Nigerian Journal of Clinical Practice
Sept 2009 Vol. 12(3):335-337

GANGRENE OF THE LIMB COMPLICATING *SALMONELLA TYPHI* SEPTICAEMIA IN A NIGERIAN CHILD

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ABSTRACT
We report an unusual case of lower limb gangrene in a pubertal boy following a typical clinical presentation of septicaemia due to *salmonella typhi*. After an initial response to presumed appropriate antibiotic and supportive therapy, the patient developed tissue ischaemia in both feet.There were no clinical or laboratory evidence suggestive of DIC or coagulopathy. Following conservative management which included oral administration of vitamin C, there was gradual regression of ischaemic changes, progressive healing and recovery of function of the left foot while the condition of the right foot deteriorated with extensive tissue necrosis and dry gangrene that extended to the distal one third of the foot. This necessitated surgical disarticulation of the metatarsophalangeal joints two months after admission. This report is to alert clinicians about this rare complication of a common curable disease with a view to anticipating the possibility of it occurring as well as considering appropriate preventive measures.

Key Words: Gangrene, foot, *salmonella typhi*, septicaemia *(Accepted March 2008)*

INTRODUCTION
Septicemia remains an important cause of childhood morbidity and mortality in developing countries.[1] Salmonella species are important cause of septicaemia particularly during wet season in some parts of Africa.[2] Various complications have been associated with typhoid septicaemia, the common ones being anaemia, perforation of the gut, bleeding and arthritis.[3] Disseminated intravascular coagulation (DIC) and gangrene of the extremities are rare complications; few reports are available on gangrene of the limbs as a complication of this illness in childhood.[4-7] We report a case of peripheral gangrene complicating *S. typhi* septicaemia in a well nourished Nigerian child.

CASE REPORT
AY was a 10-year old boy who presented to the Emergency Paediatrics Unit of Ahmadu Bello University Teaching Hospital, Zaria Nigeria with a 9-day history of a high grade persistent fever, headache, abdominal pain and diarrhoea with two episodes of meleana stools 2-days prior to presentation, but no bleeding from any other orifices. There was no vomiting but he had a mild non-productive cough. There was no history of ingestion of iron-containing drugs or traditional medication. He became weak on the day of admission and was unable to walk at the time of presentation. There were no urinary symptoms and no history suggestive of sickle cell anaemia in the patient or his family. He had received full course of antimalaria treatment and oral chloramphenicol for 5days as well as amoxicillin for 3days prior to admission, all obtained from a patent medicine store, without relief of symptoms. Physical examination revealed an acutely ill conscious child who was moderately dehydrated, mildly pale, acyanosed, not Jaundiced and had no petechiae, purpura or peripheral lymphadenopathy. He weighed 34kg with a height of 138cm, appropriate for his age. He had a respiratory rate of 26/min, pulse rate 128/min and an axillary temperature of 40°C. He had normal vesicular breath sounds. His peripheral pulses were normal with a BP of 100/70 mmHg lying down. Apex beat was not displaced and heart sounds were S_1 and S_2 only; no murmurs. He had a full abdomen, with generalized tenderness and guarding as well as scanty bowel sounds. There were no palpable organs or masses and rectal examination did not reveal any abnormality. Musculoskeletal system was essentially normal with no areas of swellings or tenderness. A working diagnosis of generalized peritonitis secondary to septicaemia was made and laboratory investigations outlined accordingly. Treatment initiated on admission included intravenous fluid 0.18% saline in 4.3% dextrose, intravenous ceftriazone and metronidazole. A nasogastric tube was passed for drainage and patient was on nil per os. Within 48 hours, abdominal signs regressed; he was commenced on oral feeding and he subsequently moved the bowels on the 3rd day of admission.Results of laboratory investigations showed a packed cell volume of 0.25 L/L, a total white cell count of 6.0 $\times 10^9$/L, (neutrophils 67% with toxic granulations, lymphocytes 33%) and platelet count that was within normal limits. Erythrocyte sedimentation rate was 21mm/hr, while antibody titers of 1:64 to *S typhi* O antigen and 1:128 to H antigen with a rise of two fold on repeat measurements a week later were obtained. Blood, urine and stool cultures did not yield any significant growth and the peripheral film showed no malarial parasites. The random blood glucose was within normal limits. His haemoglobin genotype was AA and he was seronegative for HIV. The serum biochemistry including creatinine and proteins were within normal. Plain erect abdominal x-ray did not show evidence of bowel perforation but abdominal ultrasound showed hypoactive bowel loops. His

