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Co-Morbidity of Severe Malaria and Generalised Tetanus: A Rare Case Report

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Abstract

A fifteen-year-old boy presented with a complex of clinical symptoms and signs of severe malaria; fever, convulsions, loss of consciousness, severe anaemia, hypoglycaemia and that of generalised tetanus; trismus, rigidity, reflex spasticity, tiny necrotic area on the plantar surface of the foot. The patient responded very poorly to intravenous artesunate, and blood transfusion among other measures for the management of severe malaria. A history of tetanus immunization could not be established. The patient was commenced on Intravenous (IV) metronidazole 500 mg 6 hourly after the wound was debrided and dressed uncovered. Anti-tetanus immunoglobulin was administered after a test dose. IV diazepam, Chlorpromazine, and Phenobarbitone were given to control convulsion and spasticity and to relieve symptoms. The glucose flow rate was strictly maintained via the IV route for the first 24 hours and subsequently, the Nasogastric (NG) tube was passed with the introduction of feeds. The patient responded drastically and was discharged after 15 days to complete his medication on an outpatient basis and tetanus immunization.

Subject Areas

Infectious Diseases, Pediatrics

Keywords

Malaria, Anaemia, Tetanus, Convulsion, Reflex Spasticity, Life-Threatening, Co-Morbidity

1. Introduction

Malaria is the leading cause of hospital admission in Africa [1]-[3], and consti-

tutes the greatest disease burden in the region [1] [3]. More than one hundred nations are presently affected worldwide [4], with children and pregnant women being mostly affected, and children under the age of five years suffering the severest forms. Malaria is said to be severe when the acute illness is associated with a life-threatening event(s) as shown in **Table 1** below [3]. Several organ systems could be involved [5]. Mortality in severe malaria ranged from none in well-equipped centers to as high as 45% in resource-poor facilities [2]. The main manifestations of severe malaria among semi-immune, residents of malaria-endemic countries are cerebral malaria and severe anaemia [6] (see **Table 1**).

Table 1. Features of severe malaria.

Clinical criteria
• Cerebral malaria is characterized by impaired consciousness
• or coma, convulsions, or both
• Acute respiratory distress syndrome
• Circulatory collapse
• Jaundice in the setting of other organ dysfunction
• Haemoglobinuria
• Abnormal spontaneous bleeding
Laboratory
• Hypoglycaemia [<2.2 mmol litre (<40 mg dl)]
• Severe anaemia (Hb < 5 g dl, packed cell volume < 15%)
• Metabolic acidosis (plasma bicarbonate < 15 mmol litre or
• pH < 7.35)
• Hyperparasitaemia (>2%/100,000 l in low-intensity
• transmission areas or >5% or 250,000 ulin areas of high
• stable malaria transmission intensity)
• Hyperlactataemia (lactate > 5 mmol litre)
• Acute kidney injury (serum creatinine > 265 umol litre).

World Health Organization (WHO) World Malaria report 2019.

More children particularly under-fives are now observed to present with multiple organ impairment as a component of severe malaria despite improvements in case management and malaria control programmes, in Nigeria. Survivors are commonly left with long-term morbidities [2] [3].

Tetanus is an uncommon, severe infection that poses a life-threatening risk and is primarily caused by the bacterium Clostridium tetani, and it manifests clinically within 3 to 21 days, with an average onset of 10 to 14 days following infection [7] [8]. Various routes of entry of the organism into the human body have been demonstrated, such as contaminated wounds containing dirt, feces, or saliva, puncture wounds caused by nails or needles piercing the skin, burns, crush injuries, surgical procedures, dental infection, otitis media, human and

animal bites [9]. It has a high case fatality if adequate intervention is delayed or not available. Tetanus is highly preventable through vaccination [10] [11].

2. Methodology

A case report:

We report a case of co-morbidity of Severe Malaria (Cerebral malaria, Severe Anaemia, and hypoglycaemia) and generalized Tetanus (trismus, rigidity, reflex spasticity, tiny necrotic area on the plantar surface of the left foot).

