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NEURORETINITIS ASSOCIATED WITH POST-RUBELLA INFECTION IN ADULT PATIENT

Ni Putu Ayu Reza Dhiyantari, Lukisiari Agustini, Gatot Suhartono
Department of Ophthalmology, Faculty of Medicine Universitas Airlangga, Dr. Soetomo Hospital Surabaya
**Correspondence: Lukisiari Agustini, lukisiari.agustini@fk.unair.ac.id*

ABSTRACT
Background: Neuroretinitis is an inflammatory disorder characterized by acute loss of vision associated with optic nerve head edema and a star pattern macular exudate. Flu-like illness supports viral etiology. This case demonstrates a rarely described Rubella-associated Neuroretinitis.
Case Presentation: A 39 years old woman presented with classic symptoms of a sudden painless visual loss of the right eye with visual acuity of 1/60, bilateral optic nerve head edema, and right eye macular star exudates, preceded by a history of fever and pink eye brought to the suspicion of an inflammatory post-infection neuroretinitis. There was a local macular exudative retinal detachment and central scotoma at the right eye. Serology examinations revealed IgM and IgG Rubella of 0.54 and IgG Rubella of 17.89. The patient was treated with oral Methylprednisolone 2x32 mg for 4 weeks and then tapered off. Significant improvement in visual acuity, color vision, and visual field defect was observed during the eight-week follow-up. The final visual acuity of the right eye was 5/6,5. Basal IgG Rubella value at 10 weeks follow-up was 4.27 IU/ml.
Conclusion: Acquired rubella infection may manifest as ocular pathology. A better understanding of its natural history may aid in establishing the diagnosis and promptly treating the ocular complication, especially neuroretinitis.
Keywords: *Adult Rubella Infection, Neuroretinitis, Rubella.*

BACKGROUND

Neuroretinitis is an inflammatory disorder characterized by acute loss of vision associated with optic nerve head edema and a star pattern macular exudate. The characteristic star pattern exudation on the macula is formed by penetration of lipid-rich component of the exudate into the outer plexiform layer. The exact origin of the inflammation of the optic disc vasculature is unclear.[1] Viral etiology suggested by the common prodromal flu like symptoms present in most of the patients. Neuroretinitis is usually an infectious or post-viral autoimmune process. The most common cause of neuroretinitis is *Bartonella henselae.* Viral infections such as measles, mumps, rubella, varicella, Epstein-Barr Virus (EBV), influenza A, Herpes zoster and simplex infections, and Cytomegalovirus (CMV) are also important causes.[2]

Rubella is a viral illness that can lead to complications and death. Rubella infection characterized by a mild, maculopapular rash that erupts along with enlargement of lymph node and mild fever. The rash usually starts on the face and will becomes generalized within 24 hours. It usually last for approximately 3 days. It only occurs in 50%-80% of infected people, about 25% to 50% of infections are asymptomatic.[3] Clinical diagnosis of rubella virus is unreliable as the consequences of subclinical or unapparent signs and symptoms. Adult rubella infection was poorly reported in the medical literature, moreover, clinical characteristics of an adult rubella infection are not well described.

CASE PRESENTATION

A thirty-nine-year-old woman came to outpatient clinic with chief complaint of slowly progressing blurry vision on the right eye in the last 6 months. Blurring of

the right eye vision was significantly worsened 3 days before presentation. She noted mild fever and redness of the eye a week before the onset of blurry vision. There was no complaint of rash, dyspnea, cough, pain, double vision, headache, vomiting, or nausea. History of other illnesses, past medication, and previous surgery was denied.

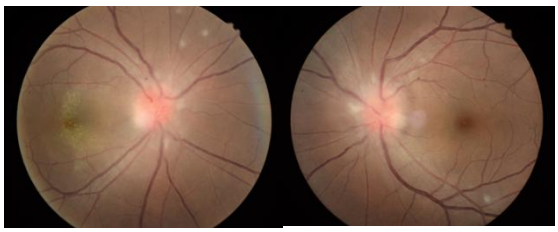

Figure 1. Fundus Photograph of the right and left eye showing swollen optic disc, with hyperemia and blurred margin. Note the star patterned exudate on the right eye macula.

