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OCULAR MANIFESTATIONS OF APLASTIC ANEMIA : RARE CASE OF ANEMIC RETINOPATHY

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Abstract

Incidence of aplastic anemia was 1-2 cases per million population per years, and showed higher rate in Asia and 10-25 years old. Anemic retinopathy can occur in 28% of patient with severe anemia, especially if accompanied by thrombocytopenia. Most cases were asymptomatic, however decrease visual acuity were also commonly found caused by haemorrhage and Macular edema.

A 65 years old female patient came with blurry vision ten days prior admission accompanied with somnolent, recurrent bleeding from nose, gum, and bluish discoloration in her extremities four years ago. Visual acuity was 1/60 on the right eye and 0.4 log on the left eye. Funduscopic examination showed vitreous haemorrhage, dot blot, hard exudate, and tortuosity of vein. Laboratory Examination showed anemia and thrombocytopenia, and peripheral blood morphology showed normochromic anisopoikilocytosis caused by chronic disease. She was scheduled to underwent anti VEGF and showed improvement in her visual acuity after injection. Fundoscopic examination later shows sub-hyaloid haemorrhage, dot blot, hard exudate, and tortuosity of vein. She was scheduled to undergo pars plana vitrectomy and were consulted to internal medicine.

Aplastic anemia is a rare disease that usually asymptomatic, thus causing late intervention and a high mortality rate. Early manifestation can be seen in retinal structure as anemic retinopathy thus ophthalmologist have valuable impact in early detection of this disease. Haemorrhage overlying the macula and macular edema is the most common cause of visual impairment. Anti VEGF treatment, transfusion of blood component, and immunosuppressive therapy is needed to prevent complication and increase patient survival rate. Patient visual acuity usually imporved after early transfusion and anti VEGF injection, however delayed intervention may cause irreversible vision loss.

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INTRODUCTION

Aplastic Anemia is a rare and life-threatening disorder that caused by depleted stem cells in bone marrow. Incidence of aplastic anemia was 1-2 cases per million population per years, and showed higher rate in Asia and 10-25 years old. Gold standard therapy were hematopoietic stem cell transplant and immunosuppressive treatment. Transplant were considered more in children or when immunosuppressive therapy has failed.

Anemic retinopathy can occur in 28% of patient with severe anemia, especially if accompanied by thrombocytopenia. The risk will increase proportionally with the severity of anemia. Most cases were asymptomatic, however decrease visual acuity were also commonly found. Pathophysiology is related to hypoxia that occurs in the retina. Clnical manifestation can occur acute or chronic. Clinical manifestation are varied, however most of the case will present with haemorrhage, vascular vasodilatation, and cotton woll spot. (1,2)

Management of anemic retinopathy includes systemic and ocular management. Systemic management includes finding and treating the etiology of anemia. Ocular management can be done with intravitreal injection of anti VEGF or vitrectomy.(1,2) The purpose of these case report is to present a case and prognosis of patient with Anemic Retinopathy.

CASE PRESENTATION

A 65 years old female patient, came to Vitreoretina department of the National Eye Center, Cicendo Eye Hospital with blurry vision on her right eye ten days ago accompanied by redness in both of her eyes. There was no pain, secretes, or loss of visual field in the eye. There was no dyspnea, headache, nausea, and vomiting. She complains history of somnolence, recurrent bleeding from nose, gum, and bluish discoloration in her leg and arm four years ago. She underwent four times of blood transfusion since the last ten years. She denied any history of trauma, operation, long term medication, hypertension and diabetes mellitus.

Figure 1. General Examination (A) Arm (B) Leg

Physical examination of the patients shows bluish discoloration in her arm and legs. Visual acuity was 1/60 on the right eye and 0.5 log on the left eye. Intraocular pressure in the right eye is 16 mmHg and the left eye is 14 mmHg. Ishihara examination was within normal limit. Patients was orthotropic with good eye movement in all directions. Examination of the anterior segment of the both eye revealed subconjunctival haemorrhage.

