Dengue hemorrhagic fever with severe ocular complication: case series

Anak Agung Mas Putrawati Triningrat*, I Ketut Agus Somia2, I Made Dwi Lingga Utama3, Ni Putu Ngurah Sri Yuliastini4, Made Paramita Wijayati5, Ariesanti Tri Handayani1

Abstract

Introduction: Ocular complication associated with Dengue Hemorrhagic Fever (DHF) is a rare condition with varied manifestations, ranging from subconjunctival hemorrhage to optic neuropathy. This condition's pathophysiological mechanism is not well understood, with several unpredictable conditions resulting in permanent visual loss. In this case series, three patients with severe ocular complications associated with DHF are presented.

Case Report: Case 1: a 16 years old girl presented with proptosis after diagnosed with DHF with no light perception. All findings were consistent with pan-ophtalmitis and retrobulbar hemorrhage. Unfortunately, the right eye turned into phthisis and spontaneous prolapse even with canthotomy with lateral cantholysis and steroid administration. Case 2: 10 years old boy presented with bilateral visual blurring within a month after being diagnosed with DHF with hand movement perception on both eyes and optic disc swelling. The visual acuity recovered to 20/20 in a month of steroid therapy with no optic disc swelling. Case 3: 52 years old man presented with propotis and dengue shock syndrome with counting finger perception, swelled optic disc, and limited eye movement to all directions. The patient was diagnosed with optic neuritis and retrobulbar hemorrhage. Canthotomy with lateral cantholysis lateral and steroid therapy were planned, but the patient died before treatment was done.

Conclusions: Severe ocular complications should be anticipated and monitored in DHF patients. Although visual recovery is possible, permanent ocular complications can be severe and cause permanent visual loss.

Keywords: Dengue Hemorrhagic Fever, Ocular Complication, Visual Loss.

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INTRODUCTION

Dengue is a systemic self-limiting disease caused by viral infection spread by the Aedes aegypti mosquito. Most cases occur in tropical and subtropical countries in which it is responsible for one of the infectious diseases with high morbidity and mortality. World Health Organization (WHO) estimated that the morbidity rate of Dengue Hemorrhagic Fever (DHF) reached 14.7 million in 2001, 26% of the total mortality. The incident rate of DHF increased by 30 times between 1960 and 2010. This increase occurred because of several crucial factors, such as rapid urbanization changes, population growth, and increased travel from endemic regions.

The clinical presentations of DHF varied with unpredictable outcomes. Its clinical manifestations are mostly fever with a saddle-back pattern, a self-limiting disease and accompanied by headache and thrombocytopenia. The severe form of this disease is Dengue shock syndrome (DSS), which can be fatal. DHF/DSS is characterized by rapid capillary leakage followed by thrombocytopenia conditions and impaired hemostasis. Atypical manifestations of dengue are infrequent, but it is expected to be increasing in the incoming decade due to the widespread distribution of the disease. The atypical manifestations of DHF include neurological, hepatic, kidney, heart, musculoskeletal and ocular manifestations.

Ocular manifestations of DHF are very rare. The most commonly reported clinical manifestations are retro Orbital pain and subconjunctival bleeding resulting from thrombocytopenia. Some conditions may cause irreversible bilateral blindness. The severity of these ocular complications require aggressive initial management and therapy. In this case series, three rare cases and the management of severe and irreversible ocular complications of DHF found in Sanglah Hospital, Bali, are reported and described in detail.
CASE REPORT

This case series reported three severe ocular DHF complications in patients at Sanglah General Hospital, Bali. The first case was a 16 years old girl who presented with pain and swelling of the right eye in the last two days before admission (Figure 1). She had been treated in another hospital with a history of fever, abdominal pain and vomiting for seven days with an episode of gum bleeding and menorrhagia. The serology test showed a positive result for immunoglobulin G (IgG) anti-dengue. Her initial ophthalmology evaluation showed no perception of light with severe and tender proptosis. USG examination revealed sub-choroidal hemorrhage, and CT-scan imaging showed retrobulbar hemorrhage.

