https://doi.org/10.48047/AFJBS.6.15.2024.5361-5363

African Journal of Biological Sciences

Research Paper Open Access

MOSKOWITZ SYNDROME MANIFESTING AS RECURRENT LARGE VESSEL STROKES IN A YOUNG MALE

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Article History

Volume 6, Issue 15, September 2024

Received: 25 Jul 2024

Accepted: 24 Aug 2024

Published: 11 September 2024

doi: 10.48047/AFJBS.6.14.2024.5361-5363

Abstract

Background: Thrombotic thrombocytopenic purpura (TTP) is a rare and life-threatening condition characterized by microthrombus formation due to a deficiency of ADAMTS13, which cleaves von Willebrand factor multimers. This deficiency leads to widespread microangiopathic hemolytic anemia and multiple organ involvement, particularly affecting the brain, heart, and kidneys. TTP can present atypically and poses a diagnostic challenge, especially in young patients with neurological symptoms and thrombocytopenia. Early diagnosis and prompt initiation of plasma exchange therapy (PEX) and steroids are critical to reduce mortality.

Case Report: A 17-year-old male presented in an altered state with weakness in the right upper arm and bilateral lower limbs for 4 days. He had a history of fever and convulsions 4 days prior, with two previous convulsive episodes in the last two years, both of which had resolved without neurological deficits. On examination, the patient was febrile, tachycardic, and drowsy, with left gaze palsy and significant weakness in the right upper limb and both lower limbs. The patient had lost bowel and bladder sensation, and plantar reflexes were bilaterally upgoing.An MRI of the brain with angiogram revealed acute large vessel occlusion in the bilateral anterior cerebral artery (ACA) territory and gliosis in the right middle cerebral artery (MCA) region. Laboratory investigations showed severe thrombocytopenia (platelet count 23k/cumm), anemia (Hb 6.2 g/dL), elevated LDH (1597 U/L), and increased cardiac troponin (35 pg/mL). The patient was diagnosed with TTP and was promptly started on plasma exchange therapy and high-dose steroids. His sensorium improved within 2 days, though weakness persisted. Plasma exchange therapy was continued daily for 11 days, resulting in gradual improvement.

Conclusion: This case highlights the importance of early recognition of TTP, particularly in young patients presenting with atypical neurological symptoms and thrombocytopenia. Prompt treatment with plasma exchange and corticosteroids is essential to improve outcomes and prevent irreversible organ damage

Key words: *TTP, vWF, PEX, ADAMTS13, HUS , LASMIC, ISTH .*

MAIN BODY

Case Report

A 17-year-old male patient was brought to a tertiary care hospital in an altered state and weakness in the right upper arm and bilateral lower limbs since 4 days. Relatives reported a history of fever and convulsion 4 days ago. The patient was a healthy, non-alcoholic, non-smoker 17-year-old male with no comorbidities, and this was his third event of convulsion in the past two years. The previous two events had resolved completely without any cognitive or focal neurological deficits.

On examination, the patient was febrile (temperature of 100.1°F), tachycardic, and breathing was normal. Blood pressure was 150/100 mm Hg. Pallor and icterus were present. Respiratory system, cardiovascular system, and per abdominal examination were all normal.

On examination of the central nervous system, the patient was drowsy but arousable. The patient was listless and responses were attenuated. On cranial nerve examination, there was left gaze palsy with gaze fixed on the right side. Cerebellar findings were not elicitable. The back and spine were normal. Plantars were bilaterally upwards. Sensory examination was not yielding in view of the poorly responsive patient.

On motor system examination, tone, power, and reflexes were all normal in the left upper limb of the body. In bilateral lower limbs and right upper limb, tone was normal but power was 0. Superficial and deep tendon reflexes were absent.

Pupils were normal in size and reactive to light. Bladder and bowel sensation was lost.

An acute cerebrovascular accident was suspected and a head MRI brain with angiogram was done. It was suggestive of acute large vessel occlusion in the bilateral ACA territory, with gliosis in regions supplied by the right MCA territory, and a small area of gliosis in the left cerebellum. Lab reports were notable for severe thrombocytopenia and a picture of hemolytic anemia. Platelet count was 23k/cumm (23,000 cells per cubic millimeter). Hb was 6.2 g/dL with peripheral smear showing few schistocytes. Total bilirubin was 5.2 mg/dL, indirect bilirubin was 4.4 mg/dL. LDH was increased (1597 U/L). Reticulocyte count was increased (3.3%). Cardiac troponin was elevated (35 pg/mL). ECG was notable for multiple leads showing symmetric T-wave inversions. Serum creatinine was 1.3 mg/dL, and blood urea was 61 mg/dL. There was the presence of microscopic hematuria. Other lab investigations were all normal.