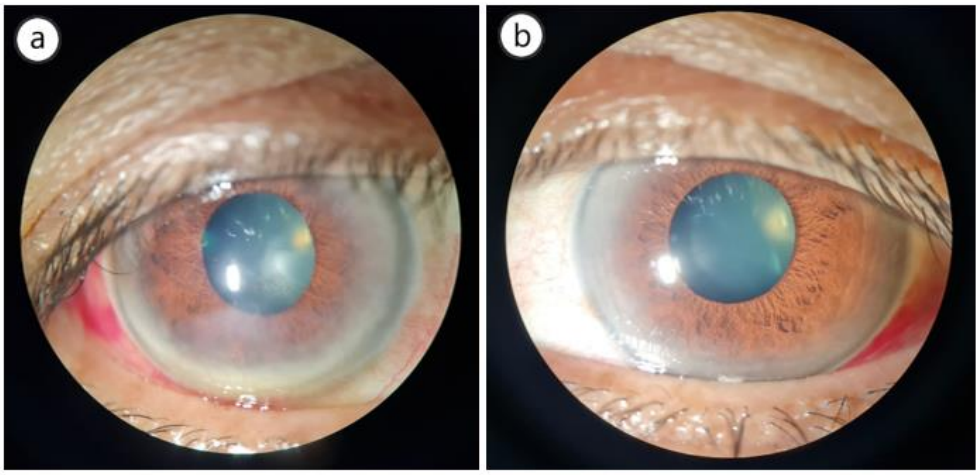

Figure 2. Ophthalmologic Examination (A) Right Eye (B) Left Eye

The pupils round with normal direct and indirect light reflexes. On fundoscopic examination of the right eye, there were vitreous haemorrhage, dot blot, hard exudate, arteriolar attenuation, and tortuosity of vein. Funduscopic examination of the left eye shows dot blot, hard exudate, arteriolar attenuation and tortuosity of vein.

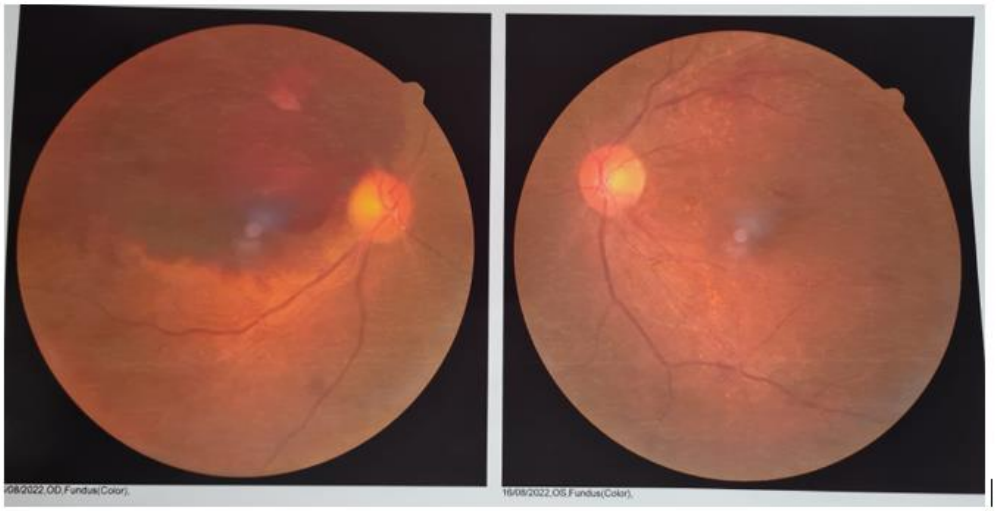

Figure 3. Fundus Photo Examination

Patients underwent OCT Macular and OCT-A. OCT Macula on the right eye showed hyper-reflective lesion in pre retina and inner retina causing shadowing effect on the outer side of retina. OCT Macula on the left eye showed thinning of the central foveal thickness. OCT-A of the right eye showed shadowing artifact caused by overlying vitreous haemorrhage.

