A CASE OF MIXED INFECTIONS IN A PATIENT WITH AFI.

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Introduction:
Concurrent infections with more than one etiological agent can result in an illness with overlapping symptoms, resulting in a situation where the diagnosis and management of such a patient could be challenging. A case of a patient who presented with fever and thrombocytopenia with multiple positive laboratory results pointing to several possible aetiologies. I would like to highlight several learning issues from this case.

Case Report
A 56-year-old male patient admitted in a tertiary care hospital, initially presented with complaints of high grade fever with rigors for six days duration which was associated with throbbing headache, pain, generalized body ache, myalgia, fatigue, and anorexia. He denied about any bleeding tendencies or skin rash. The patient worked as a driver. There was no significant past medical history. Although he lived in an urban area known to be endemic for dengue, presently, no fogging has been carried out in that area. On examination, the patient was conscious and oriented, but was mildly dehydrated. No skin rashes or hemorrhagic manifestations were observed. His blood pressure was 110/70 mmHg and the pulse rate was 100/min which was regular and of good volume. His temperature was 38.6°C. Examinations of the respiratory, cardiovascular, and gastrointestinal systems were unremarkable. An initial diagnosis of dengue in the febrile phase of the illness was made based on the presenting features of this patient and a positive dengue IgM result was found using IgM test. The patient also had thrombocytopenia which was consistent with the diagnosis of dengue. He was managed with appropriate supportive therapy and hydration with crystalloid fluids according to established guidelines for dengue. Despite this, the patient remained febrile on day 8 of illness.

| Laboratory result | Reference range | Day of illness (day of hospitalization)* |
|-------------------|----------------|----------------------------------------|
| Hemoglobin        | 13.8–17.2 g/dl | 11.6 11.4 12.8                         |
| WBC               | 4,000–11,000 cells/cmm | 3.6 4.5 6.3                         |
| Platelet count    | 1.5–4 lakh/cmm  | 60 90 189                               |
| Hematocrit        | 40–50%          | 40.9 39.2 42.1                         |
| Serum creatinine  | 0.4–1.4 mg/dl   | 1.21 1.02 0.86                        |
| Serum urea        | 10–45 mg/dl     | 32 40 42                                |

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Serum alanine transaminase  |  <45 U/L  |  55  |  40  \\
Dengue IgM (ELISA)      |  Positive  |  -  |  -  \\
Leptospira IgM rapid test |  Positive  |  -  |  -  \\
Leptospira titer (MAT)  |  -  |  1 : 400  |  Clear  \\
MPFT                      |  P.vivax detected.  |  -  |  -  \\

At this point, the differential diagnoses of malaria and leptospirosis were considered. Patient was then recommended on a daily dose of 1 g Ceftriaxone, which was administered intravenously for 7 days. On the same day, a peripheral blood smear collected and was reported to be positive for Malarial Plasmodium vivax. A dosage of oral Chloroquine at 600mg was initiated immediately followed by another dose of oral Chloroquine 300mg at 6 hours after the first dose and 300mg daily for the next two days as per established guidelines for the treatment of chloroquine sensitive vivax malaria. The patient was also started on daily oral Primaquine 30 mg for 14 days to eradicate hypnozoites in the liver. The blood cultures did not yield any positive growth while the microscopic agglutination test (MAT) for leptospirosis sent on day 8 of illness was reported to be positive with titre of 1 in 600. The MAT was repeated 25 days after the first MAT sample was still positive with a lower titre of 1 in 200. Throughout the illness, the renal and liver function tests of the patient were within normal reference range. By the eighth day of hospitalization, the blood film for malaria parasite was clear. After the commencement of antibiotics and antimalarial agents, the patient’s condition improved remarkably within 24 hours followed by normalization of platelet count over the next 48 hours.

**Discussion:--**

Patient initially presented with symptoms of a nonspecific viral-like illness. The diagnosis of dengue should be considered in a patient presenting with acute febrile illness if he originated from a dengue endemic area. Dengue infection is caused by dengue virus which is a mosquito borne flavivirus. Although the dengue IgM serology was positive, it does not necessarily indicate a recent exposure to dengue virus infection, as the dengue IgM level can remain elevated for up to several months after exposure.

In similar studies it is shown that the dengue test has been reported to cross-react with non flavivirus infections such as malaria, leptospirosis, toxoplasmosis, and syphilis. However, in this patient, several features of his illness were inconsistent with the diagnosis of dengue such as the protracted febrile phase lasting beyond a week and the absence of leukopenia and hemo-concentration in the laboratory investigation results

1. Leptospirosis is a zoonotic infectious disease caused that is transmitted directly or indirectly from infected animals (usually rodents) to human. The diagnosis of leptospirosis in this patient was made based on the microscopic agglutination test (MAT) for leptospira antigen titre of ≥1 : 400. Leptospirosis is sometimes referred to as “The Great Mimicker” and it may be overlooked and underdiagnosed due to its varied clinical presentations.

2. In a hospital-based cross sectional study conducted among 10 healthcare facilities in North eastern Malaysia, only 31% of MAT confirmed leptospirosis cases were diagnosed as leptospirosis on discharge from the hospital while another 38% were erroneously diagnosed as dengue fever or dengue hemorrhagic fever.

3. Due to the overlapping symptoms and signs, malaria may be overlooked in the presence of positive leptospirosis IgM. As malaria and leptospirosis are common in the most of the clinical manifestations, coinfections with these two pathogens are common although they have rarely been reported.

4. In this case, it was found that the positive dengue IgM serology detected early in the patient’s illness was most likely due to cross-reactivity of the laboratory test with malaria parasites, which proved to be misleading in masking the real diagnosis in this patient. The repeat MAT for leptospirosis after 25 days showed a reduction in titre from 1 : 400 to 1 : 100, indicating successful treatment of the leptospirosis

**Conclusion:--**

Co-infections with several pathogens such as dengue, malaria, and leptospirosis are not uncommon in areas of high endemicity for these pathogens in patients presenting with acute febrile illness with atypical manifestations. Interpreting the multiple positive serological results in this setting may be challenging. However, meticulous history taking, careful clinical examination, and careful interpretation of laboratory results based on available evidence will often lead to the correct diagnosis. There is a need for greater awareness amongst clinicians of the possibility of co-infections in a patient presenting with acute febrile illness with subtle atypical manifestations.