Recurrent stroke in an african female with idiopathic thrombotic thrombocytopenic purpura: a case report

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Abstract

We report on a young Ghanaian female who was diagnosed with TTP but had ischaemic stroke as initial presentation. She was successfully treated with therapeutic plasma exchange. This case illustrates how TTP can masquerade as ischaemic stroke and the application of PLASMIC score without ADAMTS 13 assay in risk prediction.

INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) is triad of severe thrombocytopenia (usually less than $100x10^9$/l), macroangiopathic hemolytic anemia and varying end organ involvement (1). Also called Moschcowitz disease, this occurs following the increase in prothrombotic state with the deficiency in the disintegrin and metalloproteinase with thrombospondin motifs 13 (ADAMTS 13), the molecule that cleaves and thereby activates the von Williebrand factor (vWF) (2). Large, uncleaved multimers of vWF forms a substrate for the binding of platelets within the blood vessels with subsequent mechanical fragmentation of red blood cell, occlusion of the microcirculatory bed and organ ischemia. The more prevalent form of this disease is acquired, with the formation of autoantibodies against ADAMTS 13 however, compound heterogeneous or homogeneous mutations may also occur: Upshaw-Schulman syndrome (3, 4). TTP usually presents acutely with rapid deterioration of the patient and has a high mortality and recurrence rate in those who survive an acute episode. Neurologic (headache, seizures and coma), cardiac (ST- elevation and non-ST elevation myocardial infarction, heart failure) and renal manifestations have been documented and many patients develop multi organ failure leading to their eventual demise within weeks if not adequately managed (5, 6). The bedrock of treatment is the use of therapeutic plasma exchange with fresh frozen plasma as this reduces the autoantibodies against ADAMTS 13 and improves the levels of functional vWF.(7)

CASE REPORT

A 40-year-old African female was referred to the Emergency on account of stroke confirmed by a CT scan. She presented with slurred speech, facial asymmetry and left upper and lower limb weakness of a day's duration. The patient had been diagnosed of hypertension 10 years ago but has been non-compliant with her medication 2 weeks prior to her presentation. Her medications included amlodipine and lisinopril. She admitted to headaches, dizziness, palpitations, and easy fatigue and reported menorrhagia for the past 10 years. Past medical history included two stroke events 5 years ago and encephalitis at age 8 months. There was a family history of hypertension and diabetes but no history of bleeding disorder.

On physical examination, she was neither in respiratory distress nor jaundiced, however was severely pale.

She had purpuric patch on the flexural areas of both elbows and knees and posterior aspect of the lower legs. The patient was afebrile with a temperature of 36.8 °C; pulse rate of 81 beats per minute; respiratory rate of 20 cycles per minute; and blood pressure 103/67 mmHg at presentation. Power grading in her left upper and lower limbs were 1/5. All other systems were unremarkable.

The complete blood count revealed a low haemoglobin level of 4.3 g/dl (11.5 – 14.5), platelet count of 18 x 109/L (150 – 450 x 109/L), white cell count of 10.47 x 109/L and a normal renal function. Samples were taken for blood film comment, blood film for malaria parasite, LDH, uric acid, clotting profile, HIV, ANA., Hepatitis B and C. Additionally, electrocardiogram, echocardiogram, abdominopelvic ultrasound, and a chest x-ray were requested. She was transfused with 1 unit of whole blood and neurological physiotherapy started. On days 2 and 3 of admission, her power improved to 4/5.