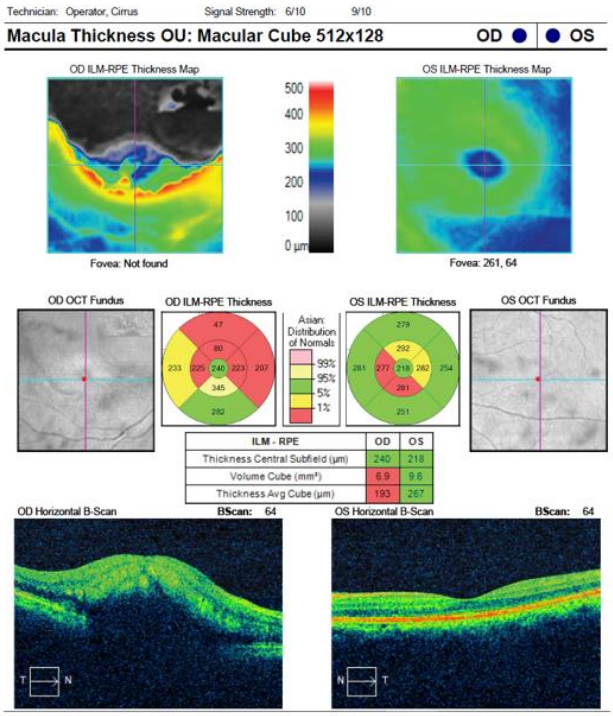

Figure 4. Macular OCT Examination

Laboratory Examination showed normal blood glucose (122 mg/dL), normal leukocyte (5.430/mm^3), severe anemia (Hb 5.8 g/dL) with severe thrombocytopenia (0/mm^3) and peripheral blood morphology showed normochromic anisopoikilositosis caused by chronic disease. Patient was diagnosed with anemic retinopathy and subconjunctival bleeding of both eyes, vitreous haemorrhage of the right eye, and bisitopenia. The patient was scheduled to underwent anti VEGF therapy and were consulted to internal medicine. Patient underwent infusion of six packs red blood cells and four packs of thrombocyte.

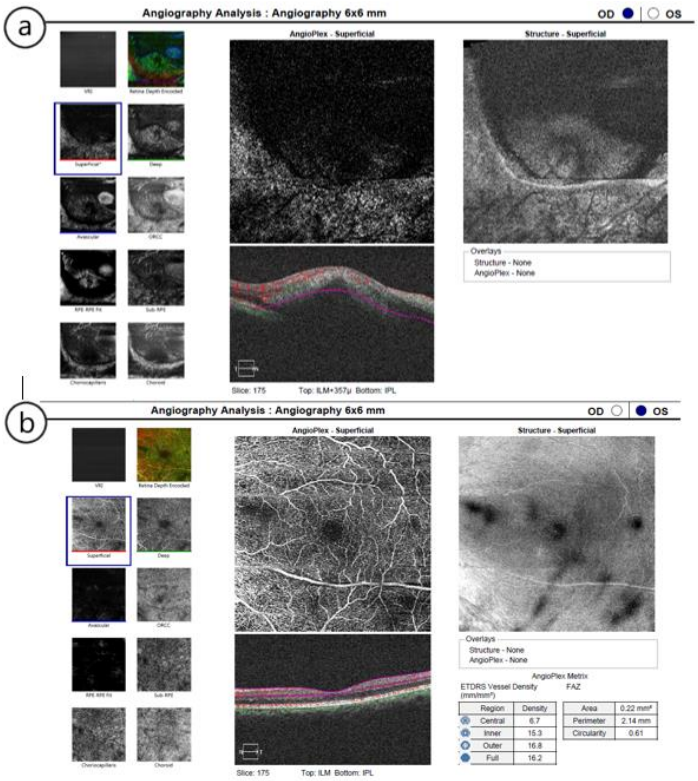

Figure 5. OCT-A Examination (A) Right Eye (B) Left Eye

One week after injection her complains improved. There were reduce redness in both her eyes and bluish discoloration of her arm and legs. She has completed bone marrow examination and showed peripheral pancytopenia caused by aplastic anemia. She was scheduled to underwent bone marrow biopsy to further investigate the cause of aplastic anemia.

