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# Branch retinal artery occlusion as an initial ocular manifestation of severe iron deficiency anemia: A rare case report

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## Abstract:

Ocular manifestations of anemia include conjunctival pallor, retinal hemorrhages, cotton wool spots, Roth spots, subhyaloid hemorrhage, venous dilatation, disc edema, and anterior ischemic optic neuropathy (AION). Retinal arterial occlusion is a very rare complication of iron deficiency anemia. We, hereby, report such a rare case of branch retinal artery occlusion (BRAO) occurring as a complication of iron deficiency anemia. A 49-year-old female presented with sudden painless diminution of vision in her right eye (RE) for 2 weeks with visual acuity of 20/120 in the affected eye and 20/20 in the left eye. Fundus examination of RE showed disc pallor, arteriolar attenuation, and retinal whitening at macula. Fluorescein angiography study demonstrated delayed filling of superotemporal branch of retinal artery, suggesting BRAO as the cause of vision loss. Thorough evaluation for underlying etiology revealed severe iron deficiency anemia (hemoglobin 3.9 g/dl). Her blood pressure, blood sugar profile, lipid profile, carotid Doppler, echocardiogram, coagulation profile, and immunological workup were all unremarkable. She was treated with packed cell transfusion and oral iron supplementation, and her vision improved to 20/40 at 1-month follow-up. Retinal vascular occlusions can occur rarely in iron deficiency anemia, and therefore anemia should be considered, while evaluation of vascular occlusion – specially in those with associated conjunctival pallor as in our case.

## Keywords:

Anemic retinopathy, branch retinal artery occlusion, iron deficiency anemia

## Introduction

Anemic retinopathy is usually observed in around 20%–25% of patients with iron deficiency anemia.<sup>[1]</sup> However, the prevalence of retinopathy may vary with the severity of anemia. With hemoglobin (Hb) levels < 8 g/dl (moderate to severe anemia), the prevalence of anemic retinopathy has been noted to be as high as 70% in various studies.<sup>[1-3]</sup> Ocular manifestations of anemia include conjunctival pallor, retinal hemorrhages, cotton wool spots, Roth spots, subhyaloid hemorrhage, venous

dilatation, disc edema, and AION. Retinal vessel occlusion is a rare complication of iron deficiency anemia. Few case reports of retinal vein occlusion in iron deficiency anemia exist in literature.<sup>[4,5]</sup> To the best of our knowledge, only one case of incomplete occlusion of central retinal artery occlusion and one more case of branch retinal artery occlusion (BRAO) occurring secondary to iron deficiency anemia have been reported previously.<sup>[2,6]</sup> Hereby, we report such a rare case of BRAO in a 49-year-old female who had severe iron deficiency anemia and had no other systemic comorbidities.

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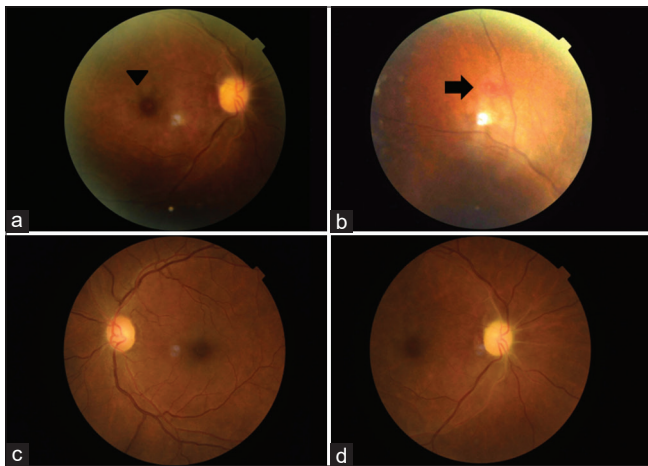
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## Case Report

A 49-year-old female presented to us with a history of sudden onset painless diminution of vision in her right eye (RE) for 2 weeks. There was no history of associated flashes or floaters. She had no history of any prior heart disease, diabetes mellitus, hypertension, or hyperlipidemia. On general physical examination, conjunctival pallor was noted. Vital signs assessments revealed a normal blood pressure (120/78 mmHg) and a bounding pulse (PR 96/min). The rest of her systemic examination was unremarkable. On ocular examination, best-corrected visual acuity in RE was 20/120 and 20/20 in the left eye (LE) with Grade I relative afferent pupillary defect (RAPD) in RE. Fundus examination of RE showed mild disc pallor, arteriolar attenuation, retinal whitening at the macula, and superficial retinal hemorrhages temporal to the disc and along the superotemporal vascular arcade. No embolus was noticed in the retinal vessels [Figure 1a and b]. LE fundus showed only arteriolar attenuation [Figure 1c]. The rest of the LE examination was unremarkable. Intraocular pressure was 13 and 14 mmHg in RE and LE, respectively. Color vision was abnormal in RE. Fundus fluorescein angiography (FFA) [Figure 2a and b] revealed delayed arterial filling of superotemporal branch of central retinal artery in the RE along with prolonged arteriovenous (AV) transit time and irregular foveal avascular zone (FAZ), which was suggestive of superotemporal BRAO. Choroidal filling and disc filling were, however, normal. FFA was normal in LE. Blood investigations revealed normal fasting and postprandial blood sugar levels and normal fasting lipid profile. Further investigations unveiled a severe iron deficiency anemia with Hb of 3.9 g/dl and serum ferritin of 3.0 ng/ml [Table 1]. Serum homocysteine was normal (12.65  $\mu$ mol/L).



