Multiple Brain Abscesses due to Salmonella Serogroup C in a Six-month-old Infant

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Abstract

Al-Shahrani Dayel A, Aderele WI, Charan RK, Farooq O, Mahaboob SG, Sharief A. Multiple Brain Abscesses due to Salmonella Serogroup C1 in a Six-month-old Infant. Nigerian Journal of Paediatrics 2007; 34: 90. Brain abscess is an unusual manifestation of salmonella infection. Salmonella typhimmuum (serogroup B), Salmonella enteritides (serogroup D) and Salmonella typhi (serogroup D) are the most frequently reported serotypes associated with brain abscesses. Conversely, reports of brain abscess caused by Salmonella serogroup C1 are rare. In this communication, we present a case of multiple brain abscesses due to Salmonella serogroup C1 in a six-month-old female infant. The abscesses probably resulted from haematogenous spread of the infection from an apparently asymptomatic intestinal focus, as the patient had no history suggestive of salmonellosis. The child responded well initially to a combination of surgical drainage and antibiotic therapy, but died from the long term complications of hydrocephalus at the age of 21 months.

Introduction

FOCAL intracranial infection caused by Salmonella species is relatively uncommon. In the recent past, we saw a six-month-old Saudi female infant with multiple cerebral abscesses that were due to Salmonella serogroup C1. In this communication, we report details of the case and review the literature.

Case Report

A six-month-old Saudi female infant presented with one-month history of poor feeding, poor weight gain, increasing head size and irritability. There was no fever, cough, vomiting or diarrhoea, neither was there any history of seizures. She was the product of a preterm delivery at 32 weeks gestation. She was delivered vaginally and admitted for six weeks after birth in another hospital. No further details of the hospital course during the postnatal period could be ascertained;

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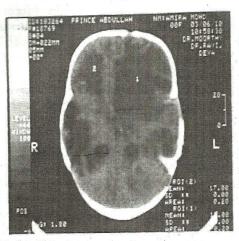
she was apparently not followed-up at that hospital after discharge. She was on formula feeding. As far as the mother could tell, the baby was unable to see, neither could she smile nor had she achieved neck control. Four other siblings were alive and healthy. She had presented in the outpatients clinic about one month earlier with fever and a tense anterior fontanelle; admission for further investigations had been strongly counseled, but was declined by the parents.

On examination, the child looked ill, pale, and marasmic, but was not in respiratory distress. Her vital signs were: temperature 37°C, respiratory rate 32 breaths/min, heart rate 120 beats per min, and blood pressure 85/45 mmHg. Her anthropometric measurements were weight 2.5kg (< 3rd percentile), length $50 \, \text{cm}$ ($< 3^{\text{rd}}$ percentile) and head circumference 40cm (<5th percentile). Neurological evaluation revealed a conscious baby who was moving the limbs, but had spastic muscle tone, exaggerated tendon reflexes and sustained ankle clonus bilaterally. The anterior fontanelle was widely open and tense; the posterior fontanelle was also palpable and tense. Cranial sutures were widely separated, while her scalp veins were prominent. She had sun-setting eyes with poor fixation. The pupils were normal in size and reacting and there was horizontal nystagmus. Her hearing was doubtful and she was not interactive. Examination of the respiratory and cardiovascular systems as well as the abdomen was unremarkable.

As intracranial pathology, probably infective in nature was suspected, initial treatment with antibiotics consisting of ceftazidime, gentamicin and metronidazole was initiated while plans were made for a CT scan of the brain. The plain scan revealed multiple hypodense rounded areas in both frontal, parietal and occipital areas of the brain (Figs. 1a & b), while enhanced scan revealed rims around the hypodense areas causing mass effect on the lateral ventricles, ambient and basal cisterns (Figs. 2). The abscesses which contained thick pus, were aspirated by the neurosurgeon through a burr hole. On the confirmation of a brain abscess, the ceftazidime and metronidazole were discontinued while ceftriaxone was substituted along with the gentamicin when Gram stain of the pus revealed gram negative

echocardiography were normal, and serum immunoglobulin levels were also normal with IgA 94 mg/dl, IgG 663 mg/dl and IgM 32.3 mg/dl. In view of the CT scan finding, lumbar puncture was not done. Follow-up CT scan five days after initial aspiration showed residual brain abscess cavity in the left parietal region. Repeat aspirations were therefore continued. Further follow-up CT scans revealed successive regression of the abscesses. A CT scan on the 33rd day of treatment revealed that the sizes of the abscesses had become very small compared with the previous scans.

