A Case of Dengue Maculopathy with Spontaneous Recovery

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Key Words
Viral infection - Dengue fever - Maculopathy - Electoretinogram

Abstract
Purpose: To report a case of dengue maculopathy, which resolved spontaneously without treatment. Methods: A 25-year-old female patient with good past health was admitted to a general hospital in Hong Kong with fever of unknown origin after traveling to Indonesia. Based on the clinical features and a positive real-time polymerase chain reaction for dengue virus type 1, she was diagnosed with dengue fever. The patient developed dengue maculopathy mainly affecting the vision of her left eye. Abnormalities on a multifocal electroretinogram showed bilateral involvement. Results: As there is no proven treatment for dengue maculopathy, the patient opted for observation. Her vision returned to normal within 3 weeks. Conclusion: Dengue maculopathy can cause severe visual loss and may resolve without treatment.

Introduction
Dengue fever is an acute viral infection caused by four closely related dengue viruses (Flavivirus) and transmitted through the bite of infected female Aedes aegypti mosquitoes [1]. Endemic areas are the Americas, Southeast Asia, Western Pacific, Africa and the Eastern Mediterranean [2].

In Hong Kong, dengue fever is not common. The principal vector Aedes aegypti is not found, but the prevailing species Aedes albopictus can also spread the disease [3]. Dengue fever has become a notifiable disease to the Hong Kong Department of Health since March 1994, and all reported cases are investigated to establish their source. The majority of the reported cases were imported from other countries. Clinical manifestations of dengue fever range from benign self-limiting fever, chills and headache to severe dengue haemorrhagic
fever and dengue shock syndrome [4]. Diagnosis can be confirmed with laboratory tests such as the haemagglutination inhibition test, immunoglobulin G or M enzyme immunoassays and polymerase chain reaction (PCR) for dengue virus.

Dengue maculopathy may develop in patients with dengue fever. Common ocular manifestations include retinal haemorrhages, macular oedema, yellow spots, optic disc swelling and retinal vasculitis [5–7]. We report a case of bilateral dengue maculopathy with spontaneous recovery in a 25-year-old female patient.

Case Presentation

A 25-year-old female with good past health presented to a general hospital in Hong Kong with a 2-day history of fever, headache and retro-orbital pain preceded by papular rash over both hands and both feet. She had recently travelled to Indonesia. Her vital signs were stable, and her body temperature was 39°C. No lymphadenopathy was noted clinically. Systemic workup revealed lymphopenia, neutropenia, thrombocytopenia and a negative culture for sputum, blood and stool, and the patient was negative for anti-HIV antibodies, malaria, leptospira and rickettsial antibodies. Immunoglobulin M for dengue virus was negative at the time of presentation. Real-time PCR for dengue virus type 1 was positive so that the diagnosis of dengue fever was confirmed. The patient received supportive treatment for her systemic disease.

Four days after admission, the patient complained of a paracentral absolute scotoma in her left eye. On examination, the Snellen visual acuity in her right and left eye was 20/25 and 20/60, respectively. There was no relative afferent pupillary defect or loss of colour perception on Ishihara test plates. Amsler chart testing showed a round, absolute scotoma inferotemporal to the fixation point in her left eye. Intraocular pressure was normal, and anterior segment examination was unremarkable. Fundal examination showed an area of retinal infiltrate and a haemorrhage superonasal to the fovea in her left eye and some retinal pigment epithelium (RPE) changes in her right eye (fig. 1). There were no signs of vitritis or vasculitis.

Spectral-domain optical coherence tomography (OCT) was performed and showed retinal thickening corresponding to the area of retinitis and haemorrhage. There was no foveolitis (fig. 2). Multifocal electoretinogram (ERG) showed a reduction in first-order kernel responses at the central maculae of both eyes (more severe in the left eye) (fig. 3). The working diagnosis was dengue maculopathy. The option of steroid treatment was discussed with the patient. In view of leucopenia secondary to dengue fever and the absence of a proven benefit of steroid treatment, the patient opted for observation.

One week after the onset of visual symptoms, the vision of her left eye deteriorated to 20/250. There was suspicion of other viral retinitis secondary to her immunocompromised state. Aqueous tapping with an aseptic technique was performed and sent for PCR for cytomegalovirus, herpes simplex and varicella zoster viruses. The patient opted for empirical treatment with oral valganciclovir 900 mg bid for a few days until the results of the PCR were negative.

