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Case Report

A rare association of dengue meningitis with *Plasmodium vivax* malaria

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ABSTRACT

Neurological manifestations in dengue are now well known. Encephalitis is the most common manifestation, but meningitis is a rare phenomenon. We described a 10-year-old child who did not have typical features of dengue and presented with meningeal signs at the end of 2nd week of fever along with raised intracranial tension. Repeat fever work up in view of persisting fever spikes was suggestive of malaria coinfection. The association of dengue and malaria is not an uncommon entity; although both diseases are transmitted by a different type of arthropod vectors.

Key words: *Dengue, Malaria, Neuroretinitis*

The association of dengue infection and neurological abnormalities was first described by Sanguansermsri and colleagues in 1976, in a patient presenting with encephalopathy [1]. Encephalitis is the most common neurological manifestation of dengue infection [2], and the main symptoms include seizures, altered consciousness, and headaches. However, unlike other viral infections, meningitis due to dengue virus is rare. We report a case of dengue with meningitis and coinfection with malaria.

CASE REPORT

A 10-year-old male patient admitted to pediatric ward of a tertiary care hospital was symptomatic with intermittent fever for the past 14 days which was associated with chills and rigors and was increasing in intensity. Fever was also associated with vomiting, which was non-bilious and nonprojectile, 1-2 episodes/day. The patient also had a complaint of a headache, neck pain, and abdominal pain with loose stools for the last 5-6 days. There was no history of seizures/joint pain/rash and/or bleed from any site.

On examination, he was conscious and oriented to time, place, and person. His weight was 28 kg (15th-50th percentile) and had height 125 cm (3rd percentile). His pulse rate was 110/min, respiratory rate 25/min, blood pressure 93/60 mm Hg, and had SpO_2 96-99% in room air. He had periorbital puffiness, neck rigidity, and positive Kernig's sign. Rest of the systemic examination was unremarkable. The patient was already evaluated outside for fever in which NS1 antigen and dengue serology were positive immunoglobulin G and M (IgG and IgM) and had thrombocytopenia (89,000/cumm). In view of meningeal signs, the possibility of aseptic meningitis or partially treated meningitis was kept.

The patient was started on ceftriaxone and vancomycin. Fundus showed papilledema grade 4 for which he was put on mannitol. Guarded cerebrospinal fluid (CSF) was done after 48 h of mannitol when fundus showed some improvement, papilledema regressed to grade 2-3, and computed tomography (CT) brain was also normal. CSF showed 30 cells/cumm (mostly lymphocytes 90%), 98 mg/dL protein, 86 mg/dL sugar against 131 mg/dL of blood sugar, and CSF culture was sterile. CSF for IgM dengue was planned, but this facility was not available in the hospital.

After 48 h of mannitol, the patient was put on acetazolamide. Patient's fever spikes continued, and he developed respiratory distress on day 5 of admission. The patient had decreased air entry on the right side, and chest X-ray (CXR) showed pleural effusion and cardiomegaly, but his blood pressure was within normal limits. Pleural tap was done which showed lymphocytic transudate. His blood culture also came out to be sterile. In view of persisting fever spikes, repeat peripheral smear for malarial parasite was sent on day 5 of admission which came out to be positive for *Plasmodium vivax*. The patient had already received chloroquine outside for fever, so he was started on injectable artesunate for 2 days followed by oral artemether-lumefantrine combination for the next 3 days. Fever spikes decreased, his distress settled, CXR cleared, and patient's general well-being improved.

Antibiotics ceftriaxone and vancomycin were continued for 14 days to give benefit of doubt to cover bacterial meningitis as we were not able to do CSF at admission because of raised ICT; although there was nothing to support the diagnosis of pyogenic meningitis. The patient was discharged after 14 days. The patient was followed after 1 week. He complained of mild decrease in vision for which repeat ophthalmological consultation was sought. His vision was 6/12 and fundus showed macular star formation which was suggestive of papilledema. Acetazolamide was continued for 2 more weeks. After 2 weeks of follow-up, he was completely asymptomatic.

