Retinal Vasculitis in Patients with Positive TB Testing in Aceh (Indonesia): A Case Series

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Abstract: Retinal vasculitis is a group of diseases characterized by inflammation of the retinal blood vessels. Although many retinal vasculitis are unknown, many systemic diseases are associated with this diseases such as tuberculosis (TB), Lyme disease, syphilis, toxoplasmosis, or viral infection. Retinal vasculitis can also be part of posterior uveitis. One of the most frequent cause of retinal vasculitis is TB, which often referred to as Eales disease. This disease is very rare in developed countries and more often found in countries with poor economic levels. In Aceh (Indonesia), the disease is quite common, but it has never been reported. Several theories have been proposed to explain the etiology of this diseases. Hypersensitivity to tuberculo-protein is the most common theory reported about the possible etiology of Eales disease. It is based on the positive results of Mantoux reactions in Eales patients. However, Mantoux examination can be positive in 67-90% of healthy adults in India (and possibly other developing countries including Indonesia). The author report 3 cases of Eales diseases with recurrent vitreous hemorrhage as the first manifestation, in patients with positive TB testing in Aceh. We also provide a brief review of the literature.

1 INTRODUCTION

Retinal vasculitis is a group of diseases characterized by inflammation of the retinal blood vessels. Although many retinal vasculitis are unknown (idiopathic), many systemic diseases are associated with this diseases such as tuberculosis (TB), Lyme disease, syphilis, toxoplasmosis, or viral infection. In addition, retinal vasculitis can also be part of posterior uveitis. One of the most frequent cause of retinal vasculitis is TB, and Eales disease is a vasculitic disease of the retina that is often associated with TB.

2 CASE 1

A 40-year-old male presented to our outpatient department with blurred vision of the left eye for 1 week. He had a history of hypertension. There were no history of trauma, other systemic diseases, or long-term drug use. Visual acuity was normal on right eye and 5 CF on left eye. Ocular examination revealed normal anterior segment of both eyes with vitreous bleeding on the left eye.

We suggested the patient to have laboratory testing and chest x-ray with no initial treatment. The patient came a week later with a strong positive result of Mantoux test (induration of more than 15 mm). We thought about Eales disease, and provided oral steroid therapy as well as photocoagulation lasers. One week later, vitreous bleeding began to subside. We continued steroid treatment, and ask the patient to come within 1 month.

One month later, bleeding has reduced. Visual acuity of the both eyes were 6/6. Slit lamp bio microscopic examination with super field lens showed minimal hemorrhage and vasculitis on the peripheral retina.

Six months later, the patient came again, complaining of floaters on both eyes. Ocular examination revealed minute vitreous bleeding in the right eye. Minimal retinal hemorrhage and vasculitis were found on the peripheral retina.

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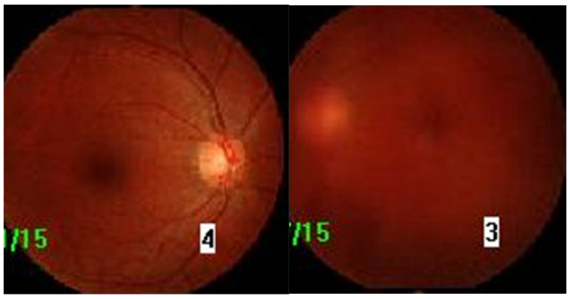

Figure 1. Vitreous hemorrhage of the left eye; right eye was within normal limit

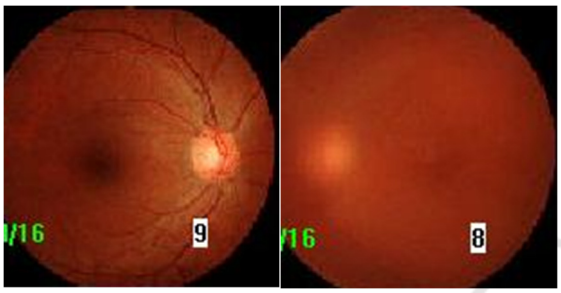

Figure 2. Vitreous hemorrhage of the left eye begins to subside

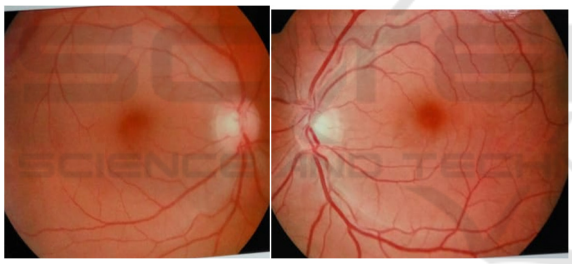

Figure 3. Minimal vitreous bleeding of the right eye six months later, the left eye was clear

