

## Case Report

# ***Haemophilus parainfluenzae*: report of an unusual cause of neonatal sepsis and a literature review**

Binu Govind<sup>1</sup>, Balaji Veeraraghavan<sup>2</sup>, Shalini Anandan<sup>2</sup>, Niranjan Thomas<sup>1</sup>

Department of Neonatology<sup>1</sup> and Department of Microbiology<sup>2</sup>, Christian Medical College, Vellore, Tamil Nadu, India

### **Abstract**

*Haemophilus parainfluenzae*, an unusual cause of early-onset neonatal sepsis, is rarely reported. Risk factors for this serious infection include prolonged rupture of membranes, choriamnionitis, and prematurity. A high index of suspicion, proper culture techniques, and rapid species identification are needed to diagnose *H. parainfluenzae* sepsis. We present the first documented case from India with a review of the literature.

**Key words:** neonatal sepsis; *H. parainfluenzae*; early-onset sepsis

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### **Introduction**

*Haemophilus* species are considered to be normal flora in the upper respiratory and urogenital tracts [1,2]. Paediatric infections due to *H. influenzae* are common in children between six months and six years of age. *H. parainfluenzae*, however, is an unusual cause of invasive bacterial disease, particularly of neonatal sepsis. Although maternal-fetal vertical transmission has been documented, there are very few reports of early-onset-neonatal sepsis due to *H. parainfluenzae* [3-8]. We report the first case of *H. parainfluenzae* early-onset neonatal sepsis from India in a very low birth weight (VLBW) preterm baby.

### **Case report**

A male baby born at 32 weeks' gestation to a 20-year-old gravida 2, abortion 1 mother was transferred to our hospital at three hours of age with severe respiratory distress. The mother had an uneventful antenatal period until she developed spontaneous labour at 32 weeks of gestation. The duration of rupture of membranes was not known; however, the mother was in active labour with the baby in the breech position so a lower segment caesarean section (LSCS) was performed. She did not have intra-partum fever and there was no documentation of intra-partum antibiotic administration. The baby weighed 1580 grams and had a weak cry at birth but he did not require resuscitation. The baby was referred to our

hospital when it appeared to be suffering from respiratory distress from birth. On admission to the hospital the baby was in severe distress and was intubated in the emergency room and transferred to the neonatal intensive care. An X-ray showed low volume lungs with a left-sided pneumothorax. The baby was started on intravenous penicillin and gentamicin after a blood culture and septic screen were obtained. Initial counts showed leukopenia with a total white blood count of 2520/mm<sup>3</sup>, absolute neutrophil count of 425/mm<sup>3</sup>, immature to total neutrophil ratio of 35%, platelet count of 72,000/mm<sup>3</sup> and a positive C-reactive protein (CRP) of 18.5 mg/L. The baby was mechanically ventilated, an intercostal tube was inserted, and one dose of surfactant administered. However, in view of worsening respiratory failure, high-frequency oscillatory ventilation (HFOV) was initiated and inotropes were administered.

As the baby was deteriorating with hypotension, falling platelet count and evidence of disseminated intravascular coagulation (DIC), he was transfused with fresh frozen plasma and antibiotics were changed to Meropenem and Netilmicin. On day 3 the initial blood culture, using the BacT/ALERT 3D system (Biomérieux, Durham, NC, USA) and X and V factors, grew a Gram-negative bacterium that was identified as *H. parainfluenzae*. An antibiotic sensitivity profile (Kirby-Bauer method) showed that the organism was sensitive to ampicillin, cefotaxime,

**Table 1.** Neonatal invasive *Haemophilus parainfluenzae* in English literature

Case	GA (weeks)	B.Wt (g).	ROM (hrs)	Chorioamnionitis	Age at presentation (hours)	Blood Counts	Maternal Culture	Neonatal Cultures	Outcome	Ref
1	Term	NS	NS	No	48	NS	No culture	CSF & Throat	Well	4
2.	NS	3460	NS	Yes	144	NS	No growth	Blood & CSF	Well	6
3.	Term	2840	20	No	29	NS	No culture	Blood & CSF	Well	6
4	Term	3400	8	No	60	Leukopenia Thrombocytopenia- NS	Blood	Blood & Scalp	Well	5
5	27	730	48	Yes	<1 hour	Leukopenia No Thrombocytopenia	Placenta Cervix	Blood	Died	6
6	29	1150	48	Yes	Birth	Leukopenia Thrombocytopenia- NS	Placenta	Blood	Died	7
7	27	900	8	Yes	Birth	Leukopenia No Thrombocytopenia	No culture	Blood & Tracheal aspirate	Well	8
8	32	1580	3	No	Birth	Leukopenia Thrombocytopenia	Urine and blood negative	Blood	Well	PC

ROM- rupture of membranes, NS-Not stated, PC-Present Case

azithromycin, chloramphenicol and imipenem; hence the antibiotics were changed to cefotaxime.