Figure 2. Fundus Photograph at 8 week follow up showing resolution of the right and left edema papil. Star patterned exudates of the right eye was persisting.

There were no enlarged lymph nodes, myalgia, stiff neck, painful swallowing, or abdominal pain. Visual acuity at first visit was 1/60 for the right eye and 6/6 for the left eye. Color vision examination with Ishihara plate was 1/38 for the right eye and 38/38 for the left eye. The intraocular pressure of the right eye was 15.5 mmHg, left eye 14 mmHg. The anterior segment of the right and left eye showed rounded pupils, isochoric 3 mm diameter, normal light reflexes, and positive relative afferent pupillary defect of the right eye. Ocular motility on each eye was normal without associated pain. Posterior segment of the right and left eye revealed swollen optic disc, with hyperemia and blurred margin. There was star patterned exudate on the right eye macula (Figure.1). She complained of generalized purpuric rash over upper body and face at second follow up. She also mentioned numbness and tingling sensation that affects the right and left wrist and fingers symmetrically.

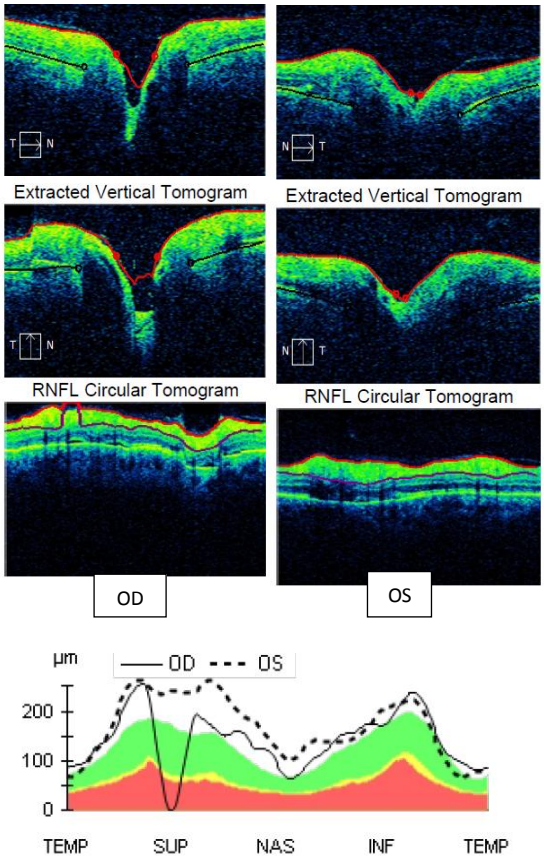

Figure 3. ONH and RNFL analysis of the right and left eye showed edema of the optic nerve head and thickening of RNFL.

Optical coherence tomography (OCT) of the optic nerve head showed an increase of RNFL thickness in both right and left eye (Figure 3). Macular OCT of the right eye taken on the first visit showing subretinal exudate causing local neurosensory retinal detachment (Figure 4). Macular OCT of the left eye was unremarkable. Humphrey Field Analyzer demonstrated bilateral enlargement of blind spot (Figure 5).