Eleven days after visual symptom onset, the patient’s condition started to improve with less retinal haemorrhage and resolving retinitis. One week later, her vision returned to normal. After 9 months, her Snellen best-corrected visual acuity was stable at 20/20, but there were a persistent reduction in retinal responses on multifocal ERG and a persistent paracentral scotoma.
Discussion

Dengue maculopathy is a rare complication. In Singapore, the prevalence of maculopathy in patients hospitalized for dengue fever was reported to be 10% [8] and there was no case of dengue maculopathy during the dengue epidemic in 2007 [9]. Ocular involvement is usually asymmetric, with a best-corrected visual acuity ranging from 20/30 to hand movements, and it usually occurs 6–7 days after the onset of dengue fever symptoms [5–7]. Time to resolution ranged from 8 weeks to 4 months. RPE discolouration over the affected area was observed on resolution [5]. In our case, the patient recovered from dengue fever within about 1 week, and her ocular symptoms lasted for about 3 weeks. There was no report on the relationship between the course of recovery of the systemic condition and that of maculopathy.

Multifocal ERG was shown to be a useful tool, especially in cases with absent or subtle clinical signs [10]. The area of reduction in first-order kernel responses corresponds well to the scotoma and represents the dysfunction of photoreceptors. In our case, the multifocal ERG demonstrated the reduction in retinal responses in the asymptomatic eye, implying bilateral involvement. Such localized retinal dysfunction may persist despite improvement of visual acuity. In a study by Chia et al. [11], there was little change or incomplete resolution in 9 out of 15 patients over 3 to 10 months.

Prognosis for dengue maculopathy varies in different series. Patients usually regain good vision. Spontaneous recovery of dengue maculopathy has been previously reported [12]. In some cases, visual recovery may be prolonged or scotomata may persist even at 2 years [10, 13]. In our case, although visual acuity recovered spontaneously, there were persistent changes on multifocal ERG. OCT patterns in dengue maculopathy were shown to be useful for characterisation and prognostication. There were three patterns of maculopathy: diffuse retinal thickening, cystoid macular oedema and foveolitis [13]. Scotomata were shown to persist longest in patients with foveolitis and shortest in those with diffuse retinal thickening [13].

There is no proven antiviral treatment or commercially available vaccine for both dengue fever and dengue maculopathy [3]. The use of steroids has been reported in some cases – with variable responses. It is postulated that there may be an immune basis for the occurrence of maculopathy rather than a direct viral infection. Low serum complement 3 levels had been found to be significantly associated with the presence of dengue maculopathy [8]. The 6- to 7-day delay in the onset of visual symptoms from the acute viral infection corresponds to the time of onset of antibody production or immune complex deposition. Direct viral infection causes apoptosis and dysfunction of endothelial cells, dendritic cells, monocytes and hepatocytes. This may lead to an aberrant immune response causing overproduction of cytokines and subsequent production of autoantibodies against platelets and endothelial cells. It is uncertain whether dengue maculopathy is associated with the production of autoantibodies against retina, RPE or choroidal antigens [14, 15].

There was a case of dengue maculopathy, who recovered rapidly from counting fingers to 20/40 while on high-dose oral prednisolone, but experienced a visual deterioration to counting fingers as the steroid was tapered [5]. This patient was lost to follow-up and the final outcome was not known. In a retrospective study of dengue foveolitis [12], 5 of 6 patients were treated with periocular steroids, oral prednisolone, intravenous methylprednisolone or intravenous immunoglobulin. All but one eye had a best-corrected visual acuity of 6/7.5 or better at a mean of 2.2 months. However, the good visual outcome may also be the natural course of the disease.
In conclusion, dengue maculopathy is a rare complication of dengue fever. The prognosis is variable, with no proven effective treatment. Immunity to one serotype of the dengue virus would not confer protection against subsequent infection with the other three serotypes [3]. Education on preventive measures such as avoiding mosquito bites and eliminating stagnant water is also important.

References

Fig. 1. Colour fundus photographs of the patient's left eye, with a localized area of retinitis with haemorrhage superonasal to the fovea in the left eye.

Fig. 2. Spectral-domain OCT of the patient's right and left maculae (Spectralis; Heidelberg Engineering).
Fig. 3. Multifocal ERG at presentation showed a reduction in first-order kernel responses at the central maculae (more severe in the left eye). a Trace arrays. b Three-dimensional response density topography plot (Veris; Electro-Diagnostic Imaging, Inc.).