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# Delayed Diagnosis in a Nigerian Female with Dyke-Davidoff-Masson Syndrome and Thrombotic Thrombocytopenic Purpura in Status Epilepticus

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***Abstract***
*Dyke-Davidoff-Masson syndrome (DDMS) is one of the disease processes that present with cerebral hemiatrophy. It may be characterized by contralateral hemiparesis, seizure, mental retardation, facial asymmetry and learning disabilities. Thrombotic thrombocytopenic purpura (TTP) is a rare blood disorder though to be characterized by thromboses resulting in a low platelet count consisting of fever, renal disease, neurological symptoms, thrombocytopenic purpura and microangiopathic haemolytic anaemia. This case report illustrates the complexity of syndrome of Dyke–Davidoff–Masson and thrombotic thrombocytopenic purpura which can constitute a diagnostic and therapeutic challenge in an emergency setting when evaluating a patient with recurrent seizures.*

***Keywords -*** *Seizure, Dyke-Davidoff-Masson syndrome, Thrombotic thrombocytopenic purpura.*

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## I. Introduction

Dyke-Davidoff-Masson syndrome (DDMS) is one of the disease processes that present with cerebral hemiatrophy. It may be characterized by contralateral hemiparesis, seizure, mental retardation, facial asymmetry and learning disabilities. Other finding include cerebral hemiatrophy on brain imaging, and sometimes frontal sinuses hyperpneumatization and calvarial thickening.[1] This was first described in 1933 were report of a series of 9 cases were done by Dyke,Davidoff and Masson.[2-5] Diagnosis has improved in the era of brain imaging. Presentation is thought to be variable, and could occur in children, adolescent and adult [2,4] and they rarely present with status epilepticus (SE). [6]

The cause of the syndrome is not fully understood but risk factors include history of perinatal hypoxia, congenital vascular anomalies, trauma, infection, stroke (ischaemic or intracranial bleed) [2,7]

Thrombotic thrombocytopenic purpura (TTP) is a rare blood disorder though to be characterized by thromboses resulting in a low platelet count consisting of fever, renal disease, neurological symptoms (alteration in mental status, seizures, hemiplegia, paresthesias, visual disturbance, and aphasia), thrombocytopenic purpura and microangiopathic haemolytic anaemia. However some studies have shown that less than 10% of patient demonstrate these symptoms, [8-10] what appears to be constant is severe thrombocytopenia (typically $<30 \times 10^9$/L) and microangiopathic haemolytic anaemia with skin and mucosal haemorrhage.

They may be idiopathic in about 50% of cases with no underlying clinical condition, [8-10] or may be associated with acquired clinical conditions which serve as triggering mechanism like Human Immunodeficency Virus(HIV), bacterial infections, pancreatitis, cancers, autoimmune diseases and drugs such as cyclosporine, quinine and clopidogrel.

This case serves as a remainder of this rare syndrome presenting at the emergency unit with status epilepticus and a rare blood disorder TTP.

## II. Case Presentation

A 23 year old female was referred to our emergency unit accompanied by her mother with history of recurrent seizures. Seizure has been recurrent since 4 years of age initially as febrile seizure. Seizures were occasional until the age of 17 years when it became more frequent about three times a month, necessitating hospital visit during which she was commenced on carbamazepine. She had noticed differential weakness of the right upper limb and lower limb at about age 4 years. Mother had an uneventful pregnancy and delivery with the child having normal developmental mile stone.

She presented to our emergency unit with recurrent seizure, unresponsiveness, low grade fever and vomiting which initially was recently ingested meal and subsequently clotted blood. Seizures were described as generalized tonic-clonic with postictal confusion and sleep of variable duration

She had an episode of haemoptysis 2 days earlier, and subsequently had 2 episodes of hematemesis (each 50-100mL, vomitus mixed with blood and blood clots). Her urine was noted to be dark coloured with no change in urine frequency or dysuria. There is mild abdominal pain and reduced bowel motion which was dark coloured. Mother had noticed reddish patches on both upper and lower limbs.

She had behavioral problems like disturbed sleep, irritability, anger outburst and intermittent outburst of inappropriate talks. She received a total of 4 units of blood from the referring hospital. She has just completed her Senior Secondary Certificate Examination (SSCE) for which the mother attributed the delay to her ill health (Poorly controlled seizures)

Her clinical examination revealed a young female who was conscious but restless, febrile with temperature of $37.9^0$ C, pale with generalized purpuric and ecchymotic patches noted on the arms and legs (shine) and the urethral catheter passed, wasbdraining dark coloured urine. Cardiovascular system exam showed a pulse rate of 106/minute, with blood pressure of 128/87mmHg and normal first and second heart sound. On neurological examination, she had intelligent quotient = 50, subtle right-sided facial palsy of upper motor neuron type and right hemiparesis involving more upper than lower extremity. (Reduced muscle bulk in the right upper limb with Power of 3/5 in the right upper and 4/5 lower limbs with a right extensor plantar response).