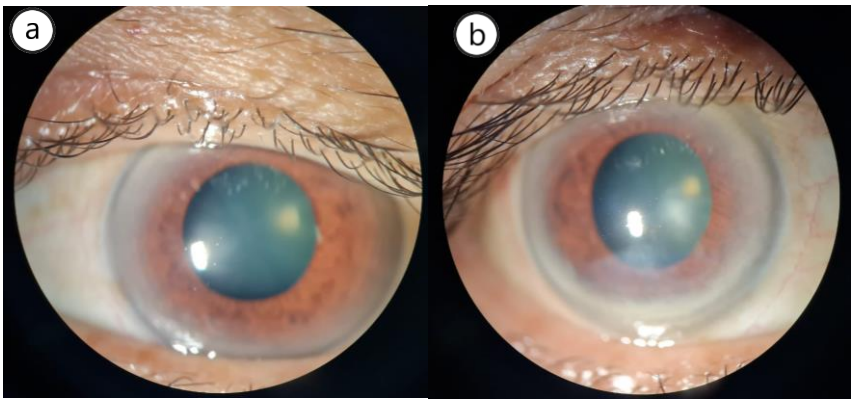

Figure 6. Ophthalmologic Examination (A) Right Eye (B) Left Eye

Visual acuity was 1/60 on the right eye and 0.4 log on the left eye. Intraocular pressure in the right eye is 18 mmHg and the left eye is 16 mmHg. Examination of the anterior segment of the both eye revealed normal conjunctiva without subconjunctival haemorrhage. On fundoscopic examination of the right eye, the vitreous haemorrhage has resolved, however there were sub-hyaloid haemorrhage, dot blot, hard exudate, and tortuosity of vein. Funduscopic examination of the left eye shows dot blot, hard exudate, and tortuosity of vein.

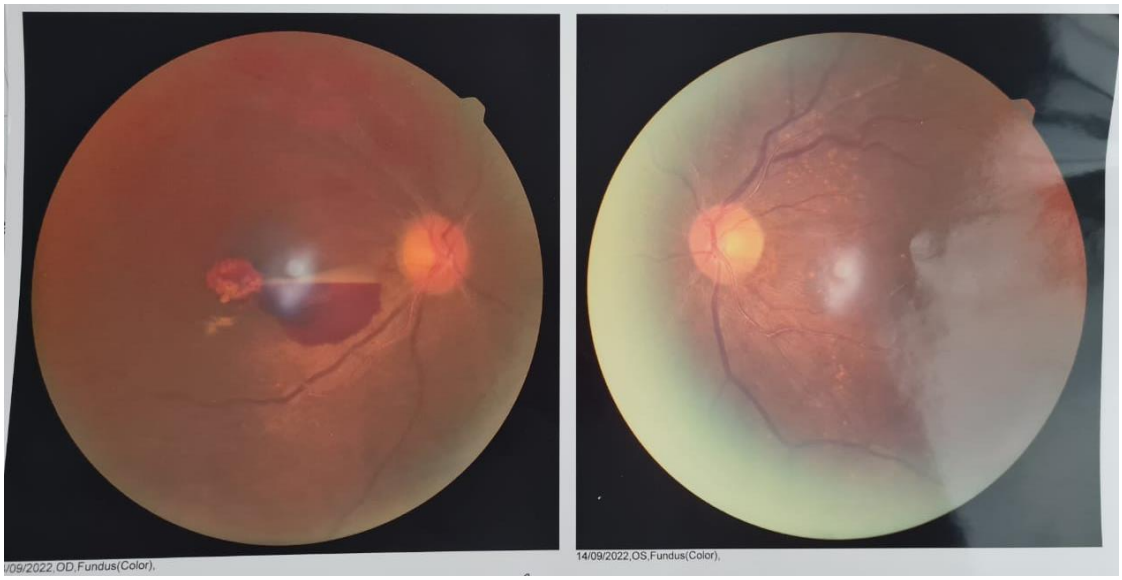

Figure 7. Fundus Photo Examination

Patients underwent OCT Macular and OCT-A. OCT Macula on the right eye showed hyper-reflective lesion in pre retina and inner retina causing shadowing on the outer side of retina. OCT Macula on the left eye showed thinning of the central foveal thickness. OCT-A of the right eyes showed ischemic area in parafovea.