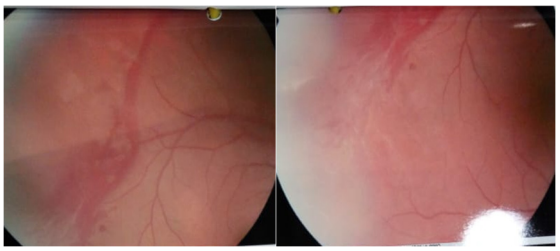

Figure 4. Retinal hemorrhage and vasculitis in far periphery of the retina detected after vitreous hemorrhage resolved

We again prescribed oral steroid therapy and planned PCR test. One week after that vision improve with minimal vitreous hemorrhage. We referred the patient to Jakarta for diagnosis confirmation and PCR test. The patient returned 3 weeks later with 6/6 visual acuity on both eyes. Vitreous was clear with retinal hemorrhage. PCR results for TB was negative and OCT examination revealed normal foveal contour of the both eyes. We suggested bimonthly examination to the patient. Two months later the patient came with vitreous hemorrhage on the left eye. We decided to observe him for 1 one month before prescribing anti-tuberculosis drug. The condition improved on the following 6 months with minimal complaint for floaters.

3 CASE 2

A 19-year-old male patient came with complaint of recurrent blurred vision of the right eye about 1 month earlier. No history of trauma and other systemic disease. The patient noted that condition always improved without medications. Ophthalmological examination revealed visual acuity of hand motion on the right eye and 6/6 on the left eye. Anterior segment of both eyes was within normal limits. We found severe vitreous hemorrhage of the right eye. Ultrasound examination showed no retinal detachment.

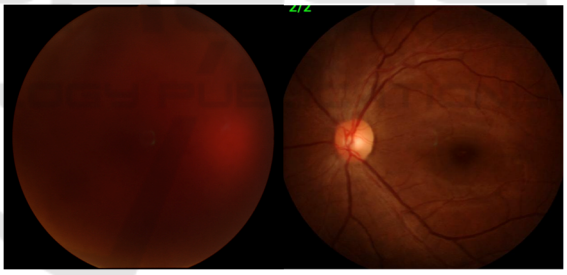

Figure 5. Dense vitreous hemorrhage in the right eye

We performed radiological and laboratory tests available at our hospital, provided anti thrombolytic, and advised him to rest in semi-fowler position. One week later the patient came with normal laboratory results and chest x-rays, except for positive Mantoux test with induration of more than 15 mm. Vitreous bleeding remains the same, there was no significant increase in vision. We diagnosed the patient with Eales' disease and prescribed prednisone 1 mg / BW with 10 mg tapering off weekly. After 1 month observation, there was no improvement. The patient was referred to undergo vitrectomy surgery. He returned two months later with clear vitreous, attached retina with giant vessels, minimal retinal hemorrhage, and laser scars on peripheral retina.

The patient returned two years later with the same complaint but on the left eye. Visual acuity was hand movement with dense vitreous hemorrhage found on the left eye. We proposed diagnostic workup that he eventually refused because he preferred to consult overseas.

4 CASE 3

A 38-year-old man presented with 1 week of blurred vision of the left eye. Initially he saw black spots. He reported no pain, redness, and lacrimation. There is no history of trauma and other systemic diseases. The patient had a history of gradually blurred vision and metamorphopsia of his other eye about one year earlier. He was diagnosed with Branch Retinal Vein Occlusion (BRVO) of the right eye and received intravitreal anti-Vascular Endothelial Growth Factor (VEGF) injection twice. He did not undergo any laboratory test at that time. As the complaint improves, the patient never regains control to the ophthalmologist until symptoms appear in the left eye.