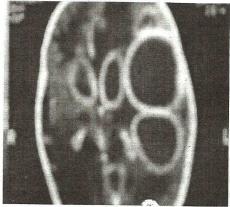
Meanwhile, she remained afebrile with no seizure activity. Her feeding gradually improved and she started gaining weight. Antibiotic therapy was continued for a total duration of two months; in addition, iron and multivitamin supplements were given. At the time of



Figs 1a & b: Plain CT scan of the brain: Axial cuts show multiple hypodense rounded areas in both frontal, parietal and occipital areas.

bacilli. In addition to the antibiotics, daily aspirates and washouts were carried out on the abscess cavities. Culture of the pus later grew Salmonella serogroup C1 which was sensitive to imipenem (Tienam) among other antibiotics. The antibiotics were then changed to imipenem which the child received until discharge. While initial stool culture also grew Salmonella serogroup C1, several follow-up stool cultures were negative. Similarly, cultures of blood and urine were sterile. Other investigations included the following: Hb 9.4g/l, WBC 9.5 x 109/l with 40 percent polymorphs, 55 percent lymphocytes, 3 percent monocytes and 2 percent eosinophils, platelets 690.0 x 109/l, while the ESR was 55 mm in the first hour. Blood and serum electrolytes, urea and creatinine were normal. HIV serology was negative, while haemoglobin electrophoresis,





Figs. 2: Enhanced CT scan of the brain showing rim enhancement around the hypodense areas seen on the plain scan. The appearance is compatible with multiple cerebral abscesses.

discharge after two months of hospitalization, she was afebrile and feeding well with normal fontanelle and a head circumference of 40.0cm. Her weight had increased to 3.9kg, while her last CBC prior to discharge showed a Hb of 12g/dl, WBC of 4.6 x 10°/l, platelet count of 465.0 x 10°/l and an ESR of 11 mm/first hour.

After discharge, she was followed in the outpatients' clinic where it was observed that she remained spastic with marked developmental delay with visual and auditory impairment. A CT scan carried out six weeks after discharge showed remarkable but incomplete resolution of the abscesses. The head circumference at this time was 42 cm. At three months after discharge, it was 44.5cm. After this, she defaulted from the clinic for a while, and when she was next seen about five months later, the head circumference had increased to 50.5cm. A repeat CT scan at this time showed dilated ventricles which remained static for the next month. However, when she presented to the clinic at the age of 18 months, the head circumference was now 54cm, and by the age of 20 months, it was 54.5cm. A repeat CT scan of the brain now showed grossly dilated ventricles with multiple loculations and very thin cortical mantle. In view of this, the child was admitted for insertion of a ventriculo-peritoneal shunt. However, on the day of admission, her general condition deteriorated as she started vomiting and developed seizures. The operation was deferred while she was managed with anticonvulsants and other supportive measures. Despite these, she died within 48 hours of admission. In keeping with the usual practice in the Kingdom of Saudi Arabia, no postmortem examination was performed.

Discussion

There are over 2400 distinct serotypes of the genus Salmonella that can infect humans. Based on their 'O' (somatic) antigens, they are sero-grouped as A, B, C1, C2, D and E. Serotypes such as Salmonella typhi and paratyphi are highly adapted to humans and have no other known natural hosts, whereas most other serotypes infect a variety of animals, including poultry (chickens, turkeys, ducks), livestock, domestic animals, reptiles, rodents, birds and humans. Animals constitute the principal source of non-typhoidal salmonella disease in humans. Many strains of salmonella have no host specificity and cause disease in both human and non-human hosts.¹

Our patient presented with non-specific features of irritability, poor feeding, and poor weight gain, features that could be due to any illness including septicaemia

and raised intracranial pressure. She was afebrile, non-toxic, and there were no symptoms of gastrointestinal infection like vomiting and diarrhoea either before or at the time of hospitalization that might have suggested salmonellosis. Although she responded to the surgical drainage and antibiotic therapy with imipenem and gentamicin initially, the course of her illness was later complicated by the development of hydrocephalus, which contributed to her eventual death. It seems that brain abscess due to Salmonella serogroup C1 is very rare as we did not come across any other report in the literature. Multiple brain abscesses are reportedly associated with high morbidity and mortality.