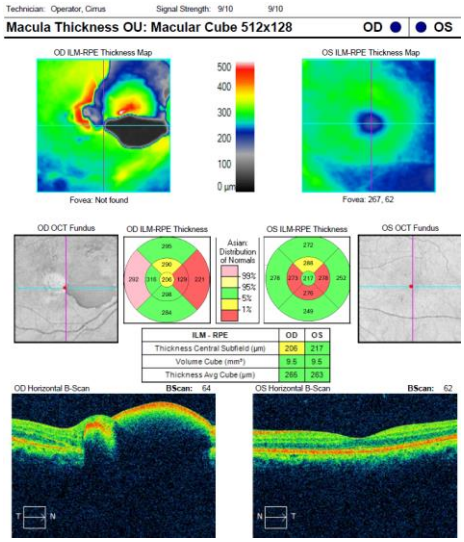

Figure 8. Macular OCT Examination

Laboratory Examination showed improvement in anemia (Hb 12.1 g/dL), leukocytopenia (1.240/mm^3) and thrombocytopenia (22.000/mm^3). Hemostasis results showed normal coagulation time. Patient was diagnosed with anemic retinopathy, sub-hyaloid haemorrhage of the right eye, and pancytopenia caused by aplastic anemia. The patient was scheduled to undergo pars plana vitrectomy and internal limiting membrane peeling to remove the chronic sub-hyaloid haemorrhage.

