CASE REPORT

Dengue Fever Manifesting as Haemorrhagic Bullae: A Rare Presentation

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Abstract

Dengue fever, a viral disease transmitted by *Aedes* mosquitoes, is a global health problem affecting millions of people each year. It is prevalent in tropical and subtropical areas, with epidemic potential due to climate change and increased travel. The disease commonly presents with cutaneous symptoms such as erythema, maculopapular rash and minor haemorrhagic lesions. This case is notable for the unusual presentation of haemorrhagic bullae, resembling drug eruption or autoimmune bullous disease. In the field of dermatology, tropical diseases like dengue have rarely been discussed. However, the recent increase in cases in Southeast Asia highlights the need for dermatologists to become familiar with dengue, as it often presents with diverse skin rashes. Herein, we report an unusual case of dengue fever presenting with haemorrhagic bullae.

Key Words: *Bullae, dengue fever, rash, tropical disease*

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Introduction

Dengue fever is an acute febrile illness caused by the dengue virus, which is transmitted by *Aedes* mosquitoes.[1] It is the most common vector-borne disease worldwide and its prevalence has increased significantly in recent decades owing to urbanization, global travel and climate change.[1] Clinical presentations vary from asymptomatic infection to severe dengue (formerly known as dengue haemorrhagic fever or dengue shock syndrome), with plasma leakage, bleeding and organ dysfunction requiring prompt management to prevent fatality.[2] Skin manifestations appear in approximately 65% of the cases, typically as a generalized morbilliform rash or confluent erythematous rash with white islands of sparing.[2] Bullae are rare in dengue and may pose a diagnostic challenge by mimicking other conditions, such as drug eruptions or autoimmune bullous disorders. Herein, we report an unusual case of dengue fever presenting with haemorrhagic bullae after travelling to Laos.

Case History

A 71-year-old Korean man who returned from a one-month trip to Laos presented with generalized pruritic morbilliform eruptions that began 4 days prior to presentation. The rash included some blisters on the abdomen, petechiae and haemorrhagic bullae on both thighs [Figure 1]. There was no mucosal involvement or Nikolsky's sign. At first, his blood pressure was 73/49 mmHg with a 110 bpm heart rate, and he had a fever of 38.2°C. A complete blood count revealed a slight decrease in platelet count to 128,000/mm3, but he was otherwise normal. To rule out autoimmune bullous disease, punch biopsies from the bullae on the abdomen and leg were done, revealing spongiosis, papillary dermal oedema and superficial perivascular lympho-histiocytic infiltration with eosinophils [Figure 2]. Direct immunofluorescence was also negative. Due to his travel history, polymerase chain reaction (PCR) for dengue, malaria blood smear and serology for syphilis, human immunodeficiency virus, hepatitis A, hepatitis B and hepatitis C were performed, and only the PCR for dengue was positive. The patient was admitted and started on intravenous fluids and inotropes because he was in shock. The patient gradually recovered from shock, and the inotropes were tapered on the second day of admission. The skin lesions began to disappear on the fourth day after admission, and the patient's platelet count improved to 333,000/mm3 at the time of discharge. After 10 days, the skin lesions nearly cleared [Figure 3], and the lesions completely resolved after one month [Figure 4]. Written informed consent

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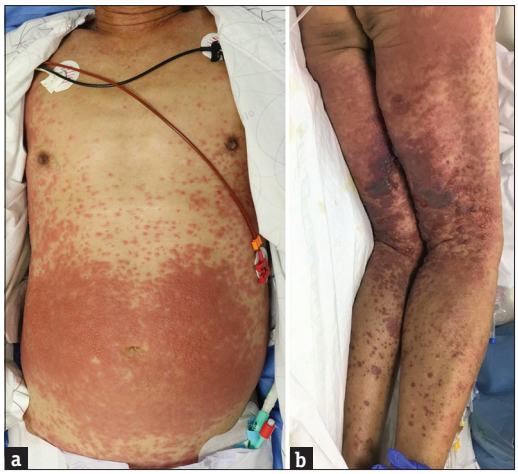

