

Relapse of Haemophilus Influenzae type B Meningitis Following Ampicillin Therapy - A Case Report

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SUMMARY

Oviawe O, Osaghae DO and Obi JO. Relapse of Haemophilus Influenzae type B Meningitis Following Ampicillin Therapy: A case report. *Nigerian Journal of Paediatrics*, 1988; 15:29 An 8-months old female infant, with relapse of H influenzae type b meningitis, following clinical and bacteriologic response to adequate ampicillin therapy is presented. It is speculated that persistence of the *Haemophilus influenzae* within the subdural tissue led to the bacteriologic relapse, and this could have been prevented had rifampicin prophylaxis been instituted prior to the initial discharge.

Introduction

ALTHOUGH bacterial meningitis is a common childhood problem, relapse bacterial meningitis is rare¹⁻². Relapse of bacterial meningitis is defined as reappearance of clinical and laboratory signs of meningeal infection within three weeks of completion of an appropriate treatment³. Most relapses are due to persistent infection in meningeal or parameningeal foci such as subdural empyema, ventriculitis brain abscess and mastoiditis or less frequently, failure to

eradicate nasopharyngeal colonisation in the patient. This report describes an infant with a relapse of Haemophilus influenzae type b (Hib) meningitis following adequate ampicillin therapy.

Case Report

Admission One

An 8-months old Nigerian female presented with a 4-day history of fever, vomiting and diarrhoea at the children's emergency room (CHER), University of Benin Teaching Hospital (UBTH), on February 17, 1986.

Physical examination at the time revealed a well-nourished infant who was irritable and mildly dehydrated. The anterior fontanelle was bulging and the neck was stiff. Her weight was 8.8kg, head

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Relapse of Haemophilus Influenzae Type B meningitist following Ampicillin Therapy

circumference 45cm and the rectal temperature was 40.2°C. The rest of the physical examination was unremarkable. Lumbar puncture yielded turbid cerebrospinal fluid (CSF) with 490 white blood cells per cubic millimeter (WBC/mm³) polymorphonuclear leukocytes; glucose concentration 10mg/dl (simultaneous blood glucose 95mg/dl) and protein, 140mg/dl. Gram stain showed numerous gram negative cocobacilli. Serum electrolytes and urea were normal and haemoglobin genotype was AA.

Cerebrospinal fluid culture grew *H influenzae* type b sensitive to ampicillin while blood and urine cultures were sterile.

Treatment was initiated with ampicillin (400mg/kg/24hours) intravenously in four divided doses. The infant became afebrile on the third day of hospitalisation and remained so for the rest of the 12-day course of ampicillin therapy. Lumbar puncture on the 10th hospital day, revealed a clear CSF with 45 mononuclear cells/mm³ glucose concentration of 37mg/dl (simultaneous blood glucose 76mg/dl and protein of 40mg/dl. The CSF culture and gram stain were negative.

On the 16th day in hospital, the patient developed typical measles rash which was managed with liberal fluids and paracetamol syrup. At the time of discharge on the 20th hospital day, she was well and had no discernible neurological sequelae. The head circumference remained unchanged.

Admission Two

Seven days after discharge, she developed fever, vomiting and convulsed for the first time. Before she was seen again in CHER, she had experienced seven episodes of seizure. Although the seizures were generalised initially, they had become restricted mainly to the right half of the body.

On examination, she was irritable, rectal temperature was 40°C and there was marked

bulging of the anterior fontanelle. Body weight was 7.2kg and the head circumference was 45.8cm. Neurologic examination revealed opisthotonic posturing in a semicomatose infant who had generalised hyperreflexia and sustained right sided ankle clonus.

Fundoscopy showed congested discs. Lumbar puncture yielded an opalescent CSF, with 850 polymorphonuclear cells/mm³. Gram stain showed numerous gram negative cocobacilli. CSF glucose concentration was less than 10mg/dl (simultaneous blood glucose 100mg/dl) while protein concentration was 400mg/dl. CSF and subdural fluid cultures grew *H influenzae* type b, with similar sensitivity pattern as the previous isolate; blood and urine cultures were sterile.