A 15-year-old male schoolchild was rushed into our facility unconscious by a team of well-wishers who found him on the ground, convulsing. He had complained of fever to his roommate five days earlier for which he was given drugs bought over the counter. A day after the presentation to our facility, the child was noticed by his roommate to have developed tremulous movement of his right hand, described as intermittent.

On arrival, he was found to be unconscious with a Glasgow Coma Score (GCS) of 3, in decorticate posturing: both arms were internally rotated, both elbows flexed to the chest with both hands fixed to the chest with curled wrist joints. He was pale with packed cell volume (PCV) of 18% and febrile with an axillary temperature of 40˚C. Laboratory results confirmed Malaria with both RDT(Rapid Diagnosis Test against *P. falciparum*) and microscopy. The child was promptly commenced on intravenous (IV) artesunate. No commensurate clinical response despite a second dose of intravenous artesunate. The child was also transfused 500 mls of parked cells.

The child was noticed to have a tiny necrotic area under the left foot, measuring about 1 mm by 1 mm. He sustained the injury while playing football barefoot two weeks earlier. The wound was left unattended. A history of tetanus immunization could not be established. The patient was commenced on IV metronidazole 500 mg 6 hourly after the wound was debrided and dressed uncovered. Anti-tetanus immunoglobulin was administered after a test dose. IV diazepam, Chlorpromazine, and Phenobarbitone were given to control convulsion and spasticity and relieve symptoms. The glucose flow rate was strictly maintained at 4 mg/kg/min via the IV route for the first 24 hours and subsequently, the Nasogastric (NG) tube was passed with the introduction of feeds. The patient responded drastically and was discharged after 13 days to complete his medication on an outpatient basis and tetanus immunization (see Table 2).

3. Objective

The objective of this paper includes:

1) Bring to the awareness of clinicians the possible co-morbidity of severe malaria and generalized tetanus, which if missed, could lead to mortality.

2) To recognise generalised tetanus as a differential diagnosis of severe malaria in the tropics.

Table 2. Tabular representation of the patient's laboratory results.

	Day 1	Day 3	Day 10	Reference value
Full blood count				
PCV (%)	18.0	32.0	34.0	42.0 - 50.0
Haemoglobin (g/dL)	6.0	8.0	8.13	14.0 - 16.7
Platelet count (/cmm)	205,000	190,000	220,000	150,000 - 450,000
TWBC (/cmm)	12,500	9400	7500	4000 - 11,000
Neutrophils (%)	78.0	60.0	59.0	40.0 - 65.0
Lymphocytes (%)	20.5	36.0	38.0	20.0 - 40.0
Eosinophils (%)	0.5	0.8	1.0	0.0 - 6.0
Monocytes (%)	0.5	1.2	1.0	0.0 - 8.0
Basophils (%)	0.5	2.0	1.0	0.0 - 1.0
Rapid malaria test				
m-RDT	positive	Positive	Positive	NA
Peripheral blood film examination				
Malaria Parasite/200WBC	+++ (≥250,000)	Nil	Nil	NA
Serum Electrolyte				
Sodium (mmol/L)	130.0	135.0	132.0	135 - 145
Potassium (mmol/L)	3.9	3.5	3,7	3.5 - 5.5
Chloride (mmol/L)	97.0	102,0	104.0	94.0 - 110.0
Calcium (mmol/L)	1.19	1.20	1.25	1.15 - 1.30
Urea (mmol/L)	5.0	4.7	4.3	1.70 - 8.3
Creatinine (mmol/L)	92.0	87.0	87.2	60.0 - 130.0

These investigations were done at the university laboratory, Federal Teaching Hospital Lokoja; g/dL: gram per deciliter; Mil/cmm: million per cubic meter; mmol/L: millimoles per liter; NA: not applicable; PVC: Packed cell volume; U/mL: Units per milliliter; WBC: White blood cell; TWBC: Total white blood cell count; %: Percentage; m-RDT: malaria rapid diagnostic tes for Plasmodium falciparum. **Note, **+++** in our laboratory stands for parasites count of 250,000 Parasite Counts/200 WBC or more**.

