รายงานผู้ป่วย/Case Report

จุดรับภาพผิดปกติ: ภาวะแทรกซ้อนทางตาที่เกิดในระยะหลังของโรคไข้เลือดออก

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บทคัดย่อ

โรคไข้เลือดออกทำให้เกิดภาวะแทรกซ้อนทางตาได้ อาการทางตาที่พบบ่อย ได้แก่ เลือดออกในตา และจุดรับภาพบวม มักจะเกิดที่ 6-7 วันหลังเริ่มมีไข้ ซึ่งเป็นระยะที่เกล็ดเลือดลดลงต่ำสุด เชื่อว่าภาวะเกล็ดเลือดต่ำนี้เป็นสาเหตุของการเกิดเลือดออกในตา คณะผู้นิพนธ์รายงานผู้ป่วยที่มีอาการจุดรับภาพบวมและมีเลือดออกในระยะหลังของโรคที่ระดับเกล็ดเลือดกลับมาปกติ ซึ่งภาวะจุดรับภาพผิดปกตินี้ เชื่อว่าอาจเกิดจากภาวะตอบสนองของภูมิคุ้มกันต่อเชื้อไวรัส **จักษุเวชสาร 2014; กรกฎาคม-ธันวาคม 28(2): 101-107.**

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รายงานผู้ป่วย/Case Report

Maculopathy: A Late Ocular Manifestation in Dengue Fever

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Abstract

Dengue fever can be associated with ocular complications. Common presentations are ocular bleedings and macular edema, which usually occurs approximately 6-7 days after the onset of fever, at the nadir of platelet count. Thrombocytopenia is believed to be responsible for hemorrhagic manifestation. The authors presented a case of Dengue fever with a late-occurring macular edema and hemorrhage at the time of recovery from thrombocytopenia. The delay onset of maculopathy raised the possibility of immune-mediated hypothesis. **Thai J Ophthalmol 2014; July-December 28(2): 101-107.**

Keywords: Dengue fever, Ocular Dengue, Macular edema, Maculopathy

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Introduction

Dengue fever (DF) is caused by flavivirus infection with four different serotypes. It is spread by mosquito bites, most commonly the mosquito *Aedes aegypti.* It is endemic in the tropic and warm climate areas of the world. Dengue infection causes flu-like symptoms. It is characterized by acute onset of high fever, headache, malaise, arthralgia, nausea, vomiting and skin rash[1]. The disease is usually self-limited with minimal systemic sequel. Bleeding manifestations are usually mild and limited to skin petechia, mucosal membrane bleeding (e.g. nose and gums), or menorrhagia. Massive life-threatening bleeding or shock syndrome may occur but are less common.

Traditionally, ocular manifestations in DF were considered to be uncommon. Therefore, it is often overlooked. In recent years, there are a handful of reports of ocular complications in dengue patients, which usually occurred approximately 6-7 days after the onset of fever, at the nadir of platelet count[1-5]. Here, the authors present a case of ocular manifestations in DF with a late-occurring dengue maculopathy at the time of recovery from thrombocytopenia.

Case report

A 32-year-old woman was hospitalized for acute onset of high fever, headache and myalgia. Minimal cervical lymphadenopathy was found. Later, she had gum bleeding and menorrhagia. The blood pressure was stable. Laboratory examination revealed thrombocytopenia (platelet count 99,000/mm^3). The clinical manifestations and presence of positive IgG and IgM antibodies established a diagnosis of Dengue hemorrhagic fever (DHF). Dengue serotype antigen 1 was detected in this patient. The patient was treated conservatively with intravenous fluids and serial hematocrit measurements for systemic viral infection.

Seven days after the initial onset of fever, the patient complained of blurring vision in both eyes, corresponding to the day which the platelet count decreased to the lowest level at 30,000 mm^3 and the fever started to subside. Visual acuity was 20/70 in the right eye and 20/200 in the left eye. The anterior segment and fundus examination were normal in both eyes. The diagnosis was inconclusive. The patient was treated conservatively and scheduled for further investigations. She noticed improvement in her visual acuity to 20/70 in both eyes on the following 2 days. Ishihara plate revealed some degree of red-green defect in both eyes. Humphrey visual field testing revealed generalized decrease in sensitivity in both eyes. Visual evoked potential test was normal. Dengue related optic neuropathy was suspected. The patient was treated conservatively with continuing improvement to 20/50 in the right eye and 20/40 in the left eye within a week. Her platelet count had increased to 124,000 mm^3.