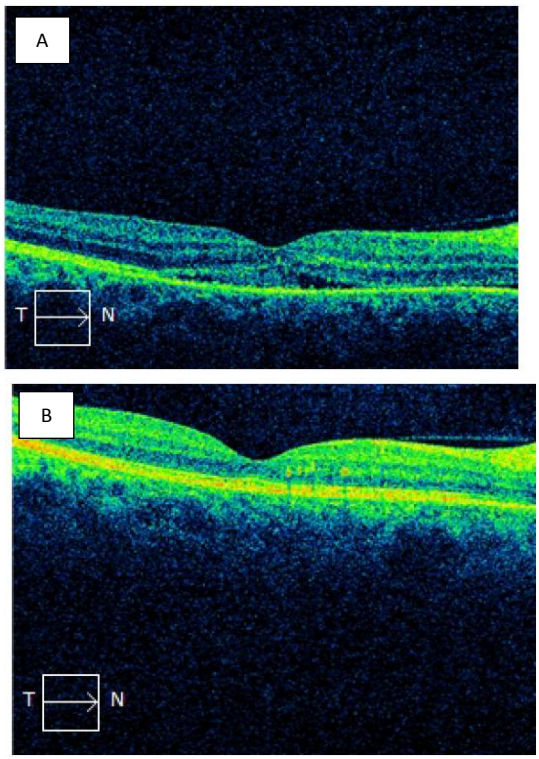

Figure 4. Macular OCT of the right eye (A) taken on the first visit showing subretinal exudate causing local neurosensory retinal detachment. (B) Macular OCT at 4th week follow up showing resolved subretinal exudate.

Laboratory investigation shows increased white blood cells (24,58 x 103), normal liver and renal function test, and normal lipid profile. The post-infection inflammatory process was suspected, therefore TORCH immunoserology was performed. Rubella IgG came out strongly positive (17.98) and Rubella IgM was 0.541. IgG and IgM for Toxoplasma were non-reactive (1.2 and 1.14 respectively) as well as anti-Cytomegalo virus IgG and IgM (0.34 and 4,00).

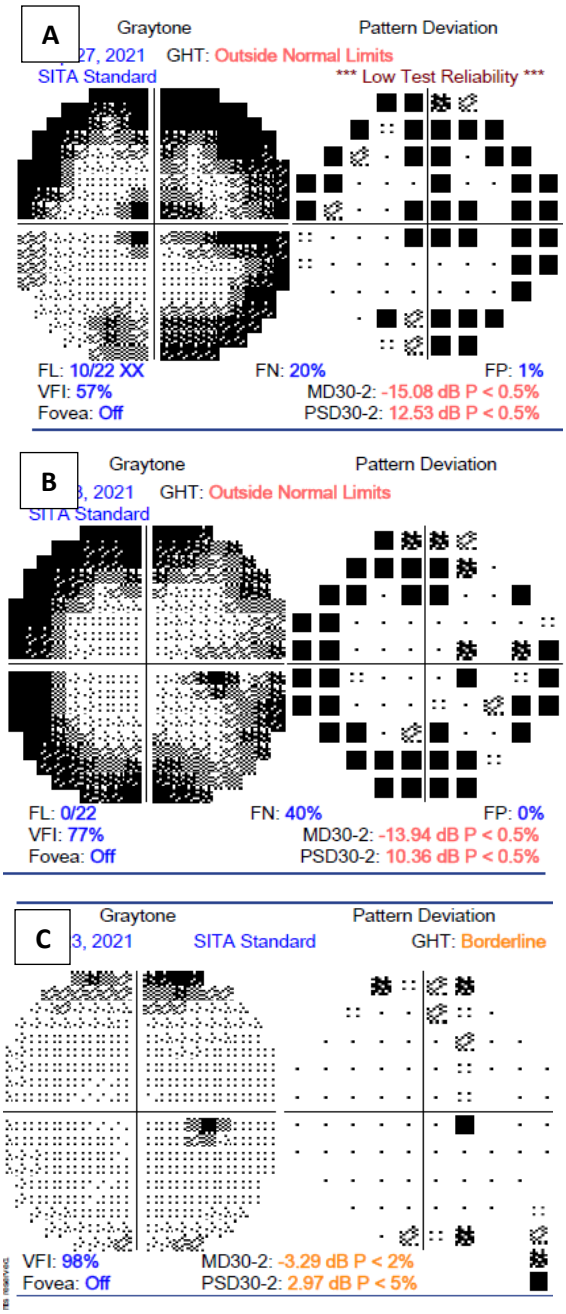

Figure 5. Guided Progression Analysis of the right eye acquired during eight weeks follow up showed improvement of the visual field defect. A. HFA acquired at presentation to the clinic; B. HFA acquired at 1 week of treatment; C. HFA acquired at 8 weeks of treatment.

