

CASE REPORT

A UNIQUE CASE OF THROMBOTIC THROMBOCYTOPENIC PURPURA ASSOCIATED WITH PLASMODIUM VIVAX MALARIA

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ABSTRACT

Thrombotic thrombocytopenic purpura is a rare disease characterized by capillary thrombosis and a pentad of findings: microangiopathic anemia, thrombocytopenia, acute renal failure, fever, and fluctuating neurologic abnormalities. We report the unusual case of a young woman with both thrombocytopenic purpura and Plasmodium vivax malaria. A causal relationship between these two diseases remains unclear. Early recognition of thrombotic thrombocytopenic purpura in patients suspected of malaria requires a high index of suspicion, which is crucial for initiating lifesaving treatment. To our knowledge, this is the first case report in Africa of thrombotic thrombocyto-

INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) is a rare disease characterized by capillary thrombosis and a pentad of findings: microangiopathic anemia, thrombocytopenia, acute renal failure, fever, and fluctuating neurologic abnormalities. Malaria, one of the leading public health problems in Ethiopia, can present with similar symptoms, especially in its severe form. The association of TTP and bacterial (*Escherichia coli*, *Shigella*, and streptococcus species) and viral (influenza and HIV) pathogens has been previously documented (1, 2). Recently, malaria has been associated with both TTP and hemolytic uremic syndrome in a series from India (3-5). However to our knowledge, our case of TTP and *Plasmodium vivax* malaria is the first to be reported in Africa. We hope that increased awareness of this association will lead to early initiation of lifesaving treatment in appropriate patients.

CASE REPORT

A 37 years old woman from a malaria endemic region of the country presented to a referral hospital in Bahir Dar, Ethiopia with a one-week history of bilateral flank pain, decreased urine output, and hematuria. Two days prior to admission, she developed high grade intermittent fever, headache, intermittent confusion, tripareisis, skin rash, jaundice, and gum bleeding.

She was found to have thrombocytopenia of 20,000/ul; she was started on Prednisolone (60 mg/day) for presumed ITP and referred to Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa for further investigation and management.

Upon presentation at TASH, vital signs included blood pressure of 120/70mmHg, pulse of 116 beats/min, respiratory rate of 40 breaths/min, temperature of 38.5°C, and O₂ saturation on room air of 78%. In addition, she had conjunctival pallor, scleral icterus, decreased air entry at both lung bases, and multiple ecchymotic lesions of both upper and lower extremities. On neurologic examination, the patient was confused and had tripareisis and exaggerated deep tendon reflexes in all but the right upper extremity.

On investigation, she had multiple laboratory abnormalities, including hemoglobin of 8.5 g/dl (12-18g/dl), platelet count of 6,000/ul (140,000-400,000ul), creatinine of 1.4mg/dl (0.5-0.9mg/dl), BUN of 119mg/dl (10-50mg/dl), total bilirubin of 5.9mg/dl (0.3-1.4mg/dl), direct bilirubin of 0.8mg/dl (0.1-0.4mg/dl), LDH of 670 U/L (115-221U/L), and urinalysis showing 2+ blood and 1+ protein.

Serum electrolytes were all normal. Rapid diagnostic testing for *Plasmodium vivax* was positive. Giemsa blood film staining revealed *Plasmodium vivax* with a low level of parasitemia. Peripheral blood smear showed microangiopathic hemolysis with multiple helmet cells and scanty platelet. Coagulation profiles were normal. Brain computerized tomography (CT) scan was normal and Chest CT showed bilateral basal lung consolidations.

With the consideration of TTP, she was started on plasma exchange treatment. Prednisolone was continued. She was also started on artesunate for malaria and broad-spectrum antibiotics for pneumonia.

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Her clinical course was complicated by respiratory failure on hospital day 2, requiring intensive care unit (ICU) care with intubation and mechanical ventilator. On hospital day 4, her gas exchange improved and she was extubated and liberated from the ventilator. The patient continued to improve with plasma exchange treatment and prednisolone. By hospital day 7, she defervesced and her mentation and strength improved. In addition, her platelet count rose to 221,000/ul and her bilirubin, LDH, and creatinine all normalized. Plasma transfusion, prednisolone and artesunate were discontinued. By day 9, broad spectrum antibiotics were also discontinued. On hospital day 10, her peripheral blood smear showed no signs of hemolysis or hemoparasites. The patient was discharged from hospital on day 14 without any residual deficits.

DISCUSSION

We believe that this is the first case of TTP complicating the course of *Plasmodium vivax* malaria reported from Africa. Although both diseases can present with similar findings, the microangiopathic hemolysis seen in our patient was not associated with disseminated intravascular coagulation (DIC), which is much more characteristic of TTP than malaria. Additionally, our case differs from previous reports in that our patient had TTP and not hemolytic uremic syndrome, and acute kidney injury that did not require renal replacement therapy or transplantation.

This case and previous reports suggest that there might be a causal relationship between *Plasmodium vivax* malaria with thrombotic microangiopathy (TMA) including TTP and hemolytic uremic syndrome (HUS). There have been several proposed

Elevated thrombomodulin, Von Willebrand factor (VWF), platelet activation, endothelial cell injury, complement dysregulation, and the impairment of vasomotor responses and microcirculatory flow may all contribute to the pathophysiology of *Plasmodium vivax* induced TMA (6 - 9). Of course, it is possible that in malaria endemic areas such as Ethiopia, there may be no causal association but just coincidental occurrence of the two disease entities.

CONCLUSION

To our knowledge, our case of TTP and *Plasmodium vivax* malaria is the first to be reported in Africa. A causal relationship between these two diseases may exist but further research is needed. We hope that increased awareness of this association by clinicians will lead to early initiation of lifesaving treatment in appropriate patients.

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