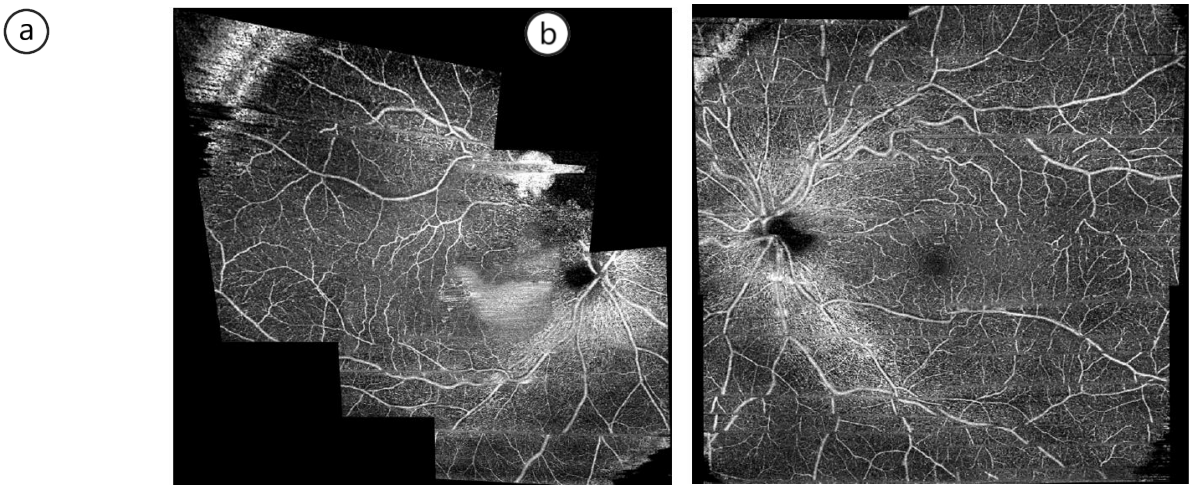

Figure 9. OCT-A Examination (A) Right Eye (B) Left Eye

DISCUSSION

Aplastic Anemia is a rare and life-threatening disorder that caused by depleted stem cells in bone marrow. Incidence of aplastic anemia was 1-2 cases per million population per years, and showed higher rate in Asia and 10-25 years old. The pathogenesis can be caused by three main mechanism that is genetic depletion of stem cell, suppression of lymphocyte, and cytokine overexpression. Classification of aplastic anemia according to Camitta criteria categorized aplastic anemia as severe, very severe, and moderate aplastic anemia. Severe aplastic anemia defines as bone marrow cellularity less than 30% and severe pancytopenia with at least 2 of the following peripheral blood count criteria such as absolute neutrophil count $<0.5\times10^9$/L; platelet count $<20\times10^9$/L; and corrected reticulocyte count <1%.

Very severe aplastic anemia if the neutrophil was less than 0.2 x 10^9, and moderate aplastic anemia defines if not meeting the definition of former two. In this study, she was diagnosed as severe aplastic anemia based on bone marrow examination. (3,4)(5)

Patients with moderate aplastic anemia usually managed by observation only, however patients with severe or very severe aplastic anemia must undergo aggressive therapy. Patients with anemia and thrombocytopenia must undergo red blood cell and thrombocyte transfusion. Gold standard therapy were hematopoietic stem cell transplant and immunosuppressive treatment. Transplant were considered more in children or when immunosuppressive therapy has failed. This patient was already being infused with red blood cell and thrombocyte infusion, however she hasn't started any immunosuppressive treatment yet. (6) (7) (4)

anemia correlates with higher risk of retinopathy. Most cases of anemic retinopathy are asymptomatic, however decrease visual acuity usually caused by haemorrhage, macular edema, or optic neuropathy. Patients complained a reduce in visual acuity in her right eye mainly caused by vitreous haemorrhage overlying her right macula, however her left eye were asymptomatic because there were no macular involvement. (1,8) (9) (10)

The clinical features of anemic retinopathy are linked to various abnormal changes within the eye that occur as a consequence of anemia. Physiologic adjustment that occurs in anemic patients are increase cardiac output, shunting of blood to vital organs, and increase 2.3 diphosphoglycerate in red blood cells which decrease oxygen affinity and increase oxygen release to tissue. Anemia will cause hypoxia in retinal structure. Hypoxia will cause

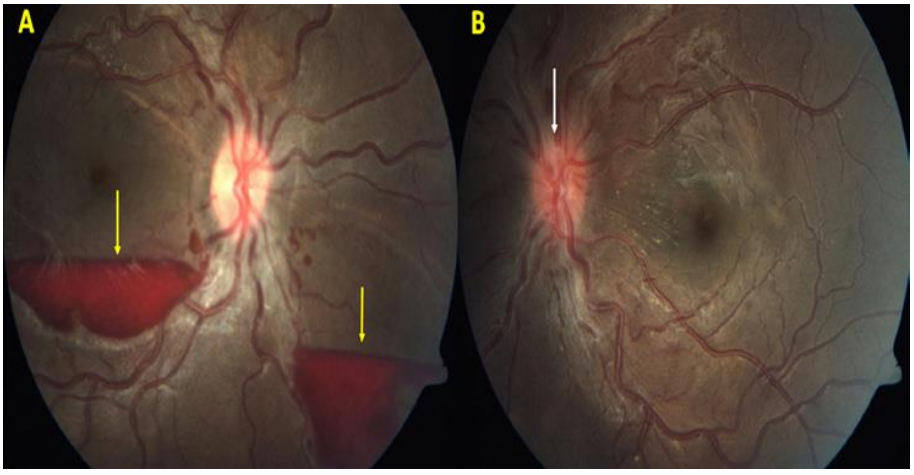

Figure 10. Sub-hyaloid Haemorrhage in Anemic Retinopathy
Cited from: Mahapatra, et al(8)