Her cranial CT scan revealed left cerebral hemiatrophy with features of encephalomalacia surrounded by gliosis. (Figure 1) Electroencephalogram(EEG) revealed a low amplitude background over the left hemisphere with intermittent bursts of generalized sharp-and-slow wave complexes.

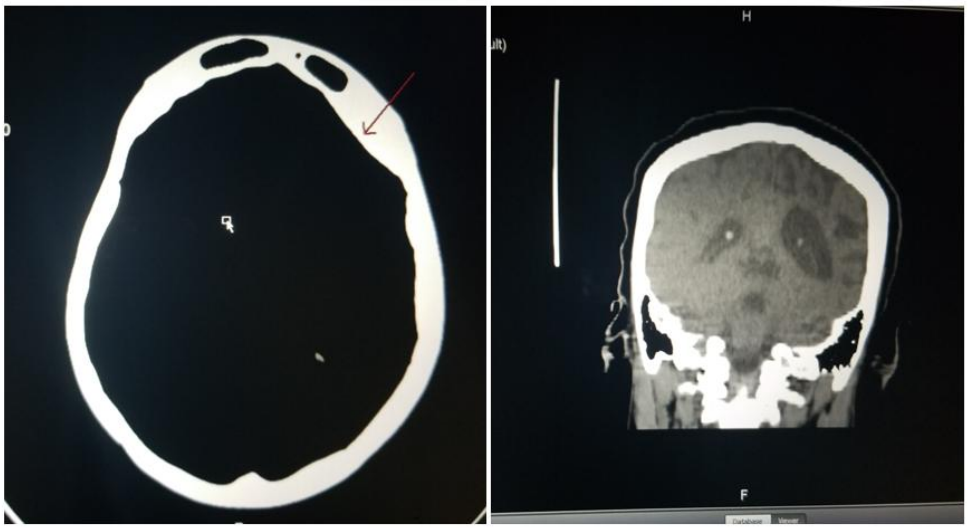
Her initial diagnosis was Status Epilepticus with drug induced Anaemia was made, while the final diagnosis was Dyke-Davidoff-Masson syndrome in Status Epilepticus with Thrombotic thrombocytopenic pupura. Liver function test, Electrolyte, Urea and Creatinine were all normal.

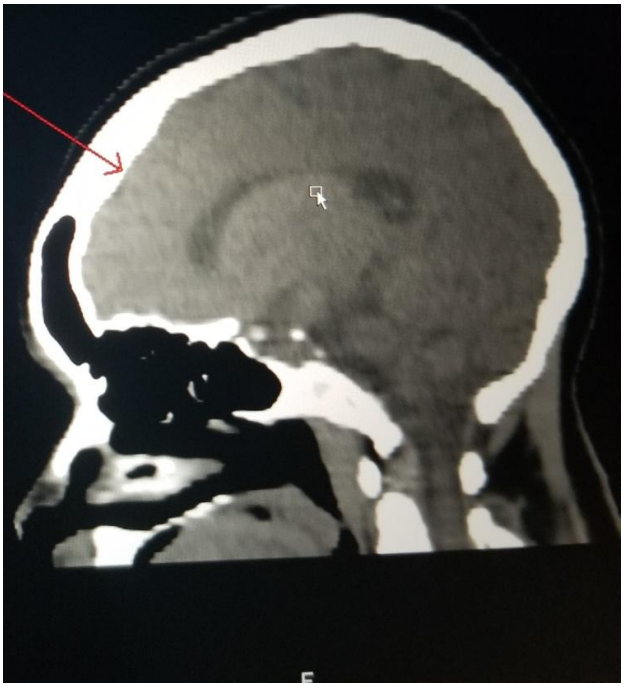
She was managed for status epilepticus and Thrombotic thrombocytopenic purpura, subsequently placed on Tranexamic acid, Methylprednisolone, Ceftriazone, levetiracetam and Lamotrigine.

LABORATORY RESULTS

| | | | |
|---|---|---|---|
| 1. | **D-Dimer** | **2.69** | **0-0.5ug/ml** |
| 2. | Calcium | 2.2 | 2.2-2.7mmol/L |
| 3. | Phosphate | 3.3 | 2.7-4.5mg/dl |
| 4. | Magnesium | 1.04 | 0.7-1.15mmol/L |
| 5. | **Lactate Dehydrogenase(LDH)** | **846** | **125-220U/L** |
| 6. | International Normalized Ratio(INR) | 1.3 | 0.9-1.3 Seconds |
| 7. | (APTT) | 32 | 25-35 Seconds |
| 8. | Direct Coombs Test | Negative | |
| 9. | Indirect Coombs Test | Negative | |
| 10. | Glucose 6 Phosphate Dehydrogenase | 22.53 | 6.97-20.5 U/g Hb |
| 11. | Rheumatoid factor | Negative | |