Salmonella organisms are responsible for a broad spectrum of clinical syndromes that include asymptomatic carriage, self-limited gastroenteritis, enteric fever, bacteremia with focal extraintestinal (metastatic) lesions. Acute gastroenteritis which is usually self-limiting, is the most common form of salmonellosis, although bacteremia and extraintestinal focal infections may also develop. Although all salmonella species can cause bacteremia, this is most commonly seen with S. typhi, S. paratyphi, S. choleraesuis and S. enteritidis and S. typhimurium.¹ Certain serotypes such as S. paratyphi A and S. choleraesuis, cause bacteremia more often than they cause gastroenteritis. Following oral infection, early invasion of the blood stream with possible focal suppurative lesions in the meninges, bones, and lungs, among other sites, can occur, but intestinal manifestations like vomiting and diarrhoea are often absent, as was the situation in the present case. Nontyphoidal salmonella gastroenteritis is complicated by bacteremia usually associated with fever, chills and toxicity in one to five percent of patients overall, and more frequently in infants.2 Metastatic foci of infection and death are more common in the first year of life, particularly if the patient has an underlying pathology. Children who are immunocompromised, are at increased risk of developing serious focal infections such as meningitis, osteomyelitis, septic arthritis, endocarditis, and pneumonia during bacteremia, than previously healthy children. 2 Similarly, there are reports of non-typhoidal salmonella intracranial infections in immunocompromised patients with HIV and chronic granulomatous disease,3-5

Focal suppurative intracranial lesions which are rare with salmonella infections include brain abscess, subdural empyema, epidural abscess and septic venous thrombosis. The most frequently isolated serotypes from these lesions are Salmonellatyphimumium (serogroup B), Salmonellatyphi (serogroup D), and Salmonellaenteritidis

(serogroup D). 6,7 Several predisposing factors seem to contribute to the pathogenesis of salmonella abscesses in the brain. Localized infections are reported to be more common in areas with impaired local defenses such as effusions, haematomas, infarctions, and tumours. Indeed, the literature contains several reports of the development of salmonella brain abscess and/or subdural empyema in preexisting intracranial lesions like tumours, 8,9 infarction, 10 congenital hydrocephalus, 11 and surgical operation site. 12,13

Lu et al, in a review of the literature, have reported that purulent meningitis is a major predisposing factor for the development of brain abscess.⁶ However, in a review of 23 cases including 22 from the literature, of salmonella brain abscesses and/or subdural empyemas in children, purulent meningitis was diagnosed in only six patients before the development of brain abscesses and /or subdural empyemas, ¹⁴ and in only three of the 23 was diarrhoea present at the time the abscess was diagnosed. It would therefore appear that meningitis is not a prerequisite for the development of intracranial abscesses in salmonella infection. Consequently, normal results of a diagnostic lumbar puncture can be misleading unless cranial imaging studies are performed.

Majority of brain abscesses due to salmonella are reported under one year of age.6 There is a male preponderance, the reported male: female ratio ranges from 2.67:1,6 to 17:5.14 Fever, seizures, change in mental status, focal neurological deficits and symptoms and signs reflecting the presence of raised intracranial pressure such as bulging fontanelle, vomiting, irritability and an enlarging head circumference are the most common clinical features. 6,7 The development of clinical symptoms depends on many factors. For example, the location of the abscess, the virulence of the pathogen and the immune status of the patient may affect the acuteness of the clinical presentation. In children, the mean duration of symptoms and signs before the diagnosis of bacterial brain abscess is about two weeks but in some cases it may be as long as four months.¹⁵ Those who are immunocompromised may have a more insidious progression. 16 Patients succumb to brain abscesses because of increased intracranial pressure and brain herniation from the volume of pus and surrounding oedema. Although it occurs less commonly, rupture of an abscess, either into the ventricular system (pyocephalus) as apparently occurred in our patient, or through the cortex into the subarachnoid space, can result in acute deterioration and death. 16 Hou et al, reported a fulminant clinical course leading to death, in a two-month-old male infant with

salmonella meningitis complicated by brain abscess, subdural empyema and purpura fulminans.¹⁷