The laboratory result showed White Blood Cell (WBC) at 11.67 x 10^3/µL, hemoglobin (Hb) 11.5 g/dL, hematocrite (HCT) 36.75%, platelet 107.1 x 10^9/µL, PTT 14.5 (13.1), APTT 37.6 (29.8), INR 1.24, SGOT 56.8 U/L (11-27 UL), SGPT 23.9 U/L (11.0-34.0 U/L), albumin 2.63 g/dL (3.20-4.50 g/dL), blood urea nitrogen (BUN) 4 mg/dl (8.00-23.00 mg/dl), serum creatinine 0.37 mg/dl (0.50-0.90 mg/dl), natrium 137 mmol/L (136-145 mmol/L), kalium 3.3 mmol/L (3.50-5.10 mmol/L), DHF IgG positive dan DHF IgM negative.

The head CT scan revealed retrobulbar bleeding in the retro-orbital and the right periorbital, which caused the prolapse bulb (Figure 2). The patient was then diagnosed with proptosis of ocular dextra et causa retrobulbar hemorrhage. From systemic condition was diagnosed with healthcare-associated pneumonia (HCAP) and grade 3 DHF (improved) Day 9. Visual acuity assessment showed no light perception, and all findings were consistent with pan-ophthalmitis and retrobulbar hemorrhage, which was also supported by the histopathologic result. Unfortunately, the right eye became phthisis and prolapse spontaneously due to extensive necrosis even after canthotomy with lateral cantholysis and steroid therapy.

The second case was a ten-year-old boy who complained of bilateral blurring of vision within a month after being diagnosed with DHF in another hospital with platelet count at 34 x 10^9/l and Dengue IgM (+). His visual acuity was at counting fingers in the right eye and 1/60 in the left eye with optic disc swelling on both of his eyes. Several additional examinations were conducted at the ophthalmology polyclinic (Fundus Photography (Figure 4.)) and Optical Coherence Tomography (OCT) of Retinal Nerve Fiber Layer (RNFL). Fundus examination showed a swelled papilla, hyperemia, and unclear CDR, while the retina images were considered normal. At OCT RNFL, swelling of the retinal nerve layer was apparent (Figure 5).

The patient was diagnosed with the right-left eye optic disc swelling et causa optic neuritis (papillitis) with Space Occupying Lesion (SOL) as the differential diagnosis. The patient was hospitalized, and some examinations such as complete blood lab check, clinical chemistry, ESR, bleeding time, PTT, APTT, D dimer, ANA, IgG
and IgM anti toxoplasmosis cytomegalovirus, as well as Magnetic Resonance Imaging (MRI), were conducted. After the examination, the patient was planned for Optic Neuritis Treatment Trial (ONTT) with Methylprednisolone 4 x 125 mg (IV), Vitamin B Complex 1x1 tab, antacids 3x1/2 and Kalk 1x1/2 tab at Sanglah General Hospital. He had an improved visual acuity within two days after therapy. The visual acuity was recovered to 6/7.5 in the right eye and 6/6 in the left eye two months after treatment with no optic disc swelling. The visual acuity was recovered to 20/20 in one month after steroid therapy.

The third case was a 52 years old man with proptosis and dengue shock syndrome. The visual acuity was at counting fingers with optic disc swelling on both eyes and limited eye movement to all directions. The patient was diagnosed with optic neuritis and retrobulbar hemorrhage. Canthotomy with lateral cantholysis lateral and steroid therapy was planned, but the patient had died before treatment was done.