On a follow up examination (24 days after initial onset of fever), she complained of a new blurring of central vision in the right eye despite stable visual acuity measurements. Fundus examination revealed macular edema with adjacent retinal hemorrhage in her right eye, with a few dot hemorrhages in the posterior pole. The fundus was normal in the left eye. Fundus fluorescein angiography of the right eye

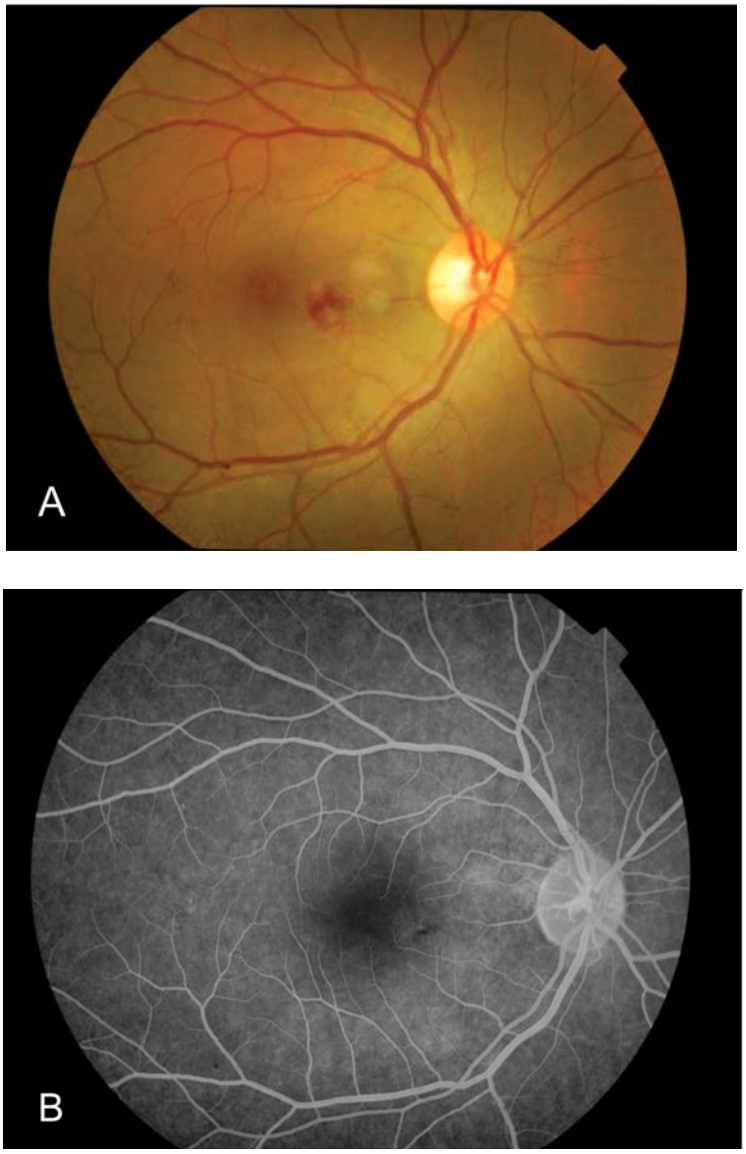

Fig 1. ***A.*** *Fundus photography of the right eye, showing intraretinal hemorrhage in the macular area.*
B. *Fundus fluorescein angiography of the right eye, showing blocked fluorescence corresponding to the hemorrhage area, with no definite points of leakage. (รูปสีหน้า 149)*

showed blocked fluorescence corresponding to intraretinal hemorrhage in the macular area, with no definite points of leakage (Fig 1).

Oral prednisolone of 60 mg/day was prescribed and slowly tapered over 4 weeks for the treatment of macular edema. Visual acuity gradually improved to 20/40 in her right eye and 20/30 in the left eye over a period of 1 month, and returned to 20/20 in both eyes after 5 months. After 26 months of follow up, visual acuity remained 20/20 in both eyes with minimal blurring of central vision. There was pigmentary change in the macular area in both eyes. Color vision testing with Ishihara plates was normal. However, Humphrey visual field testing showed persistence of cecocentral scotoma in the right eye and enlarged blind spot in the left eye (Fig 2).