Anemic retinopathy is defined as abnormality in the retina caused by systemic anemia. It has been recommended that all patient with Hb <10mg/dL undergo fundus examination. Retinopathy occurs in 28% of patient with severe anemia (<6 mg/dl) and increased by 38% if the patients have thrombocytopenia that in turn caused defective coagulation and haemorrhage. The severity of

vascular dilatation, microtrauma of vessel walls, and increase transmural pressure which in turn cause retinal edema and haemorrhage. Retinal hypoxia also caused nerve fiber layer infarction which showed as cotton woll spot. Another mechanism that can be found are venous stasis, angiospasm, increased blood viscosity (myeloproliferative disorders), and hypotension. (2) (10)(11) (6)

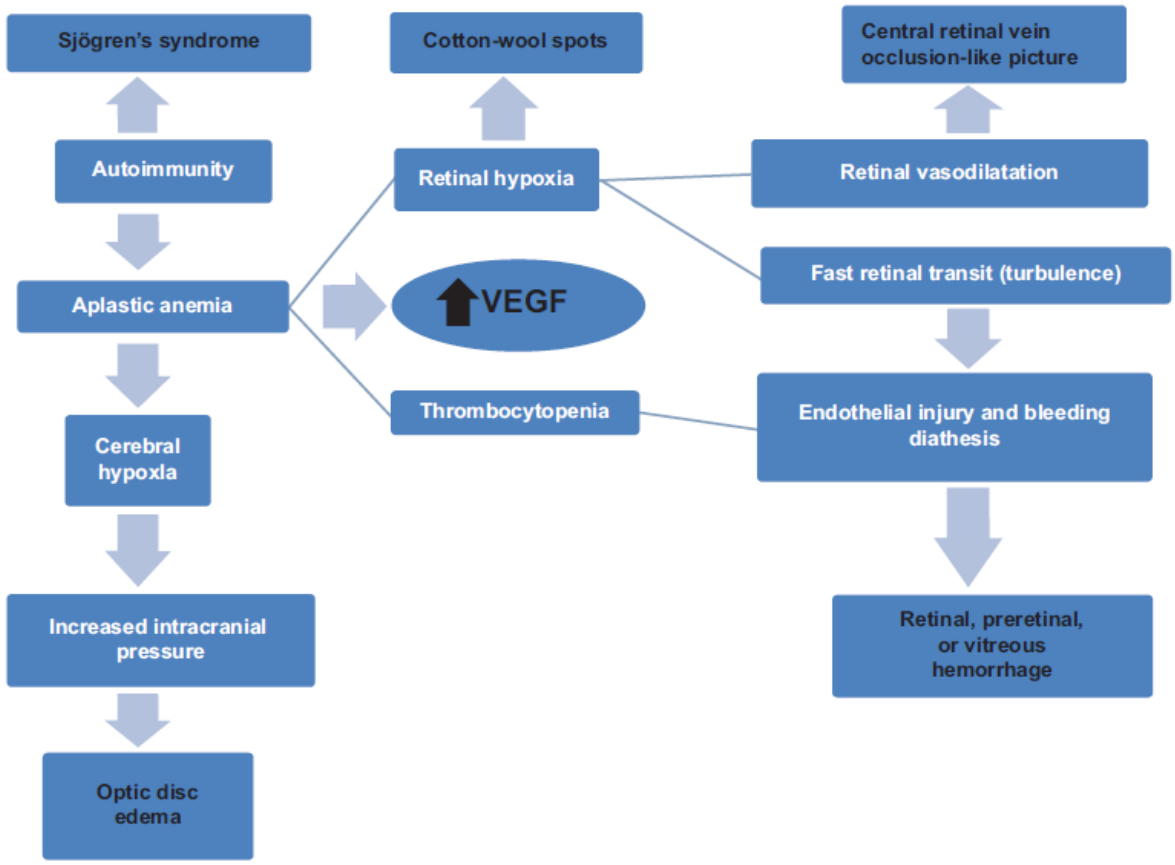

Figure 11. Pathogenesis of Anemic Retinopathy Cited from: Mansour, et al(11)