Visual acuity at the time of examination was 6/6 on the right eye and 6/20 on the left eye. Anterior segments were within normal limits. There were minimal vitreous hemorrhages, retinal hemorrhage in the supero-temporal quadrant accompanied by cotton wool spots.

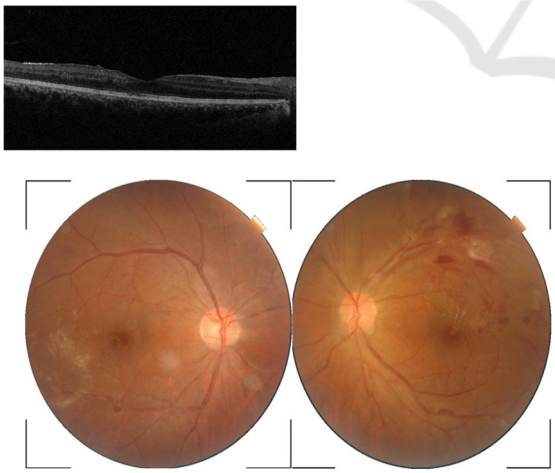

Figure 6. Retinal hemorrhage, sheating, and cotton wool spot in the supero-temporal left eye

OCT examination showed normal foveal contour of the right eye, and minimal sub retinal fluid and exudate on the left eye.

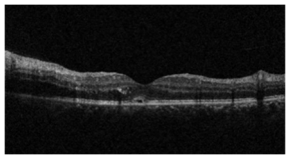

Figure 7. OCT examination of the right and left eye

The patient underwent laboratory tests and chest x-ray, and all the results were negative. Mantoux test could not be done due to technical problems in our Hospital. We performed sub tenon injection of triamcinolone acetonide, systemic metylprednisolone, and laser photocoagulation on the left eye. The condition improved but rebleeding occurred after 1 month, so did the complaint for black spots. Due to the recurrence, we referred the patient to a pulmonary specialist to determine the possibility of latent tuberculosis infection. They performed IFN-Gamma Release Assay (IGRA) examination, and revealed a positive result for tuberculosis.

5 DISCUSSION

Retinal vasculitis is a group of diseases characterized by inflammation of the retinal blood vessels. Consensus of the Standardization of Uveitis Working Group in November 2004 described retinal vasculitis as an inflammation and changes in retinal blood vessels, including perivascular sheathing, vascular leakage , or occlusion (Mir et al., 2017; Ku et al., 2012).

Although many retinal vasculitis are unknown (idiopathic), many systemic diseases are associated with this diseases such as tuberculosis, Lyme disease, syphilis, toxoplasmosis, or viral infection (Ku et al., 2012; Mesquida et al., 2017; Sharief et al., 2017). Retinal vasculitis can also be associated with other diseases like Behcet, sarcoidosis, multiple sclerosis, collagen-vascular disease, and sympathetic ophthalmia. In addition, retinal vasculitis can also be part of posterior uveitis (Pelegrin et al., 2017; Do et al., 2016).

Retinal vasculitis associated with tuberculosis is Eales diseases. It is a primary idiopathic occlusive vasculopathy, characterized by venous inflammation (vasculitis), occlusion, and retinal neovascularization that usually involves the peripheral retina. In the early stages, Eales disease often has no symptoms. Some patients may experience black spots on the eyes (floaters) 75%, or blurred vision due to vitreous bleeding (60%). Eales disease is very rare in developed countries and more

often found in countries with poor economic levels. India is one of the countries that quite often reported the case. They found that 1 of 200-250 eye diseases patients suffering from Eales. The number is also significant in Aceh (Indonesia), but has never been thoroughly reported (American, 2014; Das et al., 1994; Dalvin & Smith, 2017; Patnaik, et al., 1998).