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clinical condition continued to improve gradually but by the 5th day of admission, he developed pain involving both ankles and feet and on examination was found to have purpura with marked tenderness affecting both lower limbs from the level of the lower one-third of the legs down to the toes (Figure 1). The pulses on the dorsalis pedis arteries were palpable but weak and there was no loss of mobility or skin sensation initially. Warm compresses were then applied over both lower limbs periodically. Within 24 hours, the skin over the distal 3rd of the right leg and foot became uniformly dark due to coalition of the numerous purpuric lesions with total loss of sensations involving all toes thus forming a dry gangrene of the toes, the margin of which was not clear initially. The process was less intense on the left lower limb as mobility and sensations were preserved and the colour change was also less intense. A repeat blood count in the 2nd week of admission showed a PCV of 0.34L/L, a total white cell count of 3.0×10^{9}/L, with neutrophils comprising 37% and lymphocytes 63%. Bleeding and clotting times were normal. Coomb`s test was not done. Orthopaedic surgical consultation at this point suggested a continuation of conservative management to allow for a definitive level of demarcation of the gangrenous part from healthy tissue to emerge. Penicillin in a dose of 400,000 IU/Kg/24 hours in divided doses and vitamin C was added to the treatment at this stage. Patient was maintained on ceftriazone for a period of three weeks after which he continued with vitamin C and multivitamins. He maintained a progressive and sustained general improvement thereafter. The left foot healed completely after gradual desquamation and regeneration leaving a normal skin over it. The margins of the gangrenous segment on the right were clearly demarcated at the level of the distal third of the foot by 6th week after admission. He had surgical disarticulation of the gangrenous right foot at the metatarsophalangeal joints two months after admission figure 2. He was seen for follow-up for 1 year and had remained well.

Figure 1: **Photograph Showing Purpuric Skin Lesions Involving the Lower Third of Legs and Feet with Onset of Gangrene at the Tips of the Toes on the Right.**

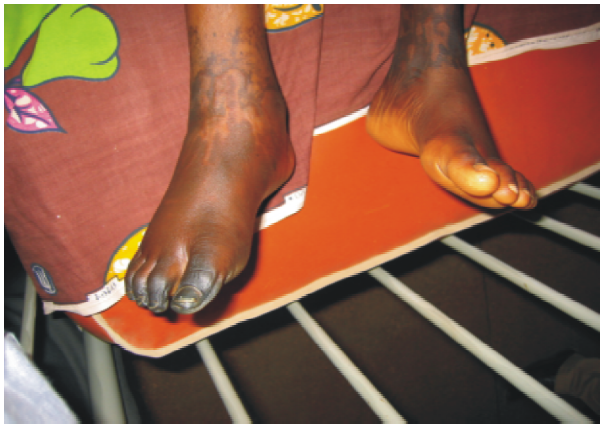
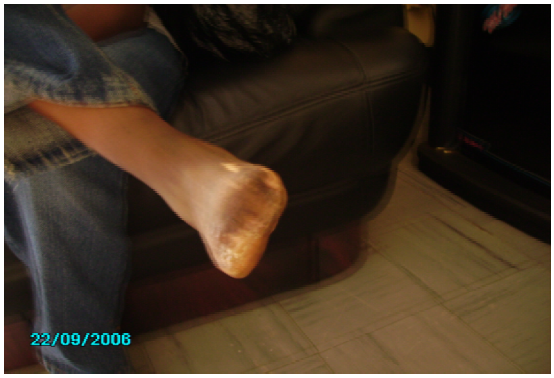


Figure 2: **Photograph Showing the Healed Stump Following Surgical Disarticulation of the Gangrenous Digits of the Right Foot.**