On day 4, the patient developed tonic-clonic seizures and she gradually developed jaundice the same day. Repeat complete blood count showed Hb of 6.2g/dl, WBC of 13.5 x 109/L, Platelet count of 22 x 109/L. Clotting profile results showed INR of 1.16, PT – 9.8s, APTT – 33.9s, PTT – 0.92s. LDH was 2,6111 u/L (135 – 214), Uric acid was 0.4 mmol/l (0.13 – 0.39), both direct(19.86 umol/l) and indirect (34.7 umol/l) bilirubin were high with low globulin levels (25.7). HIV, Hepatitis B and C, ECG, chest x-ray, blood film for malaria parasite, AST, ALT, AST, ANA were all normal. A Thyroid function test was normal. The result of the blood film comment showed normocytic normochromic RBCs, schistocytes ++ with occasional normoblast, few polychromatic cells, increased WBC count mostly neutrophils with a left shift and reduced platelets with no clumps seen suggestive of microangiopathic hemolytic anaemia. ADAMTS 13 assay could not be conducted as requested due to inadequate funds. Alternatively, the TTP PLASMIC score was used for confirmation which yielded a total score of 7 (high risk) and a 96.2% risk of severe ADAMTS13 deficiency ([?]10%). A repeat of renal function test yielded urea of 31.7 mmol/l (2.1 – 7.1) and creatinine of 492µmol/l (62 – 106). TTP was diagnosed, and the patient was transfused with 3 units of whole blood, 4 units of fresh frozen plasma and had 3 days of pulsed methylprednisolone. Subsequently, she had a total of 7 sessions of plasmapheresis and 3 sessions of hemodialysis with concomitant oral prednisolone 80mg and 1g of 10% calcium gluconate prior to plasmapheresis. Her GCS at the end of the sessions rose to 15/15. The patient was not pregnant at any time during her illness (Table 1and Table 2).

Table 1. Summary of patient's CBC laboratory reports before, during and after plasmapheresis and haemodialysis

	Date (dd/mm) from admission to last review	**Date (dd/mm) from admission to last re**
CBC parameter	**7/10**	**9/10**
Hb (g/dl)	4.3	6.2
WBC (x10^9/L)	10.5	13.5
Platelet (x10^9/L)	18	22

Table 2. Summary of patient's BUE & CR laboratory reports before, during and after plasmapheresis and haemodialysis

BUE, CR	**Date (dd/mm) from admission to last review**	**Date (dd/mm) from admission to las**
parameter	**7/10**	**18/10**
Na (mmol/l)	135	144
K+ (mmol/l)	3.97	3.7
Cl- (mmol/l)	100.1	109
Urea (mmol/l)	3.51	31.7
Creatinine (µmol/l)	150.9	492

DISCUSSION

TTP is a hematological emergency which requires prompt therapy to reduce morbidity and mortality. TTP is characterized by deposition of intravascular platelet microthrombi induced by autoantibody-mediated deficiency of ADAMTS13, a von Willebrand factor (VWF)-cleaving protease (8), resulting in thrombocytopenia, microangiopathic hemolytic anaemia (MAHA), renal abnormalities, neurologic disturbances, and fever. The pentad of clinical syndromes which was proposed to constitute the diagnosis of TTP only occurs in 5% of cases. Currently, clinical diagnosis is made when there is the presence of microangiopathic hemolytic anaemia, thrombocytopenia, with or without neurological and renal involvement and without another identifiable cause (9). Our patient presented with stroke, seizures, intracerebral haemorrhage, MAHA, thrombocytopenia, and acute kidney injury. There was no identifiable cause in our patient. TTP may also present with a transient ischemic attack (TIA) or stroke with or without hematological changes (10, 11). In a series of 47 patients with acute TTP, the most common neuroradiologic finding was posterior reversible encephalopathy syndrome (PRES), while large ischemic infarctions and hemorrhage were uncommon (12). Our patient presented with ischemic stroke and later intracerebral haemorrhage occurred. Many patients with TTP present with the triad of thrombocytopenia, microangiopathic hemolysis, and neurological abnormalities. Some of them may also have fever and renal abnormalities. However, it is important to note that neither the triad nor the pentad of presentation can be relied upon for the diagnosis of TTP. In practice, a constellation of thrombocytopenia and microangiopathic hemolysis should always raise the suspicion of TTP. Acute kidney injury requiring dialysis are uncommon (13) but our patient had an acute kidney injury and was hemodialysed whiles undergoing plasma exchange transfusion.