DISCUSSION

The World Health Organization (WHO) defines dengue hemorrhagic fever as dengue fever with thrombocytopenia (< 100x10^9 cells/L) and Hemoconcentration (Hematocrit > 20% of baseline). The diagnosis is usually established based on laboratory tests, where the most commonly used tests are hemagglutination-inhibition with immunoglobulin G (IgG) and immunoglobulin M (IgM) enzyme immunoassays. Because the symptoms are often not specific and varied, the diagnosis through laboratory tests is essential.7,8

The cases in this case series reported that the patients’ fever pattern was similar to the horseshoe fever pattern in DHF. Patients also had a history of gum bleeding and prolonged menstrual period. The laboratory examination showed positive DHF IgG in all of these patients as well as thrombocytopenia and hemoconcentration.9

The pathophysiology of dengue infection is complex in which immune-mediated reaction plays a crucial role. The virus’s invasion into endothelial cells, dendritic cells, monocytes, and hepatocytes results in apoptosis and cellular dysfunction in vascular, liver, and innate immune system.10 However, DHF ocular complications’ pathogenesis was not yet fully known, but it is hypothesized that immunogenic reaction is also responsible based on its clinical manifestations.10 In a case reported by Nagaraj (2014), pan-ophtalmitis and retrobulbar bleeding were the most common cause of proptosis in DHF patients.9
Pan-ophthalmitis is severe ocular inflammation which involved anterior and posterior segment of the globe. The inflammation will lead to some clinical manifestations such as chemosis, proptosis, hypopyon and posterior segment inflammation that potentially result in blindness.\(^1\) Ocular complications in case 1 was a severe retrobulbar hemorrhage and pan-ophthalmitis. According to Kapoor et al., retrobulbar bleeding is likely to occur when the platelet level is less than 10,000/microliters.\(^2\)

Optic neuritis optic after dengue infection is also very rare, and the reported incidence rate is only at 0-1.5\%. Ophthalmonic complications of DHF may occur two days to 5 months after the initial symptoms begin.\(^3,4\) Optic Neuritis is generally possible considering the retrobulbar part of the optic nerve. One-third of the optic neuritis occurs in the anterior chamber and appears as optical disc edema called Papillitis. Edema of the disc is usually presented as hyperemic and diffuse. In particular, children have a higher risk of optical neuritis, post-viral serous inflammation, and a decrease in bilateral visual acuity. Other potential causes of optic neuritis include multiple sclerosis, autoimmune diseases, infections, and post-vaccination reaction. Therefore, anamnesis, ophthalmology examination and laboratory examination, and Magnetic Resonance Imaging (MRI) must be carefully performed to identify the etiology.\(^5,6\)

The steroid is still the primary therapy for optic neuritis caused by a dengue infection. Systemic corticosteroids often used in ophthalmologic complications of DHF include oral prednisolone and intravenous methylprednisolone, which is usually administered for maculopathy, optic neuritis and neuromyelitis Optica (NMO). According to the Optic Neuritis Treatment Trial (ONTT) guideline, the methylprednisolone was administered intravenously at 250 mg every 6 hours for three days and continued with oral prednisolone at 1 mg/kgBW/day (tapering off) is recommended. Intravenous administration of steroids is known to have better outcomes than oral steroids in restoring the visual acuity, visual field, and contrast sensitivity.\(^8,9\)

**CONCLUSION**

DHF is still a challenging disease for internal medicine and ophthalmology because of its varied clinical symptoms and rare but severe atypical symptoms that are hard to predict. The ocular manifestations of dengue infection are rarely reported, but they can result in blindness and irreversible ocular complications. The Guidelines for ocular management of DHF is not yet established; early diagnosis and multi-disciplines management are mandatory. Although visual recovery is possible, permanent ocular complications can be severe and result in permanent visual loss.

**CONFLICT OF INTEREST**

All authors declared that there is no conflict of interest regarding this publication.

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**AUTHOR CONTRIBUTION**

All authors contributed equally in the writing and revision process of this publication.

**ETHICS APPROVAL**

This case report had been ethically approved by the Ethics Commission of Udayana University with ethic number 423/KE-PH-Lit-2/VII/2020

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**Figure 5.** a) RNFL examination of right and left eye in the first examination; b) RNFL of right and left eye after the treatment.
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