Neonatal tetanus: An old enemy still lurking around in 2021

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Neonatal tetanus (NT) is a severe but preventable disease for which South Africa achieved elimination status in 2000. It is under-reported, especially in poorly resourced areas where there is minimal surveillance and immunisation coverage is overestimated, and where traditional practices are employed. The case fatality rate is high and surviving infants often have significant morbidity. The aim of our case report is to alert clinicians to the presence of NT and its clinical presentation and to emphasise the value of notification and surveillance. Prevention of NT should be prioritised through: education around hygienic practices at delivery; ensuring adequate immunity against tetanus in all women through routine childhood immunisation; and administration of tetanus toxoid in each pregnancy. NT should be considered in any neonate who could suck and cry in the first 2 days of life and who, between 3 and 28 days of life, cannot suck normally and becomes stiff or has spasms.

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Tetanus is caused by tetanospasmin, a potent neurotoxin, which is produced by the bacterium *Clostridium tetani*. *C. tetani* spores are present globally in soil and the gastrointestinal tract of animals and this, together with the spores' inherent properties of heat and chemical resistance, makes complete eradication of tetanus improbable.[1]

Neonatal tetanus (NT) infection occurs when there are absent or low levels of maternal antibodies and unhygienic traditional practices such as cutting the umbilical cord with grass or applying cow-dung or rodent faeces to the umbilical stump.[1] NT can be prevented by adequate maternal levels of tetanus antibodies that result from immunisation with tetanus toxoid during routine childhood vaccinations, with appropriate boosters also during pregnancy. Due to the miniscule quantity of toxin that infected people are exposed to, immunity is not elicited after infection, and immunisation is necessary to ensure immunity even after recovering from tetanus.[2] Unvaccinated individuals who sustain wounds contaminated with *C. tetani* are at risk of tetanus because herd immunity does not play a role in tetanus prevention owing to the ubiquitous nature of tetanus spores in the environment and because individuals produce an insufficient antibody response.[2]

Tetanus is a clinical diagnosis that requires the exclusion of all other possible causes before the diagnosis can be made. The definition used in the maternal and NT elimination initiative is stratified into suspected or confirmed cases. A suspected case is defined with a history of tetanus-compatible illness during the first month of life in a child who previously fed and cried normally for the first 2 days of life, and between 3 and 28 days of age cannot suck normally and becomes stiff or has spasms, i.e. jerking of the muscles.[1]

Multiple risk factors for NT have been identified and include lack of medical training, poor antenatal care, placing non-sterile substances on the umbilical cord, incomplete tetanus toxoid immunisation, poverty, young maternal age and male sex.[1] Prognostic risk factors for poor outcome include young maternal age, low birthweight, delayed presentation and leukocytosis.[1]

While South Africa (SA) has achieved elimination of NT (defined by <1 case/1 000 live births) since 2000, factors that could threaten this status have been identified.[3] Inadequate access to healthcare combined with poor disease notification systems resulted in under-reporting of cases, thus the true number of cases remains unknown. Immigration from countries who have yet to achieve maternal and NT elimination adds further risk to SA's elimination status.[3]

In 2015, SA reported an NT case rate of 2.28/100 000 live births.[3] Three confirmed NT cases were notified in 2019 - 2020. In all three cases, an unknown substance was applied on the neonate's umbilical cord.[3]

This case report serves to alert clinicians to the presence of NT and to familiarise them with the clinical presentation in neonates to ensure prompt treatment, with resultant improvement in outcome. Notification and effective surveillance are critical for identifying areas or populations at high risk for NT and for monitoring the impact of interventions.

Case

A 7-day-old full-term male baby with a birthweight of 2 900 g was delivered via spontaneous vaginal delivery to a 17-year-old mother. The mother had received regular antenatal care and prenatal tetanus toxoid. The mother's immunisation history prior to pregnancy was unknown.

The infant presented to Klerksdorp Hospital casualty with his grandmother, who is the primary caregiver, with a 3-day history of irritability, poor feeding and episodes of jerkiness thought to be convulsions. The grandmother initially denied traditional practices; however, during rehabilitation she admitted to applying cow dung on the umbilical stump shortly after delivery. The family lives in an informal settlement in the North West Province, SA.

On examination, the baby was dehydrated, with a weight of 2 200 g (a loss of 700 g since birth). He was opisthotonic and had spasmic movements which were interpreted as convulsions. He was not dysmorphic and had normal male genitalia. There were no wounds or lesions, and the umbilical stump looked clean. The presumptive seizures were aborted with clonazepam and phenobarbitone. He had a metabolic acidosis with associated hyponatraemia, hyperkalaemia, hypochloraemia and hypocalcaemia.