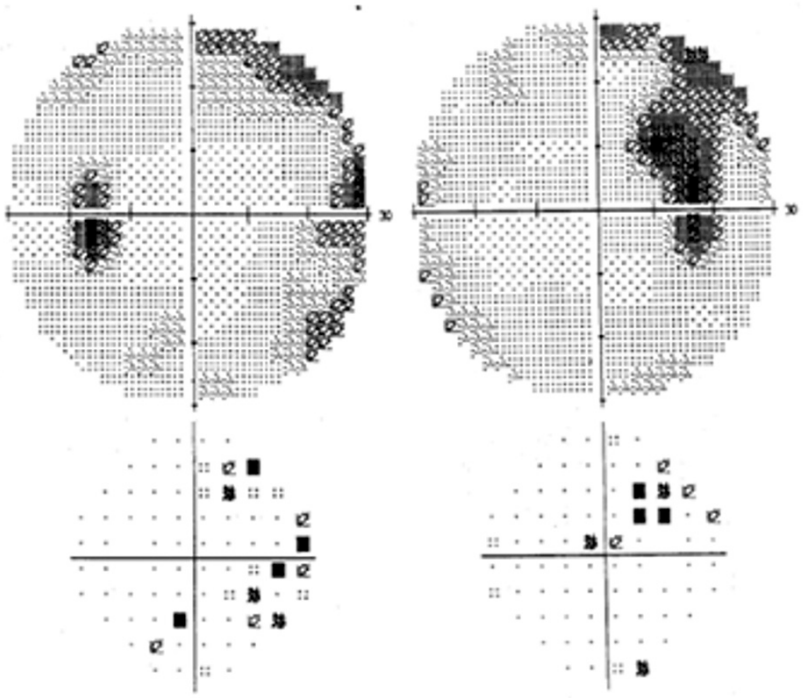

Fig 2. *Humphrey visual fields (gray scale, top; pattern deviation, bottom) at the last follow up visit showing cecocentral scotoma in the right eye, enlarged blind spot in the left eye.*

Discussion

Dengue is the most common mosquito-borne virus infection in humans, with four different serotypes. It is a major public health concern in endemic areas. The infection causes systemic symptoms which are usually self-limited. Ocular complications in DF have been traditionally overlooked. Recently, it is increasingly recognized as many reports of various ocular manifestations in dengue patients have been published.

Previous studies reported the main presenting complaint was blurring of vision[1,4,5]. In a large study of dengue patients by Kapoor et al[6], 40.3% were noted to have ocular involvement with subconjunctival hemorrhage as the most common ocular manifestation. Only 7.5% had posterior segment involvement as retinal hemorrhage, cotton-wool spots, and hard exudates with macular sparing in all patients. However, the most common pathology found was intraretinal hemorrhage (45%) by Bacsal[2] and macular edema (76.9%) by Chan[4]. A prevalence of maculopathy in dengue patients has been found 10% by Su et al[3]. Only 24.1% of patients complained of visual symptoms, occurring with a mean of 6.8 days after the onset of fever. Main findings included macular edema, macular hemorrhages, and yellow spots in the macula. Another study of dengue maculopathy by Gupta[7], reported 2 of the 3 patients had massive subhyaloid hemorrhage in the macular area with significant decrease in vision but spontaneously resolved with improved vision.

Pathophysiology of ocular involvement in DF is not clearly understood. The hypothesis of immune-mediated process, coagulopathy, and circulatory failure has been postulated. The delayed ocular manifestations, occurring approximately 6-7 days after

the onset of fever, in the convalescent phase of the systemic disease, favors the hypothesis that the pathophysiology involves immune-mediated processes rather than direct viral infection[1,3,8]. Immune response to the virus causes inflammation in various parts of the eyes, resulting in uveitis, macular edema, retinal vasculitis and optic neuritis[2,4,9-12].Exudative retinal detachment and branch retinal artery occlusion have also been reported in isolated cases of DF[13,14]. Our patient had initial ocular symptom of bilateral blurring of vision at day 7 of the course of the disease, as typical dengue ocular manifestation. Although there was no disc swelling observed, dyschromatopsia and visual field defect pattern suggested dengue-related optic neuropathy. The patient's vision improved rapidly without any specific treatments, however, a small degree of visual field loss was persistent.

Many factors are believed to be responsible for hemorrhagic manifestation in DF. Thrombocytopenia and abnormal coagulation profiles (PT, PTT) have been reported as a predictive factor for spontaneous bleeding in DF[6,7]. However, Gomber et al[15] and Seet et al[16], reported that there was no significant association between thrombocytopenia and hemorrhagic manifestation, but rather identified leukopenia and hypoalbuminemia as important risk factors for ocular bleeding[16].

Our patient had systemic bleeding at the nadir of thrombocytopenia but maculopathy including macular edema with adjacent intraretinal hemorrhage had developed over 3 weeks after the onset of fever, at the time that platelet count returned to normal level. Our findings suggest that thrombocytopenia is not the only cause of hemorrhagic manifestation. An immune-mediated process is also involved. Moreover, dengue maculopathy appears to be serotype-related. Chee[17] reported that maculopathy was more common with the virus serotype 1 compared to serotype 2, corresponding to the antigen detected in our patient. These observations suggest that dengue maculopathy is an immune-mediated disease, causing increased vascular permeability and breakdown of the inner blood retinal barrier, resulting in intraretinal hemorrhage and macular edema.

Conclusion

Dengue virus infection results in various ocular manifestations. The pathophysiology of ocular complications is not completely understood. The delayed onset of ocular inflammation and ocular hemorrhagic manifestation support the hypothesis of immune-mediated process. Further studies are needed to elucidate the mechanism of ophthalmic complication of dengue infection.