haemorrhage associated with subarachnoid haemorrhage.[5]

Retinal haemorrhages in severe anaemia have been described as 'flame shaped' haemorrhages that occur within nerve fibre layers, 'round' or 'dot' haemorrhages that are found deep in the outer retinal layers, occasionally subhyaloid haemorrhage. The pathogenesis of retinopathy in severe anaemia

could be due to hypoxic injury to the vascular endothelium causing increased permeability, capillary leakage and intraretinal bleed.[9] Age and rapid development of anaemia leads to retinopathy and it is rare in patients less than 18 years of age.[10] The present case highlights the rare occurrence of subhyaloid haemorrhage in a patient under 18 years of age with vitamin B_{12} deficiency.

Our patient a pure vegan without any history of trauma, bleeding dyscrasias but with evidence of Vitamin B_{12} deficiency who presented with bilateral subhyaloid bleed. The initial platelet count in our patient was 39,000 mm^3 and this by itself would not usually result in a retinal bleed unless there is an associated severe anaemia or platelet dysfunction due to cobalamine deficiency .

Thus, in a largely vegan population like ours, vitamin B_{12} deficiency is an important and easily treatable cause of retinal and subhyaloid haemorrhage which is reversible and easily treatable.

REFERENCES

1. Victor Hoffbrand A. Megaloblastic anemia. In: Dan LL, Dennis LK, Larry JJ, Anthony SF, Stefen LH, Joseph L, editors. Harrison's principles of Internal Medicine, 18th edition. Volume 1. New York: McGraw Hill; 2012.p. 862-72.
2. Ghosh K, Krishna V, Mohanty D. Platelet dysfunction in nutritional vitamin B_{12} deficiency. Platelets 1991;2:153-6.
3. Marwaha RK, Singh S, Garewal G, Marwaha N, Walia BN, Kumar L. Bleeding manifestations in megaloblastic anaemia.Indian J Pediatr 1989;56:243-7.
4. Gomber S, Kela K, Dhingra N. Clinico-hematological profile of megaloblastic anemia. Indian Pediatr 1998;35:55-8.
5. Duke-Elder S, Debre JH. Disturbances of Circulation in Duke-Elder S (ed):System of Ophthalmology. St Louis, CV Mosby Co,1967,vol 10,pp 145-7.
6. Rubenstein RA, Yanoff M, Albert DM. Thrombocytopenia, anemia, and retinal hemorrhage. Am J Ophthalmol 1968;65:435-9.
7. Markar MA, Peiris JB, D Silva GU. Retinapathy in megaloblastic anemias. Trans R Soc Trop Med Hyg 1969;63:398-406.
8. Lam S, Lam BL. Bilateral retinal hemorrhages from megaloblastic anemia: case report and review of literature. Ann Ophthalmol 1992;24:86-90.
9. Duke-Elder S, Dobre JH. The blood diseases. In: Duke-Elder S, editor. System of ophthalmology. Volume 10. St. Louis: CV Mosby Co; 1967;p.373-407.
10. Aisen ML, Bacon BR, Goodman AM, Chester EM. Retinal abnormalities associated with anemia. Arch Ophthalmol 1983;101:1049-52.