Figure 1: Diffuse maculopapular rash on trunk (a) with haemorrhagic bullae on both thighs (b)

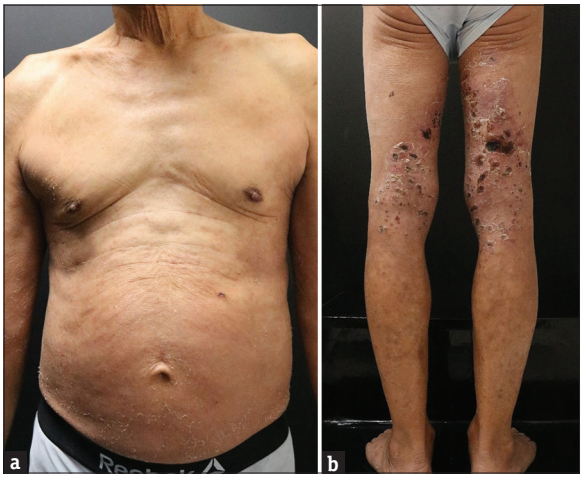

Figure 3: After 10 days, lesions had nearly cleared except for some haemorrhagic crusts (a and b)

was obtained from the patient for the publication of this case report and accompanying images.

Discussion

Dengue fever is endemic to over 100 countries across tropical and subtropical regions, with an annual incidence of approximately 400 million infections.[1] Patients often experience an abrupt onset of symptoms, including high fever, rash, headache and retro-orbital pain. Cutaneous manifestations are estimated to occur in 50–82% of patients. Classically, flushing or a macular erythematous rash affecting the face, neck and chest is noted within the first 48 hours of symptom onset, later evolving to a more maculopapular rash.[3] In a study from Pakistan,[4] the rash was generalized in 48.3% of patients, with the limbs and trunk involved in 32.8% and 18.9% of patients. In studies from Pakistan[4] and India,[5] the commonest skin finding was maculopapular (morbilliform) rash, which was

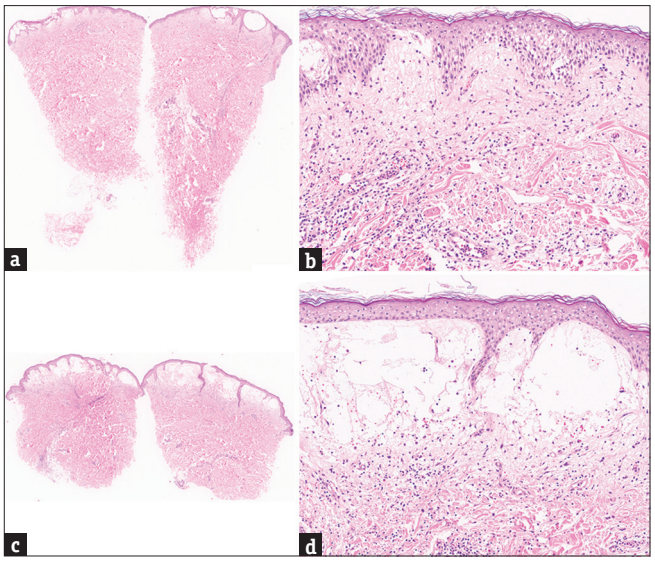

Figure 2: (a): Biopsy specimen of abdomen showing subcorneal pustules (Haematoxylin and Eosin stain × 20). (b): Spongiosis, focal vacuolar degeneration, papillary dermal oedema, perivascular inflammatory infiltrates composed of lymphocytes, histiocytes, eosinophils and neutrophils, extravasation of RBC (Haematoxylin and Eosin stain × 100), (c): Biopsy specimen of leg showing subepidermal bullae (Haematoxylin and Eosin stain × 10). (d): Papillary dermal oedema, perivascular inflammatory infiltrates composed of lymphocytes, histiocytes, eosinophils and neutrophils, extravasation of RBC (Haematoxylin and Eosin stain × 100)

