# NEONATAL MENINGITIS DUE TO NON-ENCAPSULATED HAEMOPHILUS INFLUENZAE IN A SET OF TWINS – A CASE REPORT

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*ABSTRACT*

***A set of twins born to a 24-year-old primigravida had evidence of sepsis 24 to 60 hours after birth and were treated empirically with penicillin and gentamicin. A non-encapsulated H. influenzae biotype IV strain was isolated from the blood cultures of both and from the CSF of twin II. The isolates were β-lactamase positive and hence showed resistance to ampicillin and therapy was changed to chloramphenicol only. Twin II recovered but Twin I developed a brain abscess in the left occipital region which resolved with extended antibiotic treatment. Although ampicillin-resistant H. influenzae have been reported in Malaysia, invasive disease by such strains are rare.***

*Keywords: neonatal meningitis, H. influenzae, ampicillin resistance, brain abscess.*

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## INTRODUCTION

*Haemophilus influenzae* is an important cause of invasive disease in children between the ages of 2 months and 4 years with an incidence of 52/100,000 live births[1]. Neonatal infections are rare but increasing prevalence has been reported[2,3]. At the University Hospital, Kuala Lumpur, *H. influenzae* is an important cause of childhood purulent meningitis but not of neonatal meningitis[4].

Invasive *H. influenzae* infections have been associated with capsulated strains belonging to serotypes a-f, type b being the most important. Non-encapsulated strains have commonly been isolated from the respiratory tract and less frequently from the genital tract[2,5].

The antibiotics commonly used to treat serious *H. influenzae* disease have been chloramphenicol and ampicillin. However strains resistant to ampicillin and chloramphenicol appeared in the early 1970's[6] and in the United Kingdom in 1986 ampicillin resistance was 7.8% whilst resistance to chloramphenicol was 1.7%[7].

In this paper, we describe a case of neonatal *H. influenzae* meningitis in a set of twins born at the University Hospital, Kuala Lumpur in August 1987.

## CASE REPORT

A 24-year-old primigravida went into spontaneous labour after 39 weeks' of uneventful twin pregnancy. Membranes were artificially ruptured and the liquor was clear. During labour of 20 hours duration, she was given ampicillin 500 mg 6 hourly for a probable urinary tract infection.

### Twin I

Female, birth weight of 2,250 gm, was delivered by vacuum extraction and except for a chignon was well with normal blood counts and negative bacterial cultures. However, at 48 hours of life, she became febrile and C-reative protein (CRP) was elevated to 62 mg/L. She was started on intravenous crystalline penicillin (200,000 iu/kg/day) and gentamicin (5 mg/kg/day) after blood for culture was taken. At 60 hours of life, the baby was found to be irritable and scleraemic. Cerebrospinal fluid obtained by lumbar puncture was negative for organisms both on the smear and culture, but CSF biochemical and cellular findings were suggestive of pyogenic meningitis. Antigens of *H. influenzae* type b and Group *B streptococci* were not detected in the CSF by a latex agglutination method (Slidex meningite kit, Bio Merieux, France) or a coagglutination method (Phadebact, Pharmacia Diagnostics).

However, since there were positive findings in the CSF of Twin II, penicillin was replaced by ceftazidime and the dose of gentamicin was increased to 7.5 mg/kg/day. 12 hourly and twice volume exchange transfusion was carried out for scleraemia. On day 3 of life the blood culture results were positive for *H. influenzae* and chloramphenicol (100 mg/kg/day) was started, replacing all other antibiotics. However, on day 10, fever recurred and a small abscess (estimated volume of 1 ml) was seen in the left occipital region on the CT scan (Fig 1). The neurosurgeon was of the opinion that the abscess was located in a high surgical risk area and conservative management was recommended. Chloramphenicol was continued for a total of 4 weeks and she was discharged well.

### Twin II

Female, birth weight of 2,000 gm, was in breech presentation and was well until 60 hours of life when she was found to be febrile, refusing feeds and had a raised CRP (67 mg/L). Ceftazidime and gentamicin therapy was started when the gram stained smear of CSF showed gram negative bacilli, but was replaced with chloramphenicol when CSF and blood cultures grew *H. influenzae*. *H influenzae* type b antigen was not detected in the CSF. On day 5 she developed a subdural effusion; this was tapped and 8 ml of fluid was obtained; further progress was uneventful and she was discharged well after a total of 3 weeks of chloramphenicol.

At 18 months of follow-up, both children remained well and had no neurological deficit.