When a focal intracranial suppurative process is suspected, lumbar puncture (LP) is contraindicated until increased intracranial pressure has been excluded by CT or MRI which are the most important diagnostic tests. This is because significant morbidity following LP in patients with brain abscess has been observed. ¹⁵ Since CT and MRI scans have been in use, the mortality rate from brain abscess has been reduced by 90 percent because lesions are diagnosed earlier and localized more accurately and surgical drainage is facilitated early. ¹⁵ If done, an electroencephalogram is only modestly helpful in diagnosing brain abscess, with low-frequency delta waves being the expected findings. ¹⁵

Successful management of a brain abscess requires a multidisciplinary approach that includes inputs from specialists in infectious diseases, paediatrics, neuroradiology and neurosurgery.16 A team effort allows for an early recognition of parenchymal infection, precise localization, timely surgical intervention, appropriate administration of antibiotics, monitoring of the therapeutic response, close followup for possible recurrence and neurological sequelae and rehabilitation as needed. Early identification, prompt surgical intervention and prolonged antibiotic therapy are the keys to successful management. In certain situations, antibiotic therapy alone may be the only alternative in the management of brain abscess.15 These situations may include the presence of concomitant bacterial meningitis with a known aetiology, multiple brain abscesses after aspiration of one abscess by CT-guided technique in order to identify the pathogen and optimize antibiotic treatment, presence of deep seated abscess or an abscess in a critical area not amenable to a safe surgical approach and where patients are poor surgical candidates. In this connection, Bonvin et al, have reported the successful treatment of a brain abscess due to Salmonella enteritidis in an immunocompetent adult patient with cefotaxime and ciprofloxacin, but without any surgical intervention. 18 Antibiotic therapy of severe salmonella infection can be hampered by various factors because the organism is a facultative intracellular microorganism, and inadequate drug penetration may result in progression of the infectious disease.14 In addition, multi-drug-resistant salmonella strains are on the rise. Successful treatment of salmonella meningitis and brain abscess in infants with ciprofloxacin without any adverse effects has been reported, in cases of inadequate response to other antibiotics.14,19,20

The prognosis has improved over the years. The mortality from brain abscess has improved from 32

percent in the pre-imaging era to less than 10 percent currently, largely due to the earlier, and more accurate diagnosis facilitated by CT and appropriate treatment. Higher mortality rates are associated with the presence of multiple abscesses and coma at the time of admission. Mortality is also higher in immunocompromised patients and those with intraventricular rupture of the abscess. Long term sequelae occur in at least, 50 percent of survivors; these include seizures, hemiparesis, cranial nerve palsies, hydrocephalus and behavioural and intellectual disorders which are more serious in children younger than five years of age. Less common sequelae include spasticity, ataxia, optic atrophy and visual deficits.

Impaired immune responses due to prematurity, young age and severe malnutrition might have predisposed to the development of bacteremia and multiple brain abscesses following an apparently asymptomatic intestinal infection with salmonella serogroup C1 in our case.

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COMMUNIQUE

38TH ANNUAL CONFERENCE OF THE PAEDIATRIC ASSOCIATION OF NIGERIA HELD IN WHITE CASTLE HOTELS, NENI-NNEWI, ANAMBRA STATE. JANUARY 23–27, 2007

The 38th Annual General and Scientific meeting of the Paediatric Association of Nigeria took place at the White Castle Hotels, Neni-Nnewi, Anambra State from 23rd -27th January 2007. The theme of the conference was "Mobilizing Resources for Child Healthcare". The sub-theme was "Low vaccine coverage rate in Nigeria: the way forward". The meeting was declared open by Her Excellency, the Executive Governor of Anambra State, Dame Virgy Etiaba. She noted that as the mother of all in the state, she was concerned and passionate about issues affecting children. She reported on the virtual elimination of female genital mutilation in the state and her continued interest in improving vaccine coverage rates.

There was a pre-conference workshop on improving and sustaining immunization in Nigeria that drew participants from each state of the federation.