The differential diagnoses included neonatal sepsis (possibly meningitis), convulsions, congenital adrenal hyperplasia and NT. Blood, urine and cerebrospinal fluid (CSF) cultures were negative, and a lumbar puncture and cranial ultrasound scan were normal.

Despite intubation for airway protection and benzodiazepines for the presumed seizures, he did not improve. This led to the revised diagnosis of NT made as per the World Health Organization (WHO) case definition with a grade III Ablett score.[1] Tetanus immunoglobulin (TIG) was unavailable and intravenous immunoglobulin (IVIG) at 500 mg/kg was given instead. The child received DTaP (diphtheria-tetanus-acellular pertussis) vaccine as part of the normal immunisation schedule. Spasms were initially intractable and required multiple doses of phenobarbitone, phenytoin, clonazepam, as well as infusions of midazolam, levetiracetam and lignocaine. The spasms eventually improved with the administration of magnesium sulphate, which was given as boluses and as an infusion. It was tapered, with improvement. Magnesium sulphate was opted for its muscle relaxant, vasodilatory, negative chronotropic and cardiac stabilisation properties, as well as reducing the need for other muscle relaxants. Other drugs included cefotaxime, ampicillin and benzylpenicillin.

Multiple cranial ultrasound scans were normal. Unfortunately, no amplitude-integrated electroencephalography (aEEG) monitoring was available.

The patient was nursed in an isolated, quiet environment, with minimal handling. He had episodes of apnoea, bradycardia and increased bronchial secretions which were thought to be signs of autonomic instability. He maintained a normal blood pressure throughout his admission. Hypertonicity and early hip abductor spasms with scissoring were noted after extubation. Other complications such as tendon and joint injury, fractures and hypotension were not observed.

The patient was extubated on day 29 of admission with no resultant laryngospasm. Rehabilitation was rendered using a multidisciplinary team.

The patient responded well to rehabilitation and was subsequently discharged after 85 days. Follow-up at monthly intervals showed that the baby was feeding well, with adequate weight gain. Follow-up at 4 months of age showed appropriate neurodevelopment for his age.

Discussion

NT occurs due to the use of non-sterile techniques when dealing with the umbilical stump and in children born to mothers who are inadequately immunised. As of July 2019, maternal and NT remain a public health concern in 12 countries.[4] The 80 - 100% case fatality rate among neonates is concerning, particularly in poorly resourced areas with inadequate immunisation coverage, unsanitary conditions, and poor umbilical cord care.[1]

Elimination strategies have been successful, which consist of delivering two doses of tetanus toxoid during pregnancy to confer passive immunity to the fetus. In addition, education around hygienic birth practices (using sterile equipment, skilled birth attendants and practising umbilical cord care) together with enhanced NT surveillance significantly improved outcomes.[4]

A study evaluating NT elimination in Mpumalanga Province showed that although elimination status is maintained in SA, certain cultural practices, missed tetanus toxoid vaccinations and poor notification practices are areas requiring improvement.[5] The array of case reports and case series presented in international literature is an indication that NT remains a public health problem.

In areas with a high maternal HIV or malaria population, there may be an increase in the incidence of NT due to a reduction in placental antibody transfer.[6] Therefore, important areas to address in the NT prevention programme are maternal HIV viral suppression, tetanus toxoid administration and malaria prevention in endemic areas. Enhancing the expanded programme on immunisation (EPI) and improving surveillance for NT should be prioritised. Practices for monitoring may include active and integrated surveillance (together with acute flaccid paralysis surveillance for polio) and garnering interest in notification.

The WHO has shown an increase in incidence of NT in SA from 2013, although it has remained below the elimination threshold.[4] However, it remains unclear whether this is a true increase in incidence or due to an improvement in reporting. Notification rates seem to be inaccurate as shown by Idema *et al.*,[5] who found that of the 26 cases of NT identified in Mpumalanga Province, only 14 cases were reported using the notification system.

Maintaining tetanus elimination requires continued investment in public health, which is difficult in low-income countries where there is little provision for the booster vaccination required for long-term immunity. This holds true for NT occurring in poorly resourced areas where the prevalence is underappreciated, surveillance is minimal and immunisation coverage is overestimated. Despite these challenges, there are opportunities to ensure maternal and NT elimination maintenance such as integrated service delivery, increased social mobilisation, focused health education, increased notification system awareness and assigning public health importance to prioritising NT in governments and with their stakeholders.

Since *C. tetani* cannot be removed from the environment, continued elimination of tetanus depends on universal access to immunisation and healthcare services. The maintenance of NT elimination should remain an area of focus globally to ensure that no child suffers from tetanus in this age of medical advancement.

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