In this paper, the first and second patients come with the main complaints of floaters, and blurred vision caused by vitreous hemorrhage. While the third patient came with metamorphopsia associated with macular edema caused by Branch Retinal Vein Occlusion (BRVO). BRVO in this case can occur because of the inflammation (retinal phlebitis), which is the underlying disorder of the disease. The inflammatory cells found in the branches of central retinal vein cause blockage of the blood vessels, resulting in the occurrence of BRVO. Sometimes inflammation occurs in the central retinal vein causing the occurrence of Central Retinal Vein Occlusion (CRVO) (Patnaik et al., 1998).

Etiopathogenesis of Eales disease remains controversial. Wardsworth described Eales disease as a primary vasculitis with an unknown etiology in young adults. Retinal vasculitis and peripheral retinal revascularization associated with various systemic and ocular diseases may resemble Eales disease in the inflammatory and proliferative phases.[12] Our three patients have no symptoms of tuberculosis infection seen from chest x-ray examination. However, Mantoux tests were strongly positive (induration more than 15 mm) in the first and second patients. This test is one of the major tuberculin skin tests used around the world and widely used in patients with Eales disease. Mantoux-positive rate has been reported in 42-98% of Eales disease. However, Mantoux examination can be positive in 67-90% of healthy adults in India (and possibly other developing countries including Indonesia). Therefore, the role of this examination in Eales disease still a questioned, in addition this disease has also been reported in patients with Mantoux negative (Patnaik et al., 1998; Biswas & Verma, 2007; Biswas et al., 2002; Talat et al., 2014; Murugeswari et al., 2014). In our first and second cases, the Mantoux examination results were strongly positive with induration of more than 15 mm. The third patient underwent IGRA due to technical problem in performing Mantoux test in our hospital and all hospitals in Aceh at the time. This examination is considered to have better specificity than tuberculin skin test (Banaei et al., 2016; Katyal et al., 2018). So far, we have not found a literature report about IGRA on Eales disease. In our case this test helped us establish the diagnosis. Utilization of IGRA is therefore an interesting idea.

The three major signs of Eales disease are inflammation characterized by periphlebitis or vasculitis in the periphery retina, ischemia caused by blood vessel blockage, and retinal neovascularization (in optic disc or retina) which responsible for recurrent vitreous haemorrhage (Das et al., 2010; Gadkari, 2007). In the first patient we found vitreous bleeding and signs of inflammation in the peripheral retina. Although bleeding and inflammation are not severe, an excellent response to corticosteroids coupled with strong positive Mantoux results helped us to guide the diagnosis. In the second patient, the retina couldn't be evaluated more detail due to dense vitreous hemorrhage. It is unfortunate that so difficult for us to follow up the course of the disease because the patient has undergone vitrectomy abroad, and not so good record system in our hospital at that time. The diagnosis of Eales became doubtful because there was no confirmation of the inflammatory process in the peripheral retina, until the patient came again about 1 year later and there was a severe vitreous bleeding occurred in the other eye. Male with productive age, recurrent vitreous hemorrhage, and strong positive results of Mantoux test guide us to make the most possible diagnosis of the patient. The third patient presented with symptoms characteristic with inflammation of the peripheral retina, accompanied by complications of BRVO in both eyes that do not occur simultaneously. Positive lab testing is only IGRA tests and a slight increase in total cholesterol and LDL, as well as decreased HDL. The literature suggests that young adult males with BRVO or CRVO who do not have hypertension and diabetes, and who have no signs of arteriosclerosis, and indicate the presence of phlebitis can be diagnosed as Eales. Response to oral corticosteroids helps us to confirm the diagnosis.

With all the limited facilities, we have, the first and third patients can still be well managed. The disease records describe that the retina and vision is still stable with corticosteroid and laser therapy in the first patient, as well as corticosteroids and intravitreal anti-VEGF injection in the third patient. The second patient had to undergo overseas vitrectomy surgery due to severe vitreous hemorrhage. The absence of vitrectomy machine in our province at that time made it difficult for us to manage it here. We recognize that the financial problems facing our country, especially in the province of Aceh, causes difficulties and sometimes lead to a bit of frustration in terms of diagnosing and

managing. So, it is our responsibility as an ophthalmologist, and also local governments to continuously strive to improve the facilities and human resources in our province, in order to perform good management for our patients later.

