Anemias occur when the level of healthy red blood cells (RBCs) or hemoglobin (an iron-binding, oxygen-carrying protein within RBCs) is too low. Depending on the cause, anemias can be classified as follows:

- Those occurring due to deficient production of RBCs from the bone marrow (hypoproliferative);
- Those due to increased blood loss (bleeding) or damage of red blood cells (hemolysis); or
- Those due to abnormalities in the production of the blood cells (ineffective erythropoiesis).

Iron deficiency is the most common type of anemia. A deficiency of vitamin B12 is known as pernicious anemia. In the eye, anemia can lead to transient retinal hemorrhages. These were first described by Ulrich in 1883 in association with gastrointestinal hemorrhage.

**Epidemiology and Pathogenesis**

Anemia causes retinopathy in 28% of patients, especially when there is coexisting thrombocytopenia (38%). As the severity of anemia increases, the risk of retinopathy increases, particularly when the hemoglobin (Hb) level is below 6 gm/dL.

A variety of pathologic changes occurring due to and associated with anemia are implicated in the clinical features of anemic retinopathy. Anemia causes retinal hypoxia, which leads to infarction of the nerve fiber layer and clinically manifests as cotton wool spots. Retinal hypoxia also leads to vascular dilatation; increased transmural pressure owing to hypoproteinemia; and microtraumas to the vessel walls, which cause retinal edema and hemorrhages. In many clinical situations, thrombocytopenia is associated with anemia, and that leads to defective coagulation and hemorrhages.

Other factors implicated in the pathology are venous stasis, angiospasm, increased blood viscosity (myeloproliferative disorders), hypotension (following hemorrhage), etc. Hypotension may lead to optic neuropathy.

**Clinical Findings**

Along with systemic features of anemia per se, and in relation to the primary etiology leading to the anemia, ocular findings can be classified as features common to all anemias or specific features due to specific etiologies.

**Symptoms**

Rarely, loss of vision can be a presenting complaint, because most cases are asymptomatic. At the macula, hemorrhages, edema, or hard exudates can cause impairment of vision. Alternatively, vision loss may occur due to disc edema or optic neuropathy.

**Signs**

Retinal changes common to all anemias include the following:

- **Hemorrhages**: Superficial, flame-shaped hemorrhages located in the nerve fiber layer are the most common finding in anemic retinopathy. In a few cases, dot and blot hemorrhages in deeper retinal layers may be noted. Rarely, blood may be present in the subhyaloid plane or in the vitreous. Roth spots may be seen. The white centers in Roth spots can be due to inflammatory infiltrates, fibrin and platelets, neoplastic cells, or focal areas of ischemia.
Cotton wool spots: Retinal nerve fiber layer infarction due to retinal hypoxia in anemia causes these superficial fluffy white lesions.

Retinal edema: The microtrauma of the vessel wall secondary to raised transmural pressure leads to leakage. This in turn leads to retinal edema.

Hard exudates: These may be seen due to resolved retinal edema. When these are severe and located at the macula, macular star is seen.

Vessel changes: Arteries are attenuated and pale, and veins are dilated and tortuous. These findings are seen more as the severity of anemia increases.

Optic nerve changes: Edema or, in later stages of optic neuropathy, optic disc pallor is seen.7

Retinal changes seen in special situations include the following:

Iron deficiency anemia: Besides the routine changes, other described findings include central retinal vein occlusion, retinal artery occlusion, disc edema, and anterior ischemic optic neuropathy.8,9

Vitamin B12 deficiency anemia: This condition causes optic neuropathy, which is evident as disc pallor.7

Sickle cell anemia: Proliferative changes are seen in the retina secondary to vaso-occlusion, which can lead to vitreous hemorrhage and retinal detachment. Choroidal infarcts can occur due to the sickling of red blood cells. It is interesting to note that conjunctival sickling sign and areas of iris atrophy and neovascularization occur in this disease.10

Myeloproliferative disorders: Roth spots, leukemic infiltrates in the retina, choroidal infiltration with secondary serous
in the left eye (OS). Anterior segment evaluation revealed conjunctival pallor. Fundus examination revealed thickening of the macula OD compared with OS (Figure 1). OCT documented a slight increase in macular thickness OD (Figure 2). One systemic investigation, it was found that her Hb level was 5.6 gm/dL and serum ferritin was 20 µg/dL.

The patient was diagnosed with iron deficiency anemia. She was started on nutritional supplements under supervision of a physician. At a follow-up visit 2 months later, her BCVA had improved to 6/6 OD. A reduction in central foveal thickness was seen on OCT. This case highlights the importance of the eye as a window to the body.

**Case No. 2**

A 54-year-old woman presented reporting diminution of vision OD for the past 2 months. Her BCVA was 6/24 OD and 6/9 OS. On examination, she had disc edema with hemorrhages and cotton wool spots OD. The fundus OS showed multiple cotton wool spots (Figure 3). Bulbar conjunctiva demonstrated significant pallor. On systemic investigation, she was noted to have significantly reduced Hb levels (5 gm/dL). Her serum ferritin level was 67.7 µg/dL. The physician advised peripheral blood smear, which revealed *Plasmodium falciparum*.

She was treated for the same by an internist. One year later, her Hb level had increased to 10.6 gm/dL, her BCVA improved to 6/9 OD, and the disc edema and cotton wool spots had resolved.

**INVESTIGATIONS AND TREATMENT**

Ocular investigations are indicated only if treatment is being planned. Fluorescein angiography may demonstrate a delay in the arteriovenous transit time in cases of venous occlusion. Optical coherence tomography (OCT) is useful in cases of vascular occlusion to demonstrate macular edema. Retinopathy in anemia can also be seen in oncology patients and in those with infective endocarditis or autoimmune diseases. Hence, blood investigations should include peripheral blood smear examination in addition to complete blood work. Bone marrow biopsy may be indicated in some cases.

In most cases, only treatment of the underlying etiology is needed, and retinopathy generally resolves on its own. In cases of vascular occlusion, macular edema may have to be treated. Nd:YAG laser hyaloidotomy may be indicated in cases of subhyaloid hemorrhage.

**CLINICAL EXAMPLES**

Below are two patient cases that show how different etiologies can affect the clinical findings in anemia.

**Case No. 1**

A 40-year-old woman reported diminished vision in her right eye (OD) for 1 day. Her BCVA was 6/36 OD and 6/6 retinal detachment, microaneurysms, and vascular sheathing may be seen. Thalassemia: Retinal pigment epithelial changes are seen. Malaria: Anemia and raised intracranial pressure due to cerebral malaria can cause retinal changes and disc edema.

**Figure 3. Case No. 2: Right eye color fundus photo shows disc edema with cotton wool spots (A). Left eye color fundus photo shows cotton wool spots (B), which resolved after therapy. Right (C) and left (D) eyes on follow-up.**


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