

## CASE REPORT

### TYPHOID AND MALARIA CO-INFECTION – AN INTERESTING FINDING IN THE INVESTIGATION OF A TROPICAL FEVER

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In the investigation of fever in the tropics, two important diagnoses to be ruled out are typhoid and malaria. Both cause significant morbidity, mortality and economic loss. An estimated 17 million cases of typhoid are reported worldwide each year, resulting in 0.6 million deaths. Seventy five to eighty percent of these cases occur in Asia alone. Malaria affects 1 billion people each year; out of which 1-3 million die. Although caused by very different organisms – one a Gram negative bacilli, the other a protozoa, and transmitted via different mechanisms – ingestion of contaminated food and water and via the bite of an insect vector respectively, both typhoid and malaria share rather similar symptomatology and epidemiology. Malaysia is endemic for both these diseases and one should not be too surprised when faced with a diagnosis of co-infection of typhoid and malaria, as have been described in India and Canada. Here we describe one such case of *Salmonella typhi* and *Plasmodium vivax* infection.

*Keywords* : typhoid, malaria, co-infection.

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#### Introduction

##### Case Report

A 41-year-old Malay man, working as a logger, presented with two weeks of fever, myalgia and abdominal pain. He had been diagnosed and treated for malaria 20 years ago. He remained asymptomatic until now. He had no other history of traveling to other malaria endemic country and not taking any malarial chemoprophylaxis. On examination, he was febrile with temperatures swinging between 37°C and 39.3°C and relative bradycardia. He was not jaundiced and neither were any rashes noted. There was no hepatosplenomegaly.

His full blood count showed normal Hb (14.2 g/dl) and platelet count ( $201 \times 10^9/l$ ). The white cell count, however was within normal range ( $5.2 \times 10^9/l$ ) with neutrophil predominance. Serum albumin was 34.9 g/l, alkaline phosphatase 178 IU/l, aspartate transaminase 63 IU/l, alanine transaminase 63.9 IU/l and total bilirubin 9.4  $\mu\text{mol/l}$ .

Ultrasonography of the abdomen showed hepatomegaly with a mildly echogenic parenchyma. The spleen was at the upper limit of normal (13.8

cm). Blood cultures isolated *Salmonella typhi*. The first Widal test was not significant (T(O) 1:50 and T(H) 1:50). The second Widal test taken nine days later showed T(O) 1:100 and T(H) 1:200. Serial blood smears for malaria parasites was positive for *Plasmodium vivax* (160/ul blood) on the fifth smear.

He was treated with chloramphenicol 500mg qid for 14 days and a course of chloroquine and primaquine with uneventful recovery.

#### Discussion

Typhomalaria was first described by an army doctor, J J Woodward (1833-1884) in 1862 among young soldiers during the American Civil War who were suffering from febrile illness that seemed to be typhoid (including intestinal lesions found at postmortem) but with fever patterns also suggestive of intermittent fever. He believed that it might be a hybrid rather than a new species of disease (1 - 3). However, by the end of 19<sup>th</sup> century, laboratory tests had eliminated this theory as they found that it was either one thing or the other, or in rare instances, co-infection with both *S. typhi* and the plasmodium of malaria.

Both typhoid and malaria share social circumstances which are imperative to their transmission. Therefore, a person living in such an environment is at risk of contracting both these diseases, either concurrently or an acute infection superimposed on a chronic one. A high index of suspicion is necessary to diagnose a co-infection as most clinicians are used to linking every symptom and sign to a single pathology.

In co-infections, the diagnosis of typhoid should be made from a culture specimen as false positives and overestimation occur with the use of the Widal test. Ammah *et al* reported that in 200 patients with fever, 17% had concurrent malaria and typhoid fever based on bacteriological proven diagnosis as compared to 47.9% based on the Widal test (4). This is to be expected as the Widal test being a serological test, only proves exposure to a certain antigen. It does not tell if an infection is recent or not. Samal *et al*, described 52 patients with malaria positive in the peripheral blood smear (cases consisted of vivax, falciparum or mixed vivax and falciparum), out of whom eight cases had a positive Widal test but blood cultures were negative for *S. typhi* in all. All of the cases were cured with antimalarial therapy (5). There were no complications attributed to these infections documented in the previous reported cases. Nevertheless, complications may occur even if the patients received adequate treatment. Hence, monitoring for the complications is essential especially for travelers traveling to endemic areas.

The actual and precise underlying mechanisms to explain the association between malaria and *Salmonella* species infection is still uncertain. However, there are few postulations which may explain why malaria may predispose to salmonella bacteremia and sepsis. It has 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 (6). It has been demonstrated in a murine model of infection with *Salmonella murium* that hemolysis which occur in malaria may predispose to gram-negative organism as what has been seen in hemolytic disease caused by sickle cell disease and bartonellosis (7).

In the case illustrated above, the diagnosis was from a blood smear and a blood culture, both providing objective evidence of the on-going dual infection. Fortunately, he did not developed any complications such as hemolysis.

Although cases which had been reported were

common among travelers, certain areas in our country is still considered endemic for both malaria and typhoid infections and our patient demonstrated that although he is not a traveler, these co-infection may still occur. Thus, in malarial patient with persistent fever in spite of therapy, one should consider drug resistant as well as concomitant gram-negative infection such as typhoid fever.

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