The patient was again treated with ampicillin (400mg/kg/24) intravenously in four divided doses; intravenous 20% mannitol (20mg/kg) in three divided doses. Radiographs of the skull, paranasal sinuses, chest and spine were normal. The throat and nose swabs for patient and the entire household were negative for *H influenzae*. Repeat lumbar puncture 48 hours after this admission yielded a sterile CSF, while the temperature returned to normal on the fifth day.

Lumbar puncture on the 15th hospital day revealed a clear CSF with 3 WBC/mm³, glucose of 63mg/dl (simultaneous blood glucose 100mg/dl) and protein of 30mg/dl. The CSF culture and gram stain were negative. Ampicillin therapy was continued for 17 days.

At the time of discharge on the 28th hospital day, she was spastic, deaf, blind and hydrocephalic (head circumference 46.5cm). When seen on follow up, decerebrate posturing and blindness persisted, hearing had improved but head circumference had increased to 47.5cm.

Discussion

Bacterial meningitis constitutes 2 per cent of total admission of the CHER of our hospital⁴ and since its inception 14 years ago, this patient is the

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first documented case of relapse of bacterial meningitis. This supports the observation by others¹⁻³ that relapse of bacterial meningitis is rare.

Relapse of this patient's Hib meningitis occurred despite treatment with ampicillin in a dosage and duration which are generally accepted as adequate⁵ and despite normal CSF findings at the end of therapy. The relapse was not due to bacterial resistance or inadequate CSF penetration by ampicillin since isolates of H influenzae from this patient on both occasions were sensitive to ampicillin and its reinstitution in the same dosage as used initially resulted in prompt defervescence and sterilisation of the CSF. Other possibilities such as brain abscess and mastoiditis are unlikely because of the absence of signs of these diseases.

Although lack of facilities prevented cerebral vasculitis from being excluded, the long interval between completion of initial therapy and onset of secondary fever precludes this diagnosis. In a case of localised cerebral vasculitis documented by Feldman *et al*⁶, relapse occurred within 72 hours of cessation of therapy. Furthermore, re-infection from family contacts or persistent pharyngeal colonisation in the index case was unlikely because the pharyngeal swabs obtained from these were negative for Haemophilus influenzae.

Subdural effusion was demonstrated in our patient on the second admission and this contained viable H influenzae type b, with similar sensitivity as the isolates from CSF obtained during the first and second admissions. We speculate that the bacteriological relapse was associated with a sequestered focus around the subdural space.

The occurrence of measles infection soon after the cessation of ampicillin therapy in our patient was coincidental and probably played no part in the relapse of the Hib meningitis. Besides, the immunological impairment induced by measles and the immune factors required to protect tissues against haemophilus infection are dissimilar⁷⁻⁸.

In retrospect, the relapse of Hib meningitis in our patient could have been prevented by

prophylactic administration of rifampicin prior to the initial discharge from hospital. The Committee on Infectious Diseases of the American Academy of Paediatrics recommends rifampicin at a dose of 20mg/kg once daily for four days for children who have had appropriate treatment for Hib meningitis and that this treatment should be initiated before discharge from hospital.

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Relapse of Haemophilus Influenzae Type B meningitis following Ampicillin Therapy

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Although lack of isolation prevented a definitive diagnosis, the meningitis was probably bacterial in origin. The meningitis was not due to a relapse of meningitis because the culture of the cerebrospinal fluid was negative for Haemophilus influenzae. A natural infection was demonstrated in our patient on the second admission and this contained a type B influenzae type b with similar sensitivity as the isolates from CSF obtained during the first and second admissions. We speculate that the bacteriological relapse was associated with a relapsed focus around the subdural space. The occurrence of meningitis infection soon after the cessation of ampicillin therapy in our patient was coincidental and probably played no part in the relapse of the Hb meningitis. Besides the immunological response induced by vaccines and the immune factors required to protect against meningitis infection the occurrence of meningitis is dependent on the status of the organism in the subdural space. Our patient could have been protected by