| | **HAEMOGLOBIN** | **PACKED CELL VOLUME** | **WHITE CELL COUNT** | **NEUTROPHIL** | **LYMPHOCYTES** | **MONOCYTES** | **EOSINOPHIL** | **BASOPHIL** | **PLATELETES** | **MCV** | **MCH** | **MCHC** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1st | **9.5** | 28.4 | **11.5** | 62.1 | 28.2 | 8.4 | 0.2 | 1.1 | **57** | 93.5 | 28.7 | 30.7 |
| 2nd | **7.0** | 22.8 | **9.3** | 51.9 | 40.2 | 6.6 | 0.7 | 0.6 | **109** | 89 | 26.1 | 29.4 |
| 3rd | **7.2** | 25.7 | **5.0** | 50.8 | 40.7 | 6.0 | 1.7 | 0.8 | **134** | 87.6 | 27.6 | 31.5 |
| 4th | **11** | 34.1 | **4.0** | 46.9 | 43.5 | 7.4 | 1.9 | 0.3 | **454** | 97.7 | 27.8 | 30.3 |





## III. Discussion

The index case presented with most of the typical features of DDMS: namely cerebral hemiatrophy, seizures, contralateral hemiparesis, and mental retardation. In addition this case presented with severe anaemia. Both sexes and any of the hemispheres may be affected but male gender and left hemisphere involvement are more frequent. [7] Age of presentation largely depends on time of neurologic insult, and characteristic changes may be seen in adolescence.[4,12] According to the degree of the brain damage, the clinical findings vary from patient to patient.[4,6, 13] Presentation of the disease can be divided into 2 types depending on when cerebral insult occurred either during pregnancy or early life. In the case of the congenital (Infantile) type which may be due to some genetic defect,[12] there seems to be structural changes in the vessels resulting in cerebral injury during fetal life.[2,5,13]

The acquired type which can occur during the perinatal period due to central nervous system injury or secondary to causes such as infections, injuries, tumors, vascular anomalies, prolonged febrile seizures, ischemia, hypoxia, and various kinds of intracranial bleeds.[5,13]

The etiological factor in this index case is not certain but appear to have been acquired in childhood leading to recurrent seizures. Classically patients presents with varying extent of facial asymmetry or paresis, sensory disturbances, hemiatrophy, focal or generalized uncontrolled seizures, contralateral hemiplegia, mental retardation, impaired cognition, learning and speech impairment, and psychiatric problems.

The imaging features are sometimes not apparent in early age, but will become evident as patient get older. Although MRI is preferred, CT scan is helpful in the diagnosis of DDMS, were features will include unilateral loss of cerebral volume and associated compensatory bone alterations in the calvarium, hyperpneumatization of the paranasal sinuses and mastoid cells and elevation of the petrous ridge and greater wing of the sphenoid bone[14].

Radiologists have described three magnetic resonance imaging patterns of DDMS. Pattern I corresponds to diffuse cortical and subcortical atrophy. Pattern II corresponds to diffuse cortical atrophy coupled with a porencephalic cyst, while pattern III corresponds to previous infarction with gliosis in the middle cerebral artery (MCA) territory. [15]

Furthermore this case presented with severe anaemia and generalized purpuric and ecchymotic patches, thus leading to her evaluation for TPP.

TTP is associated with a deficiency of an enzyme involved in blood clotting called the von Willebrand factor cleaving protease (also called ADAMTS13 gene). The ADAMTS13 enzyme is a plasma protease that cleaves von Willebrand factor into smaller sizes and thereby eliminates unusually large von Willebrand factor (VWF) multimers that would otherwise accumulate on endothelial cells where they can cause platelet thrombi.

The deficiency/mutation of this enzyme which is a biologic marker specific for TTP allows large complexes of the clotting protein known as von Willebrand factor to circulate in the blood, resulting in platelet clotting and the destruction of red blood cells. Mutations in this gene lead to a severe reduction in the activity of this enzyme, thus disrupts the usual balance between bleeding and clotting.

The diagnosis suggestive of thrombocytopenia, present with schistocytes on the blood smear as morphologic hallmark of the disease, elevated reticulocyte count and lactate dehydrogenase, undetectable haptoglobin concentration and negative Coombs' test which are evidence of heamolysis. In addition the activity level of ADAMTS13 may aid in diagnosis.

Treatment involves the use of plasma exchange, Corticosteroids, rituximab and Caplacizumab.

A complete response to treatment is defined by a platelet count above $150 \times 10^9$/L for 2 consecutive days, together with normal or normalizing LDH and clinical recovery.

## IV. Conclusion

This case report illustrates the complexity of syndrome of Dyke–Davidoff–Masson and thrombotic thrombocytopenic purpura a rare blood disorder which can constituting diagnostic and therapeutic challenge in an emergency setting. This constellation of symptoms should be kept in mind due to the rarity of the disease when evaluating a patient with recurrent seizures. With improved neuro-imaging modalities in Nigeria, early diagnosis is now possible and treatment which is largely supportive and aims at controlling seizures.

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