Once respiratory status improved, the chest tube was removed and the baby was extubated to continuous positive airway pressure (CPAP) after seven days. Clinical and laboratory parameters improved. A lumbar puncture performed on day 10 of life was suggestive of meningitis (cerebrospinal fluid cells, 760/mm<sup>3</sup>; protein, 319 mg%; glucose, 22 mg%). Intravenous cefotaxime was given for a total of 21 days. The baby was also noted to have bilateral grade 3 intraventricular haemorrhage, patent ductus arteriosus, hypocalcemia, hyponatremia and anaemia during the course of his hospital stay. The baby was discharged well on exclusive breast feeds after 40 days of hospital stay. He was followed up in the high-risk infant clinic at six weeks and three months of age, at which time he was growing normally with normal tone and appropriate milestones.

The mother developed high fever on the fourth postpartum day. Her urine culture grew *E. coli* but the blood culture was negative. After she was treated with intravenous antibiotics (piperacillin + tazobactam) she became afebrile.

## Discussion

*Haemophilus parainfluenzae* causes a variety of systemic infections in adults, including endocarditis, meningitis, arthritis, urinary tract infections (UTI), and genital infections. In children, commonly between six

months and four years of age, infections may include upper and lower respiratory tract infections, endocarditis, hepatic abscess, meningitis and brain abscess, with endocarditis and meningitis most frequently reported [9]. *H. parainfluenzae* meningitis has been associated with endocarditis, especially in those patients with underlying congenital heart disease. Risk factors include oral piercing, dental work, and poor oral hygiene [10].

Neonatal sepsis due to *H. influenzae* is well documented and its incidence has recently been increasing. [11]. Neonatal septicaemia caused by *H. parainfluenzae*, however, is still very rare and it is postulated to be secondary to protective maternal antibodies [12]. Since the first report in 1966 of a neonate with *H. parainfluenzae* meningitis [4], there have been only six cases of invasive *H. parainfluenzae* neonatal infections reported in the literature (Table 1). All cases were early-onset with risk factors for sepsis present. Three of the seven cases (42.8%) were preterm and maternal infection was confirmed in three. Three (42.8%) of the babies also had associated meningitis. Overall survival was 71.4%. It was interesting to note that leukopenia was seen in all cases whenever reported. Our patient was born preterm with a risk of sepsis and presented with respiratory distress from birth as well as severe leukopenia and thrombocytopenia, features of septic shock, DIC and meningitis. This clinical profile is very similar to those of previously reported cases and

our patient is the first case of *H. parainfluenzae* neonatal sepsis reported from India.

Neonatal infection due to *H. parainfluenzae* is probably acquired secondary to ascending infection through ruptured membranes, as it has been cultured from the genital tract of asymptomatic women [2]. Quentin, *et al.* isolated 30 strains of *H. parainfluenzae* from genitourinary and mother-infant infections in which premature births and premature rupture of membranes were the leading causes of amniotic contamination and neonatal infection which suggests that the latter originates from commensal flora of the genital tract [3]. In our patient the maternal source of infection could not be proved because although the mother had postpartum fever, her urine and blood cultures did not grow *H. parainfluenzae*.

There is a possibility that the incidence of *H. parainfluenzae* may be under-reported because of difficulties in isolation of the organism in culture due to lack of proper and standardized culture techniques, lack of standardization, and difficulties associated with species identification. *Haemophilus parainfluenzae* is a fastidious, Gram-negative bacilli that grows optimally on chocolate agar at 35°C in 5% CO<sub>2</sub>. Therefore, culture media using horse or human blood may altogether miss the diagnosis. *Haemophilus* strains isolated in culture should not be assumed to be *H. influenzae* and species identification should be performed using X (haemin) and V (NAD-NADP) factors. In cases where the culture is negative, diagnosis can be established by molecular diagnostic methods such as broad range polymerase chain reaction (PCR) and sequence analysis of the bacterium 16S rRNA gene [10].

*H. parainfluenzae* produces beta lactamase to a much higher degree than other organisms and is usually resistant to penicillin and ampicillin. Hence it may be necessary to treat such cases with third-generation cephalosporins such as cefotaxime. Although neonatal sepsis due to *H. parainfluenzae* is rare, it should be included as a serious pathogen that causes early-onset neonatal sepsis.

Significant risk factors for infection include prolonged rupture of membranes, choriomnionitis, and prematurity. A high index of suspicion, proper culture

techniques, and rapid species identification may help in the detection of more *H. parainfluenzae* cases.

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## Corresponding author

Niranjan Thomas  
 Christian Medical College  
 Vellore 632004 Tamil Nadu, India  
 Email: niranjan@cmcvellore.ac.in

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