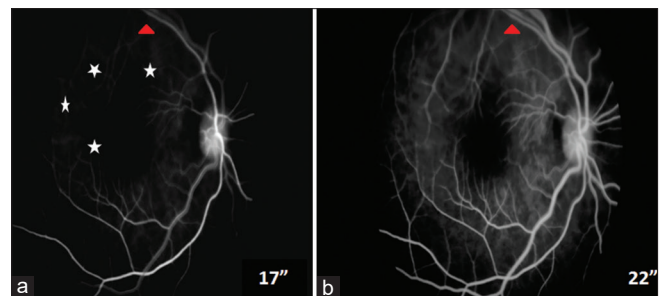
**Figure 1:** Fundus images of the right eye (a) showing mild disc pallor, peripapillary hemorrhage, arteriolar attenuation, retinal whitening at the macula (triangle), and (b) superficial retinal hemorrhage (arrow); fundus image of the left eye (c) showing normal disc and macula with arteriolar attenuation at presentation; fundus image of the right eye at 1 month (d) shows resolved retinal whitening at the macula

Coagulation profile was normal. Immunological workup including antinuclear antibody, rheumatoid factor, and antineutrophil cytoplasmic antibodies was all within normal limits. Stool was negative for any parasitic ova or cyst. Carotid Doppler study showed partially calcified atheromatous plaque with no significant luminal narrowing in the left carotid bulb, while the right carotids were normal. Echocardiogram was unremarkable. Contrast magnetic resonance imaging of brain and orbit showed mild reduced caliber of right optic nerve without enhancement. Visual-evoked potential was normal. Since she had no history of blood loss or bleeding manifestation, her anemia was attributed to her nutrition. She was transfused with two pints of packed red blood cells (RBCs) and started on oral iron supplementation (ferrous sulfate tablet 200 mg three times/day  $\times$  6 weeks) after consultation with the physician. Visual acuity in RE improved to 20/60 within 2 weeks of treatment initiation. At 1 month of follow-up, visual acuity in RE had improved to 20/40. A repeat fundus examination of RE showed mild disc pallor with arteriolar attenuation. Retinal whitening at the macular region had resolved [Figure 1d]. Repeat hemogram at 1 month revealed improvement of Hb levels to 11.9 g/dl and serum ferritin levels to 44 ng/ml.

## Discussion

Ulrich in 1883 first described anemic retinopathy in a patient with gastrointestinal hemorrhage, which had subsequently resolved following correction of anemia. The most common ocular manifestation of anemia is conjunctival pallor, followed by retinal abnormalities. Retinal hemorrhages, cotton wool spots, exudates, Roth spots, tortuous veins, posterior pole pallor, subhyaloid hemorrhage, disc pallor, and disc edema are commonly described features of anemic retinopathy.<sup>[1-3,7]</sup>

The fundus abnormalities observed in anemia are related to tissue hypoxia. Vasodilation occurs in response to hypoxia which leads to increased capillary



**Figure 2:** Fundus fluorescein angiography images of the right eye (a and b) showing delayed filling (triangles) of the superotemporal branch of the central retinal artery and normal choroidal and disc filling suggestive of branch retinal artery occlusion. Image 2a in addition shows corresponding enlarged area of capillary non-perfusion (stars) during the early phases of angiography in the macular area.

**Table 1: Complete hemogram and ferritin levels at presentation**

Parameters	Observed values	Normal range
Hb	3.9 g/dl	12-16.0 g/dl
RBC count	3.07×10 <sup>6</sup> /μl	3.8-5.3×10 <sup>6</sup> /μl
HCT	16.6%	35%-45%
MCV	54.1 fl	80-100 fl
MCH	12.7 pg	27-32 pg
MCHC	23.5g/dl	32-36 g/dl
WBC count	5.17×10 <sup>3</sup> /μl	4-11.0×10 <sup>3</sup> /μl
DLC	N47.8 E9.3 B0.6 M5.2 L37	
Platelet count	258×10 <sup>3</sup> /μl	150-450×10 <sup>3</sup> /μl
Peripheral smear	Microcytic hypochromic RBCs, moderate-to-severe anisopoikilocytosis with a few teardrop cells, elongated cells, and polychromatophils. No blasts/atypical cells seen. Platelets appear adequate. No parasites seen. Impression: microcytic hypochromic anemia suggestive of iron deficiency anemia	
Serum ferritin	3.0 ng/ml	10-120 ng/ml

