

CLINICAL SCENARIO

Post-travel acute febrile illness – dengue fever

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Clinical scenario

A 70-year-old, Asian man developed fever, rigors, profuse sweating, nausea, vomiting, and a dry cough upon return from a holiday in India to the United Kingdom. He had not taken any malaria prophylaxis prior to his trip. After being symptomatic for 2 days, he saw his general practitioner (GP) who prescribed a 3-day course of chloroquine, metoclopramide, and amoxicillin that the patient completed. Despite this, his symptoms did not improve and so after a total of 6 days, he presented to the hospital. His history is asthma, and he takes Salbutamol inhaler and Seretide 500 accuhaler.

On examination, he looked unwell, although his temperature was 37.2°C and all other routine vital sign observations were normal. His general physical examination was normal, and there was no neck stiffness or neurological deficit, and Kernig's sign was negative.

His full blood count, renal function, electrolytes, liver, and bone profile were normal except for a platelet count of $58 \times 10^9/L$ (150–450) and alanine aminotransferase (ALT) of 93 iu/L (< 41). Creatine kinase (CK) was greater than 1,000 iu/L (40–320), and Troponin T (TT) was negative at less than 0.01 µg/L. C-reactive protein (CRP) was less than 5 mg/L. Blood culture was negative. Blood film showed a red cell inclusion body, but no malaria parasites were seen. Urine dipstick, chest radiography, and electrocardiography were all normal. On advice of the infectious disease unit, Dengue immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies were detected; Rickettsial serology was negative for Spotted fever and Epidemic typhus IgG/IgM antibodies.

1. How would you manage the patient?
2. What are the differential diagnoses?
3. What are the disease variants for Dengue Fever?
4. How can this disease be prevented?

Short answers

1. Isolate in a side ward, rehydrate with intravenous fluids and regular analgesia such as paracetamol and

bed rest. Not all hospitals have an infectious disease unit, and in those situations, the microbiologist's opinion should be sought.

2. Differential diagnosis includes Dengue Fever, Rickettsial fever, Leptospirosis, Typhoid fever, Zika virus, Measles, Influenza (Flu), and COVID-19 (Coronavirus disease was not a recognised viral infection at the time this case was seen and was not tested for). The differential diagnoses above are broad and can be narrowed down as most of these do not usually cause a greatly increased creatinine kinase.

In a person with post-travel fever not responding to the initial treatment by the GP, then Dengue or Rickettsial fevers should be tested for in those who have been to endemic areas. Symptoms of Rickettsial infection classically include the triad of fever, headache, and a petechial or maculopapular rash. It may include lymphadenopathy [1]. Dengue fever can be associated with a rash, but it is more likely to be associated with thrombocytopenia than Rickettsial fever [2].

3. Classic (uncomplicated) dengue fever, dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS).
4. Mosquito control and vaccination.

Extended answers

1. Having taken a detailed history, including the evolution of symptoms, contact and travel history, you will perform viral blood serology for Dengue fever, Rickettsia virus, viral polymerase chain reaction (PCR), and viral antigen detection such as nonstructural protein 1 (NS1).

The mainstay of management is supportive therapy. Bed rest, regular analgesia, and fluid replacement for adequate hydration are essential. Aspirin and nonsteroidal anti-inflammatory drugs should be avoided as these drugs may worsen the bleeding tendency associated with some of these infections. Platelet and/or

red cell transfusion are indicated in rare cases of severe thrombocytopenia or significant bleeding [3, 4].