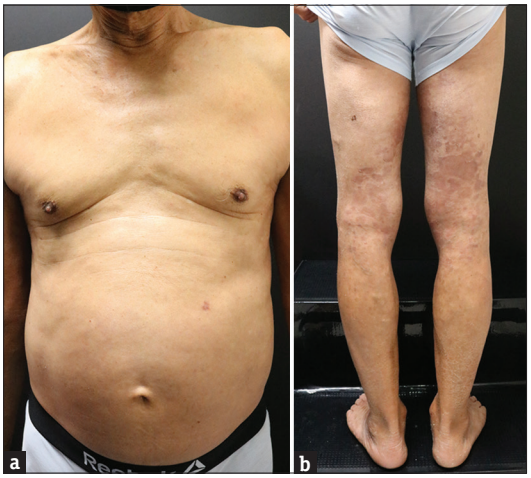

Figure 4: After 1 month, lesions were completely gone (a and b)

present in 42.9%, 48.3% of patients, followed by ecchymosis or petechiae observed in 33.8%, 41.4% of patients, respectively. In a study from France,[6] 33% of patients had a macular rash rather than a maculopapular rash. Although the rash in dengue is usually asymptomatic, pruritus is reported in different studies, ranging from 16% to 69.2%.[4,7] Moreover, in a study from Taiwan,[2] there was neither a prolonged disease course nor poor prognosis in the dengue patients with skin rash, except for increased itching scores and swelling of the palms or soles. Our patient presented with a rash resembling the 'white island in a sea of red', a typical skin manifestation of dengue. This, coupled with his travel history to

dengue-endemic areas, raised suspicion. Although blisters seemed more prominent, hypotension was also characteristic. To the best of our knowledge, only three case reports have described vesiculobullous lesions in patients with dengue fever.[8-10] However, it may be more common than previously thought. In a study from Pakistan,[4] 0.5% of a sizeable cohort of patients with dengue fever reportedly had vesicles.

Diagnosis involves a combination of clinical evaluation, laboratory tests and serological assays. Laboratory findings include thrombocytopenia, leukopenia, elevated liver function test results and hypoalbuminemia.[7] Molecular tests include the detection of viral RNA by real-time polymerase chain reaction (RT-PCR) or detection of dengue virus antigens (e.g. NS1) or antibodies by enzyme-linked immunosorbent assays (ELISA). Histopathology shows non-specific changes, such as superficial perivascular oedema, mononuclear infiltration and endothelial swelling of small blood vessels.[2] Direct immunofluorescence results are controversial. Due to non-diagnostic findings, skin biopsy is not generally performed.

Distinguishing dengue from other mosquito-borne febrile illnesses, such as chikungunya, Zika virus infection and even malaria, can be challenging due to overlapping clinical features. Bleeding manifestations are relatively specific to dengue, while arthralgia is more common in chikungunya.[1] In addition, Zika is often accompanied by conjunctivitis.[1] Our patient did not report any joint or ocular symptoms, which allowed us to rule out these diseases. Temporal correlation with drug intake, as well as histopathological features like extensive basal cell damage or necrotic keratinocytes, may favour a drug exanthem, whereas lymphocytic vasculitis suggests a viral aetiology[11] though, in this case, we were confused initially. It is noteworthy that eosinophilic infiltration, as seen in our case, may be present in up to 12.5% of viral exanthems.[11]

Dengue fever is usually a self-limiting illness with a mortality rate of less than 1% when identified early; however, it can reach as high as 20% in untreated severe cases.[1] Thus, prompt diagnosis and supportive care, including fluid resuscitation and vital sign monitoring, are integral parts of treatment.[1] From the findings of this case, dermatologists must be aware of the various skin manifestations of dengue fever and should always consider the possibility of dengue in returning travellers from subtropical regions presenting with fever and rashes.

Key messages

It is important for dermatologists to be aware of the diverse skin manifestations of dengue fever and to consider dengue in the differential diagnosis of returning travellers presenting with fever and rash, as early diagnosis and treatment are key to reducing mortality.

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Conflicts of interest

There are no conflicts of interest.

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