CASE OF THE MONTH

A Curious Case of Afebrile Dengue

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Abstract

A 50-year-old male presented to us with features of diabetic ketoacidosis which was managed with adequate hydration and insulin therapy. His routine laboratory investigation revealed transaminitis, acute kidney injury and pancytopenia. Further evaluation for hematological and biochemical derangements uncovered positive dengue test (NS1 antigen and polymerase chain reaction assay). Patient distinctively reported no history of fever and remained afebrile during the course of illness. We report this case to highlight the possibility of afebrile dengue in endemic areas.

Case Report

A 50-year-old male, nursing orderly at our hospital presented to us with complaints of fatigue for a few hours while on duty. He was a known diabetic, secondary to chronic calcific pancreatitis, on oral anti-diabetic drugs since last 12 years. He was advised insulin on multiple visits previously but he never complied. He was hemodynamically stable at the time of presentation but was found to have uncontrolled sugars (>700 mg/dl) and high anion gap metabolic acidosis. With a diagnosis of diabetic ketoacidosis (DKA), he was managed with intravenous fluids and insulin. His sugars were corrected within 24 hours of presentation and he was switched to subcutaneous insulin. On routine investigation, he was found to have pancytopenia, elevated liver enzymes and deranged kidney function (Table 1). His urine routine showed 3-9 pus cells/ high power field but the cultures were sterile. Chest X-ray was clear. Procalcitonin levels were less than 0.5 ng/ml. Vitamin B12 and folic acid levels were normal. His platelet count fell to 12,000/ cu.mm in two days of admission.

The blood samples were sent for testing dengue NS1 antigen (Panbio Dengue Early ELISA, Standard Diagnostics Inc., Korea) which came out to be positive. This was confirmed with a reverse transcription polymerase chain reaction (RT-PCR) test for dengue virus (FTD Dengue/Chik, Fast Track Diagnostics, Luxembourg) in the same blood sample. On the sixth day of illness, his blood sample was tested for anti-dengue IgM antibodies (Dengue IgM Capture ELISA, NIV, Pune, India) which was also reported positive (Table 2).

His hospital stay was however complicated with hospital acquired pneumonia due to methicillin resistant *Staphylococcus aureus* (MRSA) which was managed with intravenous vancomycin (Figure 1). His complete blood count, liver function tests and kidney function tests returned to normal by ninth day of the illness.

Discussion

Dengue is an acute febrile illness, endemic to most parts of the Indian subcontinent, frequently striking as outbreaks.[1] Although, majority of patients with dengue are asymptomatic, fever is the commonest presentation in symptomatic patients. It typically presents with an acute onset high grade fever, myalgia and retro-orbital pain.[2] However, the febrile response may be masked in certain conditions like diabetes, old age and other immune-compromised states.[3] Here, we present a case of afebrile dengue with severe manifestations in a diabetic patient with uncontrolled sugars.

Since, DKA is usually precipitated

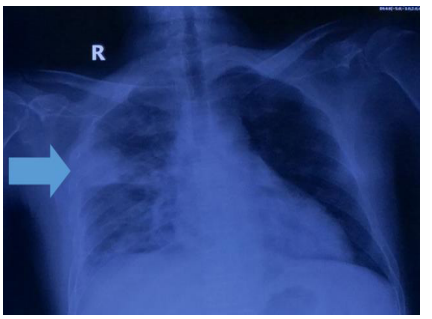

Fig. 1: Chest X-ray on seventh day of illness showing diffuse infiltrates in the right hemi-thorax with consolidation in the right middle zone suggestive of hospital acquired pneumonia

Table 1: Laboratory parameters of the patient with reference values

Laboratory parameters	At admission	At discharge	Reference values
Hemoglobin (g/dl)	9.7	8	12-15
Hematocrit (%)	28.2	21.8	40-50
Total leucocyte count (/mm^3)	2500 (N66, L25, M8)	4700 (N84, L7, M9)	4000-11000
Platelet count (/mm^3)	50,000	1,82,000	150000-400000
Total bilirubin (mg/dl)	0.5	1.1	0.8-1
Aspartate transaminase/ Alanine transaminase (IU/l)	132/62	30/12	Up to 50
Urea/ Creatinine (mg/dl)	81/1.2	20/0.6	0-40/0-1

Abbreviations: g/dl- gram per deciliter, mm^3- cubic millimeter, mg/dl- milligram per deciliter, IU/L- International units per liter

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Received: 20.04.2018; Accepted: 30.04.2018

Table 2: Dengue tests done on different days of illness

Test	Day of illness	Result
NS1	3	Positive
Reverse transcriptase polymerase chain reaction assay	3	Positive
IgM capture Enzyme linked immunosorbent assay	6	Positive

by an infection in the urinary or respiratory tract, the patient was evaluated for both. He had no localized symptoms for either and his routine urine examination and chest X-ray were normal, at the time of presentation. There was no evidence of sepsis at the time of evaluation, with patient being hemodynamically stable and reports showing normal serum procalcitonin. As the patient presented during the ongoing outbreak of dengue, he was evaluated for dengue and was found to be positive.

Classically, dengue is suspected in patients with high grade fever with or without haemorrhagic manifestations and features of plasma leakage. However, it has been observed in certain reports that some patients may not mount a febrile response but have other clinical, biochemical and hematological features consistent with dengue.[4] In a series of children with mild symptomatic dengue from Thailand, over 20% of the children were afebrile but had other symptoms.[5] It has been observed in few studies that the mononuclear cells of diabetic patients secrete less inflammatory cytokines (IL-1 and IL-6) and consequently may not mount fever in response to infections.[6] It is possible that the febrile response could have been blunted due to the presence of concurrent diabetic keto-acidosis. Dengue fever is associated with multiple organ involvement including hepatic and renal dysfunction. Transaminitis is a very common manifestation of dengue fever with frequencies as high as 90% reported in the published literature.[7] Aspartate transaminase (AST) is commonly more elevated than alanine transaminase (ALT) in dengue as AST is also secreted from other sources besides liver (myocytes, cardiac myocytes). While, AKI is reported in about 0.8 to 14% of dengue patients, its etiopathogenesis is still uncertain with no single superior hypothesis.[8] Both, leucopenia and thrombocytopenia have been used in differentiating dengue from other febrile illnesses, especially in adults.[9] The presence of these features, in the setting of dengue outbreak, prompted us to evaluate the patient for dengue. The presence of dengue NS1 antigen in the first five days and seroconversion to IgM positivity on the sixth day led us to the diagnosis of dengue. Detection of dengue RNA by RT-PCR further confirmed our diagnosis.

Therefore, in an endemic area, dengue should always be kept as an important differential diagnosis in patients with leucopenia and severe thrombocytopenia, even in absence of fever, especially during period of outbreak. We present this case to highlight the possibility of afebrile dengue in immunosuppressed patients.

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