Based on the clinical findings, the patient was diagnosed with neuroretinitis associated with Rubella infection. The patient was treated with Methylprednisolone 32 mg tablet every 2 hours, Neurotropic tablet every 12 hours, and folic acid supplementation. The

patient was referred to an internist clinic but no additional treatment was given because of the absence of fever and lymphadenopathy. Methylprednisolone dose of 2 x 32 mg was maintained for four weeks before tapering off. The patient showed a good response to therapy, and visual acuity and color vision of the right eye gradually improved. Visual acuity of the left eye was improved to 3/60 at the second visit (10 days after the first visit), 4/60 at the third visit (14 days after the first visit), and eventually 5/6.5 at the 8th follow-up, approximately 2 months after therapy. Serial fundus photograph showed decreasing edema of the optic nerves, and edema of the right and left optic nerve head was completely resolved within 8 weeks of follow-up. Subretinal fluid was completely resolved at two weeks follow-up (as seen on macular OCT), but the star pattern exudates persist.

DISCUSSION

Determination of the cause of neuroretinitis should be undertaken early in the course of medical assessment, as this will guide the approach to treatment and long-term management.[2] Although cat-scratch disease caused by *Bartonella henselae* has consistently been shown to be the most common etiology for neuroretinitis, another infectious agent including viral, fungal and parasitic should be considered. Concurrent systemic signs and symptoms can help to distinguish the etiology of the disease.[3]

Neuroretinitis is primarily a clinical diagnosis with characteristic findings of unilateral disc edema and a macular star 1. The case illustration presented a rare clinical findings of bilateral swollen optic nerve head and macular star pattern exudates associated with unilateral sudden onset painless vision loss. Visual disturbances were experienced in the past six months before presentation, it is suggestive of recurrent neuroretinitis. Neuroretinitis typically presents following a febrile illness in which patients may present with lymphadenopathy, rashes, arthralgia and headache.[2] Post-viral inflammatory etiology was suspected in this case because of the positive history of fever and eye redness (suggestive of conjunctivitis) one weeks before the onset of blurry vision.

The classic ocular findings suggestive of neuroretinitis are painless decreased visual acuity, dyschromatopsia, relative afferent pupillary defect and visual field abnormalities, most commonly a cecocentral/central scotoma.[4] Optic disc could show pallor or edema with peripapillary internal limiting membrane folds and perivascular hemorrhage. Macula may manifest hard exudates in a star pattern with associated retinal thickening or subretinal fluid. Ocular examination in this patient revealed initial visual acuity of 1/60, total color blindness, presence of relative afferent pupillary defect, and visual field abnormality of the right eye. All four symptoms suggestive of neuroretinitis were only found on the right eye despite bilateral optic disc edema. Poor visual acuity of the right eye might be caused by local macular exudative retinal detachment. Classically, the optic nerve head edema begins to decrease 2 weeks after onset, and by 3 months, most patients demonstrate complete resolution.[1] The presumption of inflammatory etiology is supported by leukocytosis, increased erythrocyte sedimentation rate (ESR), and also slightly increased liver function test results.

Rubella has a global distribution and remains an important cause of blindness in resource-limited regions and nations, nonetheless its incidence drops dramatically after the introduction of Rubella vaccine in 1969.[5] The incidence of rubella varies according to age and geographical zone. The Indonesian Health Ministry reported 30.463 cases of Rubella

in Indonesia in the period of 2010-2015. The number of cases is estimated to be lower than the actual number in the field, considering that there are still many unreported cases, especially from private health services.[6]

