



Case Report

Concomitant Triple Infection Of Dengue, Malaria And Enteric Fever- A Rare Case Report

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ABSTRACT

Dengue, malaria and enteric fever are the important causes of fever in Maharashtra especially during rainy season. Each of these diseases can substantially contribute to mortality if not diagnosed and treated early. Co-infection of dengue with malaria, other viral infections, enteric fever, leptospira etc has been described in many parts of the world but triple infection with dengue, malaria and enteric fever in the same patient is very uncommon. We report a rare case of 38 year old male, who came to our hospital for continuing fever of more than a week with rash, breathlessness and pain in abdomen.

He was febrile, conscious and coherent and his other vitals were stable. His blood picture showed leucopenia and thrombocytopenia, while other biochemical tests were normal. Dengue NS1 antigen and IgM ELISA were positive. Malarial antigen was positive for *P. falciparum* and widal test showed a titre of TO-1:240 and TH- 1:240. His blood culture showed growth of *Salmonella Typhi*, confirming typhoid co-infection. He was treated with intravenous Artesunate, Ceftriaxone, along with symptomatic treatment. He responded to treatment and was discharged after near normalization of general condition.

Key Words: Dengue, NS1 Antigen, MAC ELISA, Malaria, Enteric fever, Triple infection

INTRODUCTION

Malaria and enteric fever are common causes of fever in many parts of Maharashtra. Vidarbha region reported maximum deaths due to malaria in the past decade and the figure is unlikely to change in future. Recently, the incidence of dengue fever is on the rise in these regions. Co-infection with dengue with malaria and malaria with enteric fever are reported in

literature from many parts of the world. [1,2] We report a rare case of triple infection with dengue, malaria and enteric fever in the same patient. Only one case of dengue, malaria and enteric fever co-infection is reported in literature, to our knowledge. [3]

CASE REPORT

A 38 year old male patient came to our hospital with unrelenting fever for eight

days with rash, breathlessness and pain in abdomen. Patient was admitted and complete blood count, peripheral blood smear, dengue rapid test, dengue ELISA test, widal test and blood culture were done. During hospital stay, he continued to have high grade fever with chills, rigors and severe prostration. Fever was intermittent, associated with headache and joint pains, nausea and diffuse pain in abdomen. Rash was diffuse erythematous, blanchable and disappeared two days later. On examination his vitals were stable. He was conscious and coherent. There was no cardiac murmur and lungs were clear. There was a palpable spleen four cm below the left costal margin and abdomen was diffusely tender.

Investigations showed hemoglobin 10.2 gm/dl, total count was 2,800 cells / mm³, neutrophils- 52.4 %, lymphocytes-30.5%, eosinophils-7.1%, ESR-35mm/hr, platelet count 1, 07,000/ mm³. Malarial antigen (paracheckpf rapid test for *P. falciparum* malaria (ver.3) dipstick, 98.2% sensitive and 99.3% specific to *P. falciparum* malaria against microscopy) was positive for *P.falciparum* and peripheral blood smear showed gametocytes of *P.falciparum* (**Figure-1**). He was positive for dengue NS1 antigen and dengue IgM antibody but negative for dengue IgG antibody by dengue rapid test (Dengue Day 1 Test kit by J. Mitra and Co. Pvt. Ltd. India. Dengue NS1 Ag – Sensitivity 100%, Specificity 99.94% and Dengue IgM/IgG Antibody -Sensitivity 100%, Specificity 99.88%). IgM Capture ELISA was positive for dengue (NIV DEN IgM Capture ELISA kit by NIV, Pune, India Sensitivity - 98.53%, Specificity - 98.84%). Widal test had shown a titre of TO-1:240, TH-1:240. On first subculture only, blood culture showed the growth which with further biochemical testing and serotyping was confirmed to be *Salmonella Typhi*. (**Figure-2**). Antibiotic sensitivity test was done on

Mueller Hinton agar plates by Kirby Bauer disc diffusion method as per CLSI guidelines 2014 [4] and was susceptible to Ampicillin, Cotrimoxazole, Cefotaxime, Ceftriaxone, Chloramphenicol and Ciprofloxacin. Ultrasonography of abdomen showed mild hepatomegaly and moderate splenomegaly.