DISCUSSION

The neurological manifestations of dengue are mainly associated with dengue virus type 2 (DENV-2) and DENV-3. Although rare (1-5% of dengue cases), the neurological involvement have been increasingly reported in dengue epidemics. Furthermore, the cases may be underestimated [3]. The neurological complication can occur in patients with few or no signs of previous dengue infection. The age of patients ranging between a few months to 79 years old, being more frequent in children. In most of the cases, the neurological manifestations appear between 2 and 30 days after the onset of the fever [4].

In our case, the patient presented with neurological manifestation on day 12-13 days of fever that is the end of 2nd week of fever with neck rigidity, headache with normal sensorium. Our case did not have the typical clinical features of dengue infection. There was no history of arthralgia and bleeding manifestations. The main symptoms were high-grade fever with severe generalized headache. A headache is a very common symptom in patients with dengue fever, and severe or very severe headache is reported in 79% of patients with dengue fever [5]. As CSF analysis is not done routinely to differentiate "non-specific dengue headache" from dengue meningitis, a number of patients with dengue meningitis may remain undiagnosed [6]. However, in addition to a headache, the presence of neck stiffness with a positive Kernig's sign with normal sensorium in our patient pointed toward the clinical diagnosis of aseptic meningitis because of dengue.

The exact mechanisms by which dengue virus causes central nervous system (CNS) involvement are unclear, but experimental evidence suggests direct tissue lesion caused by the virus because of its neurotropicity, capillary hemorrhage, disseminated intravascular coagulation, and metabolic disorders, which might play a role [7]. Encephalitis, myelitis, and meningitis are the most important neuroinvasive diseases associated with dengue. However, unlike other viral infections, meningitis due to dengue virus is rare, being more frequent in children. In these cases, the clinical manifestation is similar to the other viral meningitis [6].

The presence of dengue IgM, viral antigens, or virus ribonucleic acid (RNA) in patients with acute neurological symptoms is sufficient for the diagnosis of neurological disease associated with dengue virus infection. Regarding specific tests for dengue infection in CSF, specific antibody (IgM and IgG), RNA or viral antigen should also be evaluated. Antibodies can be detected in CSF in the early stages of dengue CNS infection up until 5-7 days after the onset of neurological symptoms [8]. The dengue IgM detection by enzyme-linked immunosorbent assay presented a high specificity (97-100%) but the sensitivity varied between 0% and 73%, depending on the method used. The absence of specific IgM detection in CSF, however, does not exclude dengue as the causative agent of neurological disorder [8]. It is important to note that the detection of specific IgG in CSF is not a useful diagnostic tool, since, they may be due to a prior infection and they can cross the blood-CSF barrier [9].

Other point of discussion, in this case, is the presence of papilledema which later on developed into macular star formation which was confused with neuroretinitis which is again more uncommon entity associated with dengue infection. Differentiating point was that patient complained of mild vision loss that too after discharge. He only complained of diplopia and headache during admission which was suggestive of raised intracranial tension. He had grade 4 papilledema with no exudates. Neuroretinitis is a particular form of optic neuropathy characterized by an acute unilateral visual loss in the setting of optic disc swelling and hard exudates arranged in a star figure around the fovea [10]. Neuroretinitis is commonly associated with an antecedent viral syndrome, suggesting a possible viral etiology for up to 50% of the cases [11]. It is usually unilateral but may be bilateral in 5-30% of the cases [12].

Finally, this patient had co-infection of malaria and dengue. Both are arthropod-borne diseases. It would be expected that coexisting malaria and dengue infection would be common in areas where both illnesses are endemic. Dual infections with two infectious agents can result in an illness having overlapping symptoms, resulting in a situation where both diagnosis and treatment of a patient may become difficult for a physician. The patients with combined infection had prolonged fever of more than 7 days, myalgias, bleeding manifestations, rash, and anemia. Carme et al. [13] reported the specific rate of concurrent infection of malaria and dengue from overall febrile patients equal to 0.99% that means there is high chance of malaria–dengue coinfection in South-East Asian region, including India, yet these are unusually reported. Coinfection of malaria and severe dengue has been reported to be in the range of 20% to as high as 80% [14-16]. The reason may be both the illnesses present with acute febrile illness with overlapping symptoms and when one particular infection is diagnosed; the possibility of concurrent infection may not be suspected.

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