Over 300 delegates from various parts of Nigeria and the West African sub-region attended the conference. Over 76 papers were presented, and three symposia held. His Excellency, Professor Chigozic Ogbu, Deputy Governor of Ebonyi State and Professor of Paediatrics gave a keynote address on the conference theme, while Professor Ilochi Okafor SAN (represented) delivered a guest lecture on the Rights of the Nigerian child under Nigerian Jurisprudence. An eminent paediatrician, and then President of the International Paediatric Association, Professor Adenike Grange was honoured with the Distinguished Paediatrician's Award.

The Conference observed as follows:

- 1. Nigeria is endowed with abundant human, material, financial and other natural resources.
- These resources have however, not been adequately mobilized to deal with the multiple problems militating against child survival in Nigeria, especially in the rural areas. This was identified as being responsible for the slow pace of activities towards the attainment of Millennium Development Goal (MDG) 4.
- 3. The high burden of both communicable (such as malaria, HIV/AIDS, tuberculosis) and non-

- communicable (e.g. malnutrition, sickle cell disorders) diseases have continued to contribute to the poor child survival statistics in the country which rank among the poorest in the world.
- 4. There are increasing cases of children being denied access to timely and quality health care (sometimes life saving) due to extreme religious and socio-cultural practices with their attendant contribution to the burden of avoidable mortality.
- 5. Although the School Health Programme is a valuable strategy for promoting child health, this has been virtually non-existent in the country.
- Although the National Health Insurance Scheme (NHIS) is a potentially viable means of mobilizing resources for child health care in Nigeria, the coverage is inadequate for any meaningful impact.
- 7. The Child Rights Act which was passed into law by the National Assembly lacks the 'teeth' to make it enforceable across the Federation.
- 8. The improved vaccine coverage rates remain insufficient to eradicate the diseases for which the vaccines are given.
- 9. Malnutrition remains a major problem among children in Nigeria and there is need to pay attention to the silent burden of micro-nutrient deficiency.
- 10. Despite the continued high incidence of diarrhoeal diseases, there has been a significant reduction in diarrhoea related mortality and this is attributable to improvement in case management.
- 11. The regulatory role of the NAFDAC in safeguarding the health of the nation is noted with satisfaction. However, the recent regulation regarding the marketing of infant and young children food and other designated products is considered too intrusive. This is inimical to fruitful public and private sector partnership in dealing with the challenges that face child nutrition and survival in Nigeria.
- 12. Despite the inclusion of paediatricians in some policy decisions bodies, the level of representation on child health care issues is still inadequate.

The Conference recommends that:

- Resources should be adequately mobilized and equitably distributed at all levels of governance, especially in the rural and underserved populations.
- Corporate organizations and multinational agencies should engage in widespread activities such as infrastructural development, capacity building, provision of supplies that would impact positively on the health of the Nigerian child.
- 3. Government should increase the NHIS coverage to all sectors and should in particular underwrite the premium paid on children aged less than five years
- 4. Special consideration should be given to children with chronic conditions such as HIV/AIDS, tuberculosis and sickle cell disease in the provision of care and free drugs, not forgetting their psychosocial needs.
- 5. Paediatricians at all levels should get involved in the planning and distribution of resources starting from their local environment. Local hospital budgets should be based on activities, programmes and needs of children catered for by the respective paediatric departments.
- 6. State governments should as a matter of urgency, adopt the Child Rights Act as have been done by Lagos and Ogun states.
- There should be a categorical legal provision to protect the rights of children to life saving medical care.
- Promotion of exclusive breastfeeding until the age of six months and the introduction of

- appropriate (fortified) complementary feeds thereafter, should be continued.
- To further consolidate the gains of improved diarrhoea case management, the use of zinc should be promoted.
- 10. Routine immunization should be strengthened as a cardinal strategy for sustainable vaccine coverage in Nigeria.
- 11. Urgent attention should be paid to school health programme as an avenue for promoting the health of school-age children.
- 12. There should be a review of the NAFDAC regulation on the marketing of infant and young children food and other designated products regulation of 2005, by all stakeholders.
- 13. The involvement of the Paediatric Association of Nigeria (PAN) with its network of experts on child health matters is critical to the attainment of MDG 4. PAN should therefore constitute a strong advocacy group to liaise with Government at all levels, Development Partners and International NGOs to ensure appropriate representation of, and partnership with it on all child health care issues.
- 14. There should be coordination of all activities through involvement of all stakeholders, intersectoral collaboration and community participation.

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