REFERENCES

American Academy of Ophthalmology staff., (2014-2015). Other Retinal Vascular Diseases. In: American Academy of Ophthalmology staff, ed. *Retina and Vitreous. Basic and Clinical Science Course. Sec 12.* Sanfransisco: American Academy of Ophthalmology. pp. 113-55

Banaei, N., Gaur, RL., Pai, M., (2016). Interferon Gamma Release Assays for Latent Tuberculosis: What are the Sources of Variability? *Journal of Clinical Microbiology.* **54**, 845-850.

Biswas, J., Sharma, T., Gopal, L., Madhavan, HN., Sulochana, KN., Ramakrishnan, S., (2002). Eales disease—an update. *Survey of ophthalmology.* **47**(3), 197-214.

Biswas, J., Verma, A., (2007). An Update on Eales' Disease. *Kerala Journal of Ophthalmology*. **19**, 300-307

Dalvin, LA., Smith, WM., (2017). Intraocular manifestations of mycobacterium tuberculosis: A review of the literature. *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*. **7,** 13-21.

Das, T., Biswas, J., Kumar, A., Nagpal, PN., Namperumalsamy, P., Patnaik, B., Tewari, HK., (1994) Eales' disease. *Indian J Ophthalmol*. **43,** 3-18.

Das, T., Pathengay, A., Hussain, N., Biswas, J., (2010). Eales' disease: diagnosis and management. *Eye.* **24** (3), 472.

Do, BK., Giovinazzo, J., (2016). Retinal Vasculitis. *Adv Ophthalmol Optom*.**1**(1), 69–84.

Gadkari, S., (2007) Inflamatory vascular disease. Eales' disease. In: Joussen, AM., Gardner, TW., Kirchhof, B., Ryan, SJ, ed. *Retina Vascular Disease*. Berlin: Springer.p.613-627

Katyal, M., Leibowitz, R., Venters, H., (2018). IGRA-Based Screening for Latent Tuberculosis Infection in Persons Newly Incarcerated in New York City Jails. *Journal of Correctional Health Care.* **24**(2),156-170.

Ku, JH., Ali, A., Suhler, EB., Choi, D., Rosenbaum, JT., (2012). Characteristics and visual outcome of patients with retinal vasculitis. *Arch Ophthalmol.* **130**(10),1261–1266.

Mesquida, M., Llorens, V., Adán, A., (2017). New imaging techniques in retinal vasculitis. *Med Clin (Barc)* **149**(6), 261–6.

Mir,TA., Reddy, AK., Burkholder, BM., Walsh, J., Shifera, AS., Khan, IR., Thorne, JE., (2017). Clinical Features and Incidence Rates of Ocular Complications in Patients With Retinal Vasculitis. *Am J Ophthalmol* **179**,171–178.

Murugeswari, P., Shukla, D., Kim, R., Namperumalsamy, P., Stitt, AW., Muthukkaruppan, V., (2014). Angiogenis Potential of Vitreous from Proiferative Diabetic Retinopathy and Eales' Disease Patients. *PloS ONE.* **9**(10), 1-8.

Patnaik, B., Nagpal, PN., Namperumalsamy, P., Kalsi, R., (1998). Eales disease: clinical features, pathophysiology, etiopathogenesis. *Ophthalmology Clinics.* **11**(4), 601-617.

Pelegrin, L., Hernández-Rodríguez, J., Espinosa, G., Llorenç, V., Sainz-de-la-Maza, M., Fontenla, JR., (2017). Characterization of isolated retinal vasculitis. Analysis of a cohort from a single center and literature review. *Autoimmun Rev*. **16**(3), 237–243.

Sharief, L., Lightman, SUE., Blum-hareuveni, T., Bar, A., Tomkins-netzer, O., (2017). Clinical Outcome of Retinal Vasculitis and Predictors for Prognosis of Ischemic Retinal Vasculitis. *Am J Ophthalmol* **177,** 206–212.

Talat, L., Lightman, S., Tomkins-Netzer, O., (2014). Ischemic Retinal Vasculitis and its Management. *Journal of Ophthalmology.* **7**, 1-13