DISCUSSION

Salmonella septicaemia characteristically evolves from local infection in the gastrointestinal tract after faeco-oral transmission which becomes widespread and systemic via the blood stream.[2, 3] With initial clinical features of gastrointestinal disease, progressing to features of systemic manifestation, the patient's presentation followed the common pattern in typhoid septicaemia. However, the development of peripheral ischaemic process of the lower limbs is rather unusual even amongst the complications that may follow salmonella infections.[4, 5, 7, 8] The rise in specific antibody titres to *S. typhi* O and H antigen, the blood picture of leucopenia with relative lymphocytosis in our patient were highly suggestive of the diagnosis of *Salmonella typhi* septicaemia as described in the literature.[3, 7, 8] It was not surprising that cultures of specimens were negative in this case as the patient had received chloramphenicol and amoxicillin at the onset of illness when he presented to a patent medicine store. It is also known that the yield of the blood culture is only 60.0% in the first week of illness while low level and intermittent bacteraemia are well known contributory factors to having negative cultures in typhoid septicaemia.[1, 3] Cultures of bone marrow and duodenal aspirates often yield the organism even with prior antibiotic therapy but this was not done in our patient. Cases of peripheral gangrene complicating *Salmonella* infections have been reported in infants from The Gambia,[4] Ile-Ife[5] and in adult patients from our hospital.[8] The postulated mechanisms for the development of gangrene in these reports include cardiogenic shock, stasis as a result of sluggish blood flow from the effect of endotoxins on the micro-vasculature, vascular spasm or disseminated intravascular coagulation (DIC) associated with bacterial, viral and parasitic infections. The cases reported by Colman et al[7] were caused by DIC complicating *S. paratyphi* septicaemia similar to reports by Onyemelukwe et al.[8] In contrast to these observations, the clinical and laboratory features in our patient did not suggest DIC as the cause of gangrene. However, the finding in this report is similar to what was reported by Okoko et al[4] from The Gambia who also did not find DIC as the likely cause of gangrene. The disease severity in our patient was somehow less than that in the reports from The Gambia[4] and Ile-Ife.[5]

The reasons for this difference may include the older age, normal nutritional status and the near normal haematological status of our patient, all of which are features that confer a stronger immunity. Although our patient had bilateral involvement of the limbs at the onset of the ischaemic process, only the right foot became severely affected. It is well known that endotoxins produced during septicaemia could also activate the classical and alternate pathways of the compliment system and lead to initiation of thrombotic process (DIC) or local thrombosis in peripheral vessels.[4] Furthermore, it has been suggested that the effects of endotoxaemia in septicaemia may include tissue response with production of free radicals that may lead to endothelial damage, initiating thrombotic phenomena and ischaemic process.[9] The use of vitamin C, known for its antioxidant effect through arresting free radical regeneration from tissue reaction was probably influential in limiting the progression of the ischaemic process in the less affected limb. Brighthope[9] in a recent review, compiled evidences from several research trial studies where the use of antioxidant nutrients including vitamin C at greater than recommended daily allowance levels demonstrated favourable outcome in diseases involving thrombosis, embolism and ischaemia, and in the treatment of angina and prevention of primary and secondary myocardial infarction, intermittent claudication and retinopathy. Thrombolytic therapy with fresh frozen plasma, a source of tissue plasminogen activator, along with the use of anticoagulant such as heparin have been successfully used to arrest and reverse the progression of peripheral gangrene following *Klebsiella* septicaemia.[10] Some other reports have recommended that such non surgical management may be more effective where there are intact arterial pulses in an affected limb.[11, 12] We presume that our patient may Have had a local thrombotic phenomenon especially as clinical examination at the time of appearance of purpuric lesions revealed weak pulses in both dorsalis pedis arteries in spite of having shown good response to initial antibiotic therapy. Although tissue plasminogen activator and heparin were not used in the patient reported, the limitation of apparent response to the left limb following administration of vitamin C may be because the thrombotic process in the right limb was already advanced.

CONCLUSION

The management of peripheral gangrene complicating *Salmonella typhi* septicaemia is difficult and challenging in resource-limited settings. The use of antioxidants such as vitamin C initiated as soon as ischaemic changes suggestive of local thrombotic phenomenon appear may be beneficial in preventing the progression to formation of gangrene. However, the early recognition and prompt treatment of septicaemia as well as a high index of suspicion and close vigilance for development of complications remain the most important measures for prevention of adverse sequalae in all settings.

ACKNOWLEDGEMENT

We wish to thank Profs AM Yakubu and HA Aikhionbare for reading through the manuscript and for their valuable suggestions.

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