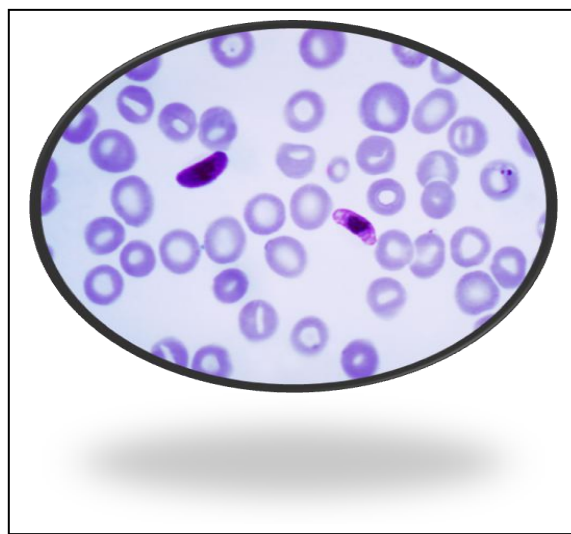


Figure 1- Peripheral blood smear showing gametocyte of *Plasmodium falciparum*

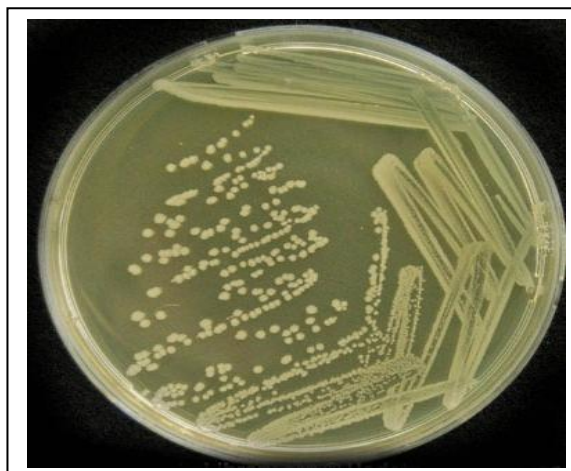


Figure 2 – Colonies of *Salmonella Typhi* on Nutrient agar plate

Therefore, the diagnosis of mixed infection of Dengue and *P.falciparum* malaria and enteric fever was concluded.

Patient was started on Tab. Primaquin 45 mg stat for gametocyte

eradication of *P.falciparum*, Inj. Artesunate 120 mg, Inj. Ceftriaxone 4 gm/day. Sufficient I.V fluids were given and Tab Paracetamol was given as required. Treatment was continued for seven days. At the time of discharge he was afebrile and his platelets were normalized. At follow up after one week he had no complaints.

DISCUSSION

Dengue, malaria, and enteric fever are endemic in South Asia and represent a major public health problem. Concurrent infection of dengue with malaria [5-7] and malaria with enteric fever [2] have been reported in past and acquisition of both infections is not uncommon among inhabitants in these regions. They are major etiological considerations in both acute and prolonged fever of unknown origin (PUO) in the tropics. In our case, we found the concurrent infection by dengue, malaria and enteric fever, which is unusual.

Dengue infection is caused by dengue virus which is single stranded RNA virus belonging to family flaviviridae and genus flavivirus. It has four serotypes - DENV-1, DENV-2, DENV-3 and DENV-4 which are closely related but antigenically distinct. Principle transmission vectors are arthropods of the *Aedes* genre, especially *Aedes aegypti*. [8-10] Malaria is caused by parasite *Plasmodium*, most commonly by *P. falciparum*, *P. vivax*, *P. malariae* and rarely by *P. ovale* which is relatively common in Western Africa. [11] The etiological agent of typhoid fever is *Salmonella enterica* sub-sp *enterica* serotype *Typhi*. Human beings are the only reservoir and host for typhoid fever. [12]

Dengue fever occurs predominantly in monsoon and post monsoon period because of mosquito burden and corresponds with the peak incidence period for malaria and typhoid. Short term changes in temperature, precipitation and humidity

are often correlated with dengue incidence. Other important factors include population growth, urbanization, lack of sanitation, increased long distance travel, ineffective mosquito control, deforestation and agricultural settlements in peri-urban areas. [13,14] Enteric fever is transmitted by feacally contaminated water and food in endemic areas especially by carriers handling food. [12] Because these infections share social circumstances which are imperative to their transmission, individuals in areas endemic for these diseases are at substantial risk of contracting these, either concurrently or an acute infection superimposed on a chronic one. [15]

The actual and precise underlying mechanisms to explain the association between dengue, malaria and enteric fever infection is still uncertain, although there are few postulations which may explain why malaria may predispose to *Salmonella* bacteremia and sepsis. Dengue virus, like many other viruses can reduce the total lymphocyte count and transient bone marrow suppression can result in marked neutropenia. It can induce IL-10 production which down regulates monocytes and promotes alloantigen specific unresponsiveness of human CD8+ T cells, the effect lasting upto two weeks. [16] This can result in increased susceptibility to secondary infections, especially during the convalescence period. It has also been shown that antibody response to O antigen of *S. Typhi* was markedly reduced in acute episode of malaria compared with that in controls where humoral immunity is transiently impaired. [17]