TTP results from either a congenital or acquired decrease/absence of the von Willebrand factor protease ADAMTS13. Low levels of ADAMTS13 result in microthrombi formation which leads to end organ ischemia or damage (14, 15, 16). This is due to inability of the ADAMTS13 to cause an inactivation of the large multimer von Willebrand factor (vWF) that is necessary to prevent spontaneous coagulation. These larger multimers have a high avidity to bind platelets and initiate thrombi formation. However, the availability of ADAMTS13 activity assays are not available in many developing countries (17), making the confirmation of the diagnosis difficult. In attempting to solve this problem, prognostic scores are now being used to reduce the chance of mistakes and increase the clinical diagnosis accuracy. Among these developed scores is the PLASMIC score which has been shown to be practical and effective, according to some validated studies (18, 17). Since our patient couldn't afford the ADAMTS13 assay, and this assay is not readily available in the country, the PLASMIC score was used as an alternative to confirm our diagnosis of TTP. She had a risk score of 7 which is categorized as a high-risk for TTP and a 96.2% risk of severe ADAMTS13 deficiency ([?]10%). (Table 3 and Table 4)

Table 3. PLASMIC Score

	PLASMIC SCORE	
Parameters	**Results**	**Score**
Platelet count	18	1
Creatinine	150.9	1
INR	1.16	1
MCV	76.4	1
Presence of haemolysis variable	Raised LDH (2,6111 u/L) Raised Indirect bilirubin(34.7umol/l)	1
History of stem cell or solid organ transplant	Nil	1
Active cancer	Nil	1

Table 4 . Risk of severe ADAMTS - 13 deficiency score

SCORE	RISK CATEGORY	RISK OF SEVERE ADAMTS- 13 DEFICIENCY ([?]10%)
0-4	Low	4.3%
5-6	Intermediate	56.8%
7	High	96.2%

Measuring ADAMTS-13 activity levels may not guarantee initial diagnosis and therapeutic decisions, but it is important for the prognosis. An ADAMTS-13 activity level $< 5\%$ - 10% seems to have increased specificity for TTP, but it does not identify all patients at risk for relapsing. ADAMTS-13 activity levels of $> 10\%$ makes the diagnosis of TTP unlikely in patients presenting with acute thrombocytopenia (10, 19, 20). Sometimes transfusion of fresh frozen plasma may increase ADAMTS-13 activity levels which may alter diagnosis.

Therapeutic plasma exchange is the main therapy for patients with TTP (21). Plasma exchange delivers elevated ADAMTS-13 dose without circulatory overload and removes antibodies to ADAMTS-13, recovering ADAMTS-13 activity. The treatment approach consists of a 1 to 1.5 plasma volume exchange with plasma daily until clinical symptoms have resolved and the platelet count has reached a normal level (22). Our patient's condition resolved after undergoing 7 sessions of plasmapheresis. LDH levels should also be monitored since it reflects ongoing tissue ischemia as well as haemolysis. Treatment with immunosuppressive agents is reserved for patients suspected of having ADAMTS-13 autoimmune deficiency. Glucocorticoids are the immunosuppressive agents initially administered. Other agents such as rituximab and cyclosporine are used for more critically ill patients and patients with recurrent disease (23, 24).

CONCLUSION

This case report shows how TTP can present as ischaemic stroke which is an atypical presentation. It is interesting to note that our patient is the first Ghanaian to undergo plasmapheresis and the only case described in literature and this makes our reported case a unique one. This may be due to late or missed diagnosis, the unavailability of screening tools or inadequate funds to patronize plasma exchange. Rapid diagnosis and treatment are necessary for decreasing the risk of fatal outcomes in patients with TTP. This case illustrates the potential of TTP masquerading as Ischaemic Stroke and it is necessary that Clinicians are familiar with the clinical presentation and laboratory abnormalities of TTP, to make early diagnosis and initiate appropriate therapy.

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Declaration

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and material

All data generated or analysed during this study are included in this published article (and its supplementary information files).

Conflict of interest

The authors declare that they have no conflict of interest

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Authors' contributions

1. Kwabena Oteng Agyapong - provided direct patient care, planning, writing up the manuscript, discussion, and reviewing the literature

2. Aba Folson - worked on manuscript revision, and final approval. All authors read

3. Kate Fiador - provided direct patient care, planning and reviewed manuscript

4. Roland Wonkyi – provided direct patient care, planning and reviewed manuscript

5. Kelvin Amenyedor - reviewed the final manuscript

6. Jefferey J. Boateng – reviewed the final manuscript

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