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Case report

Severe malaria in a Nigerian neonate and treatment with intravenous artesunate

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Abstract

Severe malaria in neonates is a rare occurrence because of the protective effect of fetal haemoglobin and passively acquired maternal antibodies. Despite this protection, severe malaria can still occur and may be confused with neonatal sepsis due to an overlap of clinical manifestations. Therefore, febrile neonates in malaria endemic region should be routinely screened for malaria because any delay in making a diagnosis and instituting adequate and effective treatment can lead to the death of the neonate. This is the first clinical report and successful use of parenteral artesunate for treatment of severe malaria in a Nigerian neonate that is documented in literature to the best of our knowledge.

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Introduction

Malaria has been documented as a leading cause of infant morbidity and mortality in Africans [1]. Nonetheless, infants appear to be relatively protected from clinical malaria, and from the severe consequences of malaria infection, for the first 3-6 months of life because of the preponderance of fetal haemoglobin in their red blood corpuscles, which are relatively resistant to penetration by the malarial parasite [2,3]. Furthermore, maternal antibodies also protect infants in the first 3 months of life [2]. Therefore, severe malaria is an unusual occurrence in children below 3 months of age especially neonates. However, this protection from malaria is not absolute and the protective mechanisms can be overwhelmed by very high transmission intensities [4]. Severe malaria is a life-threatening medical emergency and requires institution of prompt and effective treatment to avert death. The rarity of severe malaria in neonates is buttressed by the fact that standardized management guidelines are not readily available for this age group. We hereby report an unusual case of severe malaria in a Nigerian neonate as well as highlight challenges in the management of such cases in a resource constrained setting.

Patient and observation

NC, a 25 day old male presented at the children outpatient clinic of Madonna University Elele , Niger Delta region of Nigeria, in company of parents with, a five day history of fever and reduced activity. The pregnancy history was unremarkable and the mother had no febrile illness during pregnancy. The child was on exclusive breastfeeding and his immunizations were up to date. The mother administered paracetamol and vitamin C prior to presentation. The child was brought to the hospital for expert care because his fever persisted despite self-medication. NC is the 3rd child in a monogamous family and both parents a attained primary level of education. NC lives in an apartment and he does not sleep under an insecticide-treated net. A diagnosis of presumed late-onset neonatal sepsis was made and the baby was admitted to the children ward for investigation and treatment. However, the parents initially declined admission on grounds of financial constraint and opted to seek alternative care elsewhere. About 18 hours later, they presented again at the children emergency department with worsening of the child's condition. The patient had developed difficulty with breathing and had become weaker. On examination, the child's weight was 3.8 kg, he was febrile (38.50C); Pulse rate 140 / min; Respiratory rate,70/minute. He was moderately pale, anicteric, acyanotic and not dehydrated. Anterior fontanelle was patent and slightly depressed; muscle tone was normal and primitive reflexes were present and intact. The Liver was palpable 4 cm beneath right costal margin and was tender. The Spleen was tipped. Available laboratory results showed: Numerous trophozoites of *Plasmodium falciparum*, Haemoglobin of 7g/dl, WBC 10,700/mm^3, Neutrophils 36%, lymphocytes 48% and monocytes 16%. Random blood sugar was 80mg/dl and urinalysis was normal. Blood culture could not be done due to lack of funds. A diagnosis of severe malaria with severe anaemia in anaemic heart failure was made with late-onset sepsis as a differential diagnosis. The patient was transfused with sedemented cells and was given intravenous furosemide stat alongside. He was also commenced on intravenous artesunate 2.4mg/kg/dose given at 0, 12, 24, and 48 hours, and later changed to oral artemeter- lumefantrin (20mg/120mg) combination one tablet twice daily for three days. He was also placed on I.V ceftriazone 50mg/kg daily for five days. He was discharged home after five days of admission in a stable condition and the parents were advised to get an insecticide-treated net for use. The child is currently on follow-up on an outpatient basis and is asymptomatic with no malarial parasites detectable in peripheral blood smear.

Discussion

Severe malaria usually occurs as a result of a delay in instituting effective and adequate treatment of uncomplicated malaria caused by *Plasmodium falciparum* [5]. The delay in seeking early medical attention by the parents of NC may have played a contributory role in the progression to severe malaria. Unless parasitemia is severe, clinical malaria is a rare occurrence in neonates because of the presence of passive maternal antibodies and fetal haemoglobin [2,3]. Additionally, most nursing mothers stay indoors with their babies, wear protective clothing on their babies and lay them under bed nets. These measures drastically reduce the chances of a mosquito biting a child. Baby NC may have acquired malaria because parents neither owned nor used insecticide treated nets. This was not surprising because of the low socioeconomic status of the parents. Furthermore, NC had severe parasitemia, and this could explain why he developed severe malaria despite the protection from maternal antibodies and fetal haemoglobin. No standardized management guidelines are currently available for treatment of severe malaria in neonates. Parenteral artesunate was preferred over parenteral quinine because of the World health organization (WHO) recommendation that intravenous artesunate should be used in preference to quinine for the treatment of severe *P. falciparum* malaria in children [5]. This was based on the observation that intravenous or intramuscular artesunate has been shown to significantly reduce the risk of death in children from severe malaria compared to intravenous quinine [5]. Additionally, intravenous artesunate offers a number of advantages over intravenous quinine in terms of not requiring rate-controlled infusion or cardiac monitoring [5]. Concurrent parenteral antibiotics were used, though blood culture was not done and the full blood count result of the patient did not show evidence of bacterial infection. The routine use of antibiotics in severe malaria is controversial. It is noteworthy that invasive bacterial infection is a recognized complication of *Plasmodium falciparum* malaria and may increase the case fatality substantially [6]. The signs and symptoms of malarial infection in neonates closely mimic neonatal sepsis. Therefore, a high index of suspicion is required to diagnose severe malaria in neonates. This can explain why presumed late onset neonatal sepsis was the initial diagnosis when patient presented to the hospital. The initial refusal of admission by the parents lead to a delay in instituting therapy for a life-threatening illness in the neonate. Also, difficulty by the parents in paying for some necessary investigations due to financial constraint brings to fore the issues with out-of-pocket spending for health services. It is pertinent to note that the National health insurance policy does not cover every citizen in Nigeria especially in the informal sector where these parents belong.

Conclusion

Though severe malaria is a rare occurrence in neonates, paediatricians caring for children in malaria endemic regions should routinely screen febrile neonates for malaria, because any delay in making a diagnosis and instituting adequate and effective treatment can lead to the death. We found I.V artesunate safe and effective in the treatment of severe malaria in a Nigerian neonate. There is need for further studies so that a standard protocol can be

developed for use in neonates. We recommend the use of I.V artesunate for the treatment of severe malaria in neonates. We advocate a free or subsidized health care service for children under five years of age especially and for neonates. Insecticide- treated nets should be made readily available and affordable for use in households. This will help in reducing unacceptably high neonatal deaths from malaria in Nigeria, which is a significant contributor to the high under five mortality rate in general.

Competing interests

The authors declare no competing interest.

Authors' contributions

All authors equally contributed to the management of the case and have read and agreed to the final version of this manuscript to be published.

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