- Differential diagnoses have been listed in the short answer and will now limit discussion here to Dengue fever, which is also known as breakbone fever or bonecrusher disease. It is an acute onset febrile viral illness prevalent in the tropics and subtropics. It is caused by four closely related virus serotypes of the genus *Flavivirus* – DEN 1, 2, 3, and 4. There is no cross-protection against each serotype. An individual can be infected by all 4 types at different times during their lifetime, but only once by the same type. However, the individual develops lifetime immunity to the particular serotype to which the patient was exposed. It is transmitted to humans by the bite of an infected *Aedes* mosquito. The incubation period ranges from 3 to 15 days before signs and symptoms of dengue fever appear [2, 5].
- The classic (uncomplicated) dengue fever presents with high fever with no localising source of infection, headache, low backache, petechial rash, myalgia, arthralgia, abdominal pain, nausea, vomiting, or diarrhoea. Thrombocytopenia and relative leucopenia can occur. The acute phase lasts for 1–2 weeks; convalescence may take several weeks. DHF presents with features of classic dengue, in addition to marked damage to blood and lymph vessels. It

causes bleeding from the nose, gums, and under the skin. DSS presents with features of DHF in addition to massive bleeding and hypovolaemic shock. It is common in children and has a mortality rate of about 6–30% [5–7].

- Prevention is mainly by mosquito control. Avoid mosquito bites by using mosquito nets, insect repellents, and wearing protective clothing. Screen windows and close doors. Reduce mosquito breeding sites by avoiding water collecting in containers such as flowerpots, bottles, cans, etc. Use insecticides to reduce the adult mosquito load.

Two vaccines have now been approved for use. They are Qdenga, a live tetravalent attenuated vaccine for adults, adolescents, and kids from 4 years of age [8] and Denagvaxia for people with previous infection, in populations with a high rate of prior infection by age 9 [9].

Patient outcome

The patient got better with supportive management, and his platelet normalised at discharge.

Epidemiology of dengue fever

Dengue fever is endemic in more than 100 countries in Africa, the Americas, South-East Asia, The Western Pacific, and eastern Mediterranean (Fig. 1). It is found in