Rubella infection commonly occurs in children and is transmitted via respiratory tract droplets.[7] The infectious period extends approximately 8 days before to 8 days after the rash onset.[8] Rubella infection in adults may show typical symptoms such as rash, low fever, nausea, and mild conjunctivitis.[9] Polyarthritis and polyarthralgia is the most common complication of rubella infection, affecting up to 70% of adolescents and adult women. It is usually symmetric and involves the wrists, fingers, knees, and ankles.[10] The most frequent ocular complication of acquired rubella is conjunctivitis (70%), followed by a rare occurrence of epithelial keratitis and retinitis.[5] A delayed onset of optic neuritis after the initial infection and prompt response to corticosteroid therapy may suggest the involvement of an immune process in the pathogenesis of post-rubella optic neuritis.[12] The high percentage of asymptomatic or unapparent clinical sign symptoms might lead to the rarity of cases reported.

Confirmation of rubella infection relies on the detection of the virus or evidence of rubella infection by serologic testing. Confirmed rubella infection was described as a case with or without symptoms with one or more of the following: (1) rubella virus isolation; (2) rubella-virus specific nucleic acid detection by reverse-transcription polymerase chain reaction (RT-PCR); (3) significant rise between acute and convalescent-phase titers in serum rubella immunoglobulin G (IgG) antibody level by any standard serologic assay; or (4) positive serologic test for rubella immunoglobulin M (IgM) antibody without a history of MMR vaccination in 6–45 days prior. The most common diagnostic test for recent postnatal infection is the detection of rubella-specific IgM antibodies by using an enzyme immunoassay.[13] Rubella-specific IgM antibodies are usually detectable 4 days after the onset of rash. In addition, rubella infection and reinfection can be demonstrated by a four-fold or more significant increase in rubella-specific IgG titers between acute and convalescent sera.[13] Rubella IgM of 1.21 or more was considered a strong positive. A weak positive result was defined by an IgM titer of 0.8-1.2. A titer of <0.8 was considered negative.[11] The diagnosis of post-viral neuroretinitis associated with rubella infection, in this case, was suspected based on clinical signs and symptoms, it was later confirmed by rubella-specific IgG strong positive result (17.98).

Most patients with neuroretinitis recover excellent visual acuity with or without intervention, to the visual acuity of 20/40 or better in 90% of reported cases.[1] Neuroretinitis treatment and its efficacy are not established, yet idiopathic neuroretinitis is treated with high-dose oral corticosteroids.[1] Treatment should be directed towards the underlying cause if a specific etiology is found.[4] Patient, in this case, was consulted to the internal medicine department but was not given particular treatment due to a lack of systemic signs and symptoms at presentation, also there is no specific antiviral therapy exists for rubella infection.[14] Management of rubella-associated neuroretinitis was not mentioned in any study. However, rubella retinitis and optic neuritis may respond well to systemic corticosteroids.[5] Recent studies comparing the efficacy of high-dose oral corticosteroids vs high-dose intravenous methylprednisolone stated that both are bioequivalent.[15] Oral corticosteroid has the benefit of being less expensive and more convenient to

administer than an intravenous regimen, it is considered an equally viable treatment for acute optic neuritis.[15] The patient illustrated in this case was initially treated with a high-dose oral corticosteroid, which was methylprednisolone 2 x 32 mg per day for four weeks and tapered off slowly, following significant improvement of visual and ocular pathology.

CONCLUSION

Neuroretinitis has been typically associated to infection or post viral autoimmune process. Infectious neuroretinitis most associated *to Bartonella henselae*, syphilis, tuberculosis, toxoplasmosis, measles (rubeola), and other viruses. Rubella associated optic neuritis was rarely reported in medical literature. We conclude that the case presented was a neuroretinitis associated with adult rubella infection because of a classic sign and symptoms of neuroretinitis with a strong positive titer of Rubella specific IgG during the sub-acute phase. We suggest this case has several important medical implications to be discussed. First, it demonstrates the necessity to correlate inflammatory posterior segment findings to viral etiology, especially when history or concomitant viral illness is present. Second, it may confirm the possibility of rarely described cases of rubella neuroretinitis. Although there is no specific antiviral therapy exist for rubella infection, rubella neuroretinitis may respond well to oral corticosteroids.

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