The patient was diagnosed as a case of TTP presenting with recurrent large vessel occlusions and promptly started on therapeutic plasma exchange therapy. Steroids were also started in high doses (Inj MPS 1 gm/day) for 3 days. The patient's sensorium showed prompt improvement within 2 days but the weakness did not seem to improve much. Plasma therapy was continued every day for 11 days. The patient gradually improved with residual weakness.

Discussion

TTP is a rare and life-threatening disorder of intravascular thrombus formation, leading to microangiopathic hemolytic anemia and several organ involvements. It occurs due to a qualitative or quantitative deficiency or increased lysis of ADAMTS13, which cleaves the multimers of von Willebrand factors. The disease can manifest in a number of ways and atypical presentations are also seen. The array of clinical features and the absence of the classical pentad of symptoms in most of the patients pose a diagnostic dilemma and challenge with respect to starting treatment. It is potentially lethal if not diagnosed and treated on time. Pre-PEX mortality was close to 90%, but the advent of therapeutic plasma exchange and transfusion has dramatically reduced the mortality and the way we look at the disease. It is notorious for relapses but is mostly considered a manageable condition as of now.

Pathobiology

The primary defect in TTP is a qualitative or quantitative deficiency of ADAMTS13, which can be congenital or acquired (either immune-mediated or secondary to many systemic illnesses). The common endpoint is a deficiency in functional ADAMTS13, leading to a failure to cleave the multimers of von Willebrand factor, which is a highly prothrombotic molecule and induces the formation of microthrombi in small vessels of the body. The primary organs involved seem to be the brain, heart, kidneys, and mesentery. The lung and liver seem to be less involved or not involved in most cases. The classical pentad described for TTP consists of fever, neurological involvement, thrombocytopenia, hemolytic anemia, and kidney involvement in the form of acute kidney injury or failure (very rare). This pentad is only found in 10% of cases, and 90% of patients either do not have all these symptoms or have an atypical presentation altogether. Literature is available stating several atypical presentations that were eventually diagnosed as TTP and responded to therapeutic plasma exchange.

Of particular interest is an array and range of neurological symptoms that can confuse the clinician with regard to diagnosis. They can range from confusion, memory lapses, cognitive and behavioral disturbances to major neurological disorders causing convulsions, stroke, coma, and death. Strokes in TTP are generally not limited to any vascular territory. They are small in size and the neurological deficits caused are mostly reversible. Large vessel occlusions occur very rarely in TTP and large infarcts are also uncommon, although they are described. If they occur, the neurological damage caused is not completely reversible even after successful treatment, and some neurological deficits always persist.

Renal involvement can range from asymptomatic microhematuria to acute kidney injury, raised creatinine, and acute renal failure. Renal features are typically less severe and occur less commonly in contrast to its close differential of HUS, where kidney involvement seems to be the primary manifestation. Anemia occurs due to shearing forces in the microvasculature causing lysis of circulating red blood cells. The anemia is typically Coombs-negative hemolytic anemia

at first, which can coexist with nutritional-type anemia due to increased demand for iron, B12, and folate by the marrow to compensate for lost cells by premature lysis. The hallmark for this is increased lysed RBCs seen on peripheral smears—schistocytes. More than 1% are typically seen in the relapse of TTP, although many centers do not quantify these, but their presence is an indicator of active hemolysis.

Thrombocytopenia occurs due to the consumption of platelets in the formation of microthrombi throughout the microvasculature. This results in severe thrombocytopenia, and the majority of patients have platelets less than 50k/cumm. Clinical manifestations range from asymptomatic to minor petechiae or purpura to GI bleeds or genitourinary bleed, and can also cause major bleeds like intra-abdominal or intracranial bleeds, although it is very rare. ICH occurring in TTP mostly happens in an attempt to thrombolyse the primary stroke and not de novo. Therefore, the possibility of TTP should always be considered and entertained, especially in young patients without classical risk factors for stroke who present with stroke and thrombocytopenia, because thrombolysis in this setup can be useless and potentially life-threatening. The incidence of young stroke is increasing, and this cause of young strokes should always be kept in mind and entertained whenever there is a reasonable margin of suspicion because this is a very much reversible and manageable condition if addressed on time. If not, it can lead to irreversible organ sequelae and even death

Conflicts of Interest: The authors declare that there are no conf l icts of interest regarding the publication of this paper.

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