Hb=Hemoglobin, RBC=Red blood cell, HCT=Hematocrit, MCV=Mean corpuscular volume, MCH=Mean corpuscular hemoglobin, MCHC=MCH concentration, DLC=Differential leukocyte counts, WBC=White blood cell, N=Neutrophil, E=Eosinophil, B=Basophil, M=Monocyte, L=Lymphocyte

permeability and abnormal vascular leakage, thereby causing fundus abnormalities. Ischemia of nerve fiber layer due to tissue hypoxia manifests as cotton wool spots. Associated hypoproteinemia results in increased transmural pressure and thus retinal edema. Microtrauma and associated thrombocytopenia result in retinal hemorrhages. Severity of anemia, associated thrombocytopenia, and acute rather than chronic anemia are important risk factors for the development of retinopathy. Vascular occlusion is a rare manifestation of iron deficiency anemia, and it can cause significant vision loss.<sup>[1,6,7]</sup>

Our patient had conjunctival pallor and arteriolar attenuation on examination in both eyes. In addition, RE showed Grade I RAPD, mild disc pallor, retinal whitening at macula, and superficial retinal hemorrhages. Our initial differential diagnosis based on poor vision, RAPD, and fundus findings included BRAO and AION. FFA confirmed diagnosis of BRAO as there were delayed arterial filling, irregular FAZ, and prolonged AV transit time along the superotemporal branch of central retinal artery. There was no obvious arterial filling defect or involvement of all four branches of the central retinal artery as would be expected in CRAO.<sup>[8]</sup> There was neither any delay in optic disc filling nor any choroidal filling defect as would be expected in AION.<sup>[9]</sup>

As far as probable etiology for the retinal manifestations is concerned, we had done extensive systemic and laboratory evaluation and ruled out autoimmune diseases, hypercoagulable states, polycythemia, cardiac disease, hypertension, hypercholesterolemia, and

diabetes mellitus. Severe iron deficiency anemia was diagnosed in our case based on her detailed systemic and laboratory evaluation (Hb 3.9 g/dl, serum ferritin 3.0 ng/ml, and microcytic hypochromic RBCs in peripheral smear). Microvascular occlusion of retinal vessels similar to other vascular occlusions in severe anemia is the probable pathogenesis of BRAO in our case.<sup>[2]</sup> Thrombocytosis due to disinhibition of thrombopoietin, anemic hypoxia, and angiospasm are the proposed mechanisms for microvascular occlusion in severe anemia.<sup>[10]</sup> In the laboratory evaluation of this case, there was no thrombocytosis or hypercoagulability state. Hence, anemic hypoxia or angiospasm due to severe anemia may be the probable cause of microvascular occlusion in our case.

Two prior case reports of arterial occlusion secondary to iron deficiency anemia have been described in literature. Matsuoka *et al.* reported a case of incomplete CRAO in a 13-year-old girl with iron deficiency anemia who presented with features of LE gross diminution of vision; engorged tortuous retinal veins, attenuated retinal arteries, retinal hemorrhage, milky-white posterior pole with a cherry-red spot at macula, optic disc edema; and delayed filling and prolonged AV transit time with normal choroidal filling on FFA.<sup>[6]</sup> Imai *et al.* reported a case of BRAO in a 35-year-old male with iron deficiency anemia and rectal carcinoid. He presented with a sudden gross reduction in visual acuity in his LE with fundus examination showing retinal whitening and cherry-red spot at macula and FFA showing delayed arterial filling time, no arterial filling defect, and a normal choroidal filling time.<sup>[2]</sup> The findings in our case were identical.

Treatment of BRAO is directed toward the management of underlying etiology. As many improve spontaneously, aggressive management in BRAO is not pursued frequently. Surgical and laser embolectomy has been tried with varying success. However, our patient was treated with blood transfusion and oral hematinics alone. She had responded well to these measures with early improvement of visual acuity during the initial 2 weeks of therapy. Reversal of anemic hypoxia and angiospasm may be the possible explanation of the improvement of vision in our case. However, close follow-up to detect neovascularization at the earliest is required in such cases.

In conclusion, retinal occlusive events may be the first manifestation of an underlying systemic disease. Hence, a complete and thorough systemic examination is warranted. Although rare, retinal vascular occlusions can occur in iron deficiency anemia. Anemia should be considered while evaluation – specially in those with associated conjunctival pallor as in our case.

### Ethical approval

This study is approved by the Institutional Ethics Committee (IEC) of Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India. The approval number is IEC/JIP-01-20-189.

### Declaration of the patient consent

Informed consent was obtained from all individual participants included in the study. The authors certify that they have gathered all necessary patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal.

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Nil.

### Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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