Although dengue, typhoid and malaria are caused by very different organisms - one a RNA virus, a gram negative bacilli and the other a protozoan and are transmitted via different mechanisms, they share rather similar symptomatology. Clinically two major types

of the dengue fever are recognized - Primary and Secondary. Primary dengue infection typically results in a self limiting disease with sudden onset of fever, severe headache, retro- orbital pain, body aches, joint pain and rash. Secondary dengue infection is caused by a second exposure by a different serotype, more serious and can result in Dengue Haemorrhagic Fever [DHF] and Dengue Shock Syndrome [DSS]. [18-20] Malaria and typhoid fever often present with mimicking symptoms especially in the early stages of typhoid fever characterized by an acute illness, the first typical manifestations of which are fever, headache, abdominal pain, relative bradycardia, splenomegaly and leucopenia. [21-24] Co-infected patients presented similar days of fever as compared to malaria patients. That means that a patient with the diagnosis of dengue presenting with prolonged evolution should raise the suspicion of co-infection with malaria or enteric fever.

Dengue is diagnosed by NS1 antigen kits which are commercially available, which are highly specific but sensitivity drops after first week of fever and may become negative subsequently. The accuracy of serological diagnosis of dengue fever in cases of malaria has been questioned previously, because of some nonspecific reactivity of certain rapid serological assay. In this case, NS1 antigen and IgM antibody positive for dengue by the rapid test was further confirmed by NIV DEN MAC ELISA, which has > 95% specificity.

Conventional light microscopy is the established method for the laboratory confirmation of malaria. The careful examination by an expert microbiologist of a well-prepared and well stained blood film remains currently the “gold standard” for detecting and identifying malaria parasites. It is sensitive, informative, relatively an inexpensive general diagnostic technique.

[25] We were able to detect *P.falciparum* and its gametocyte in thick and thin smears.

The definitive diagnosis of typhoid fever requires the isolation of *Salmonella enterica* serotype *Typhi* from the patient. Cultures of blood, stool, urine, rose spots, blood mononuclear cell-platelet fraction, bone marrow and gastric and intestinal secretions can all be useful for diagnosis. [23] Widal test is readily available and an inexpensive test, introduced as a serologic technique. It has been used for more than a century. Enteric fever in this patient was diagnosed on significant titres of Widal test and subsequent confirmation was done with isolation of *Salmonella Typhi* in blood culture.

This makes us believe that the patient was suffering from dengue, malaria as well as enteric fever.

Supportive treatment for dengue fever is sufficient while monitoring for complications is a must. Thrombocytopenia in this case might be caused by both dengue and malaria. Thrombocytopenia requires correction preferably with single donor platelets if there is systemic bleeding or if platelets are below 20,000-30,000/mm³, depending on clinical judgment. On the other hand, severe *P. falciparum* malaria should be aggressively treated with Artemesin based combination therapy as delayed treatment can substantially increase the mortality. [26]

Typhoid infection shows variable patterns of fever in the first week and if untreated, can result in serious complications like encephalopathy and bowel perforation later on. [27] Occasional resistant strains had been identified in the laboratory so antibiotic susceptibility testing should be carried out in each case. In the present study, it was found to be susceptible to Ampicillin, Cotrimoxazole, Ceftriaxone, Cefotaxime, Chloramphenicol and Ciprofloxacin.

It is estimated that 2.5 billion people are at risk for dengue infection of which nearly 100 million people contract dengue fever annually and over 250,000 progress to DHF and DSS. [28,29] About 95% population in the country resides in malaria endemic areas and 80% of malaria reported in the country is confined to areas consisting 20% of population residing in tribal, hilly, difficult and inaccessible areas. [30] It is estimated that there are more than 13 million cases of enteric fever occurring annually in Asia alone of which a large proportion occur during childhood and in the wake of emerging multidrug resistant strains, the disorder is known to be associated with significant morbidity and mortality. [31-33]

CONCLUSION

Concurrent infection of these three infectious agents resulting in an illness having overlapping symptoms should be kept in mind. So, it is very essential to make early and confirmed diagnosis to initiate prompt treatment to prevent resulting morbidity and mortality in otherwise misdiagnosed or untreated cases.

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