Almost all patient with anemia retinopathy shows superficial flame shaped haemorrhage, however dot blot, subhyaloid haemorrhage and roth spot also seen in several cases. Clinical manifestation of anemic retinopathy also can be classified as acute or chronic. Acute manifestation shows cotton woll spot and blurred optic disc margin that leads to non arteritic anterior ischemic optic neuropathy. Chronic manifestation includes haemorrhage, dilatation of retinal blood vessel, and hard exudate. Some study also classified the manifestation based on the etiology. Iron deficiency anemia can cause central retinal vein occlusion, disc edema, and anterior ischemic optic neuropathy; Vitamin B12 deficiency usually cause optic neuropathy and disc pallor; sickle cell anemia caused proliferative changes secondary to vaso-occlusion and manifest as vitreous haemorrhage, retinal detachment, roth spot and leukemic infiltrates; Aplastic anemia caused venous dilation and ischemic retina. In this patients, the manifestation was chronic that showed by haemorrhage, hard exudate and dilatation of retinal blood vessel.(1,2,11) (9) (10)

Additional examination such as fluorescein angiography may demonstrate a delay in arteriovenous transit time. Optical coherence tomography can be used to monitor macular edema. Management of anemic retinopathy includes systemic and ocular management. Systemic management includes finding the appropriate etiology and therapy of pancytopenia. Blood transfusion is the mainstray treatment and usually followed by visual recovery. Vitrectomy can be done in non-clearing vitreous haemorrhage. Anti VEGF intravitreal will decrease the number of VEGF that in turn prevent neovascularization in retina.

This patient underwent blood transfusion, anti VEGF injection, and was scheduled to undergo pars plana vitrectomy for the sub-hyaloid haemorrhage. Prognosis for the right eye is dubia ad malam, because of the widening of fovea avascular zone. However we still cannot investigate further due to the presence of sub-hyaloid haemorrhage overlying the macula. Left eye prognosis was also dubia ad malam caused by the presence of macular atrophy. She was scheduled to undergo fundus fluorescein angiography to further evaluate the retinal perfusion. (1,2) (10) (6)

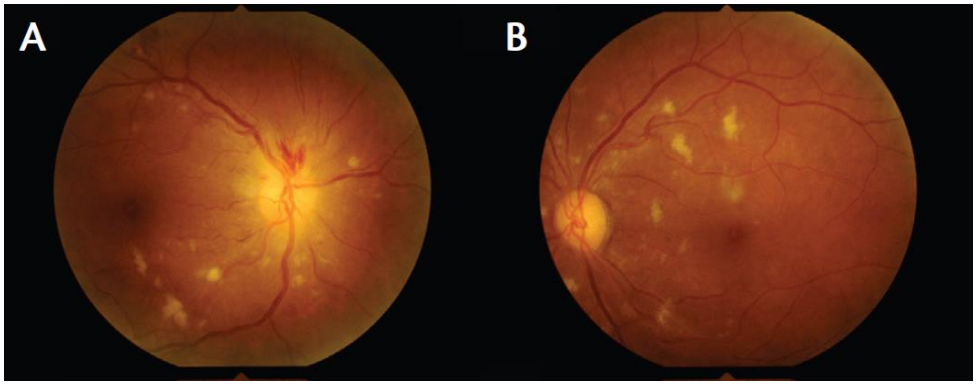

Figure 12. Anemic Retinopathy Cited from: Gaurav, et al(10)

CONCLUSION

Aplastic anemia is a rare disease that usually asymptomatic, thus causing late intervention and a high mortality rate. Early manifestation can be seen in retinal structure as anemic retinopathy, thus ophthalmologist have valuable impact in early detection of this disease. Anemia will cause hypoxia in retinal structure that in turn produce vessel dilatation, microtrauma of vessels wall, and increase anti VEGF. Clinical manifestation were mostly asymptomatic unless there were involvement of macula.

Haemorrhage overlying the macula and macular edema is the most common cause of visual impairment. Anti VEGF treatment, transfusion of blood component, and immunosuppressive therapy is needed to prevent complication and increase patient survival rate. Patients visual acuity usually improved after early transfusion and anti VEGF injection, however delayed intervention may cause irreversible vision loss.

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