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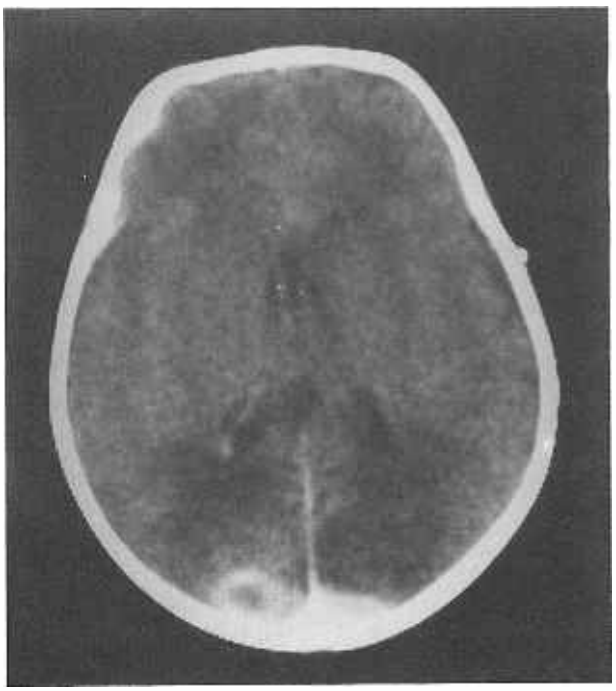
**Bacteriology**

The organisms isolated from the CSF of Twin II and blood cultures of both babies were identified as *H. influenzae* using standard bacteriological techniques. Agglutination with *H. influenzae* polyvalent antisera (Difco) was negative and there was no iridiscence of growth on Levinthal agar indicating a non-encapsulated strain. Using the method described by Kilian[8] the isolates were identified as biotype IV. A high vaginal swab taken post-partum from the mother grew a similar organism. The isolates were sensitive to chloramphenicol, erythromycin, cotrimoxazole, gentamicin, ceftazidime, cefotaxime and ceftriaxone but resistant to ampicillin and tetracycline by the disc diffusion method. The MIC for ampicillin by the agar dilution method was > 32 mg/L. β-lactamase activity of the isolate was detected by the acidometric method (Oxoid, UK).

**Fig 1 – CT scan of the brain of Twin I, showing an enhancing ring lesion, indicative of an abscess in the left occipital region.**



## DISCUSSION

Neonatal infections due to *H influenzae* are rare but increasing prevalence had been reported by several authors[2,3]. In our hospital only two cases have been reported[9]. Non-encapsulated strains have been mainly responsible for neonatal sepsis[3,10] especially those belonging to biotypes II and III[3] but two other reports implicate biotype IV in 25% to 38% of neonatal septicaemia[2,11]. Biotype IV strains have characteristic peritrichous fimbriation and a homogenous outer membrane protein pattern which may help in colonisation of the genital tract[11].

*H influenzae* is believed to be transmitted from mother to the baby either *in utero* or during delivery[2,3,10,12]. Prematurity, early rupture of membranes, prolonged labour and maternal genito-urinary infections all contribute to the development of neonatal sepsis[3,10]. Early onset fulminating infection and pneumonia with respiratory distress are the usual clinical manifestations of neonatal *H. influenzae* infections[2,3,12]. Neutropenia, a feature in early neonatal sepsis, and CRP values are useful in evaluating and monitoring the progress of such infections[12]. Complications such as brain abscess following meningitis are rare and only about four such cases have been reported[13].

The drugs of choice in the treatment of *H. influenzae* meningitis have been ampicillin and chloramphenicol. However, ampicillin resistance due to β-lactamase production has been reported to be 6.2% of *H influenzae* strains in the UK in 1986[7]. In addition there was a high prevalence of β-lactamase production amongst biotypes IV and V strains[7]. Chloramphenicol resistance due to the production of acetyl transferase is extremely unusual with a reported rate of 1.7% in 1986 in the UK[7].

In our experience, the prevalence of ampicillin and/or chloramphenicol resistance among all isolates of *H. influenzae* is less than 5% and thus these antibiotics are still useful in the empirical treatment of *H. influenzae* infections. However, in neonates in whom non-encapsulated strains of *H. influenzae*, gram-negative bacilli and group B streptococci are important pathogens, then perhaps a cephalosporin such as cefotaxime, ceftriaxone or ceftazidime may be a better choice. *Listeria monocytogenes* may not be effectively treated with the third generation cephalosporins but is a rare cause of neonatal infections in our setting.

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