4. Discussion

The World Health Organization (WHO) World Malaria Report 2019 estimates 228 million cases of malaria worldwide, causing 405,000 deaths in the year 2018, significantly under the age of 5 years 1. In 2018, nineteen sub-Saharan African countries and India carried approximately 85% of the global malaria burden [1] [2]. Malaria is said to be severe when the acute illness is associated with life-threatening event(s) [3]. Severe malaria, therefore, is rapidly lethal if left unattended. Tetanus, on the other hand, is another rapidly fatal disease. Both malaria and tetanus still constitute a high disease burden in Sub-Saharan Africa,

they are completely preventable diseases [1] [2] [8] [9]. Several organ systems including the kidney, nervous system, respiratory, cardiovascular, and gastrointestinal can be involved in both tetanus and malaria [8]-[14]. This case report highlights the importance of considering tetanus infection, in cases of severe malaria with clinical and laboratory evidence without commensurate response to appropriate treatment. Particularly, when immunization status is unclear, with features such as trismus, rigidity, and reflex spasticity as in this case. The clinical signs of this patient were a combination of that of severe malaria and generalised tetanus [2] [10] [11]. Although, patients with cerebral malaria often develop one form of neurologic sequelae or the other, no permanent neurological damage has been reported among survivors of tetanus [2] [3] [12]-[14]. Autonomic dysfunction posed a huge challenge in the management of this patient, which could be due to severe malaria, or generalised tetanus, or both [1]-[3] [10] [14]. These reports underscore the challenge of recognizing generalized tetanus co-morbidity with severe malaria where gross similarity of symptoms and signs exist. This co-morbidity carries a significant risk of rapid clinical deterioration and death if unrecognised. In addition to diagnostic challenges, distinguishing between severe malaria and generalized tetanus clinically presents a significant difficulty. This patient presented a serious clinical challenge as he was rushed into our facility unconscious. History of his illness was not available. The appropriate treatment of generalized tetanus includes neutralizing the free-circulating tetanus toxin, performing surgical debridement, eliminating the bacterial burden with 500 mg of Intravenous metronidazole, and appropriate adequate supportive care. Human Tetanus-Specific Immunoglobulin (TIG) is very potent in neutralising tetanospasmin [13], although there is conflicting information regarding the most effective dosage and administration method [12] [15]. According to a recent meta-analysis, the combined administration of TIG via both intramuscular and intrathecal routes has demonstrated superior efficacy in reducing tetanus-related mortality when compared to intramuscular treatment alone [16]. The patient had six IV doses of artesunate followed by 3 day course of artemisinin-based combination therapy [2] [3]. The anaemia was corrected with a transfusion of 500 ml packed cells. The most significant factor in reducing mortality associated with generalized tetanus is the provision of treatment in a modern paediatric intensive care unit that implements aggressive sedation protocols and offers advanced ventilatory support. Benzodiazepine derivatives serve as the primary method of sedation in such cases [17]-[20]. There have been reports of damaged muscles or peripheral nerves in generalised tetanus [21] but this was not present in the patient described, as he achieved full recovery of both muscular and neuronal functions.

5. Conclusion

Severe malaria and generalised tetanus are life-threatening clinical conditions that require prompt diagnosis and treatment. Diagnosing generalized tetanus co-morbidity with severe malaria in children can be challenging even in the best

centres of the world, as either can be missed with grave consequences. The early identification and prompt initiation of appropriate therapy are key to preventing swift clinical decline. It becomes more tasking when the history of illness is not available. Therefore, when evaluating children with severe malaria whose immunization history is unknown, present with a sudden onset of trismus, rigidity, and reflex spasticity as in this patient, it is imperative to consider generalized tetanus in the differential diagnosis. This case report seeks to bring to the knowledge and understanding of healthcare providers about the lethality of this co-morbidity if not recognised with prompt therapeutic interventions. We, therefore, advocate that generalised tetanus should be recognised as a good differential diagnosis of severe malaria in the tropics. More resources should be deployed at national and sub-national levels for the prevention of these diseases.

Limitation of the Study

There is paucity of data on severe malaria comorbidity with generalised tetanus, making comparative analysis of the outcome of this case difficult.

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Conflicts of Interest

The authors declare no conflicts of interest.

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List of Abbreviations

NG	Naso-gastric
PCV	Packed Cell Volume
IV	Intravenous
RDT	Rapid Diagnosis Test