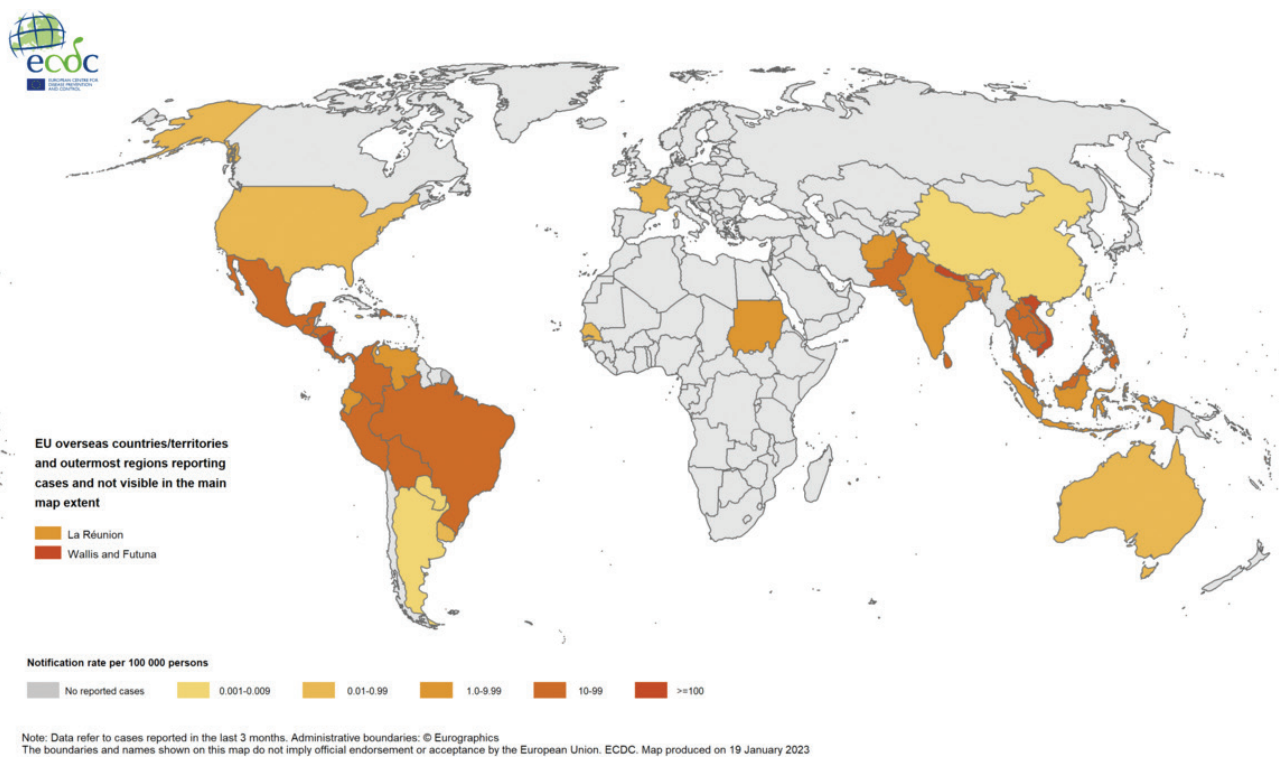


Fig. 1. Geographical distribution of Dengue cases reported Worldwide. Three-month dengue virus disease case notification rate per 100,000 population, to January 2023 [12].

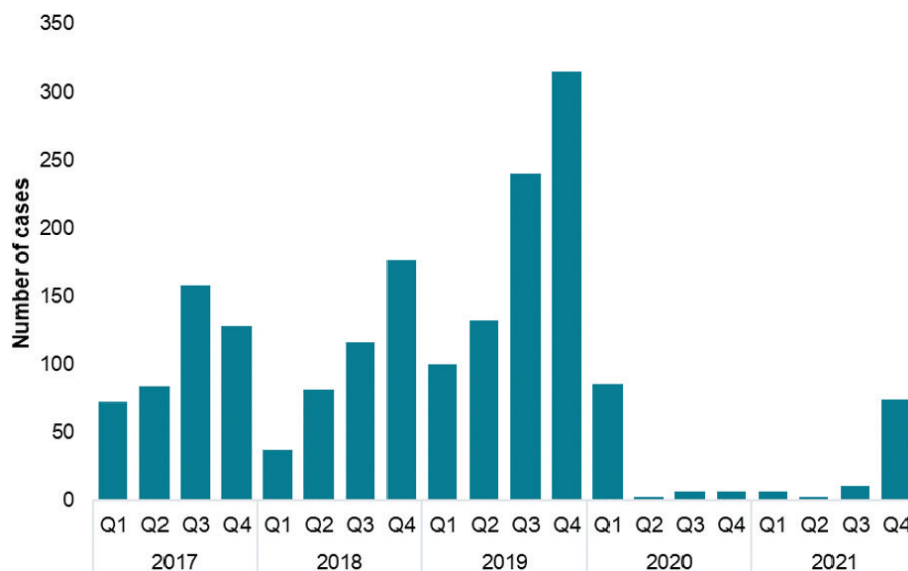


Fig. 2. Total case of dengue reported in England, Wales, and Northern Ireland by quarter: 2017–2021 [13].

tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas. Global incidence of dengue has grown dramatically with about half of the world's population now at risk. It is estimated that 100–400 million infections occur each year, and 40–80% of dengue infections are mild or asymptomatic [10, 11].

In UK, between 2015 and 2019, there were an average of 505 dengue cases reported each year, with a peak in 2019 of 787 cases. There were 102 dengue cases reported in 2020 (101 in England and 1 in Wales), which was an 87% decrease compared to 2019. Of these, 86 (84%) were confirmed cases, and 16 (16%) were probable cases. There were 95 cases reported in 2021 (93 in England, 1 in Northern Ireland, and 1 in Wales), of which 87 (92%) were confirmed cases and 8 (8%) were probable cases. The large decrease in cases in 2020 and 2021 (Fig. 2) compared to 2019 coincides with the COVID-19 pandemic where international travel greatly reduced and so there were fewer cases of travel-associated infections [13].

Learning points from this case scenario

1. In recent decades, the incidence of dengue has grown dramatically around the world.
2. Many cases are underdiagnosed as other febrile illnesses.
3. Have a high index of suspicion in patients with a history of travel to/residence within 2-week period of onset of symptoms in an area it is known to occur.
4. It is a notifiable disease in Europe.

Conflict of interest and funding

There are no conflicts of interest.

Consent: The patient illustrated in this case gave his consent.

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