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Case Report

Hafnia alvei causing late onset sepsis in neonates: report of two cases and review of literature

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ABSTRACT

Hafnia alvei, a Gram negative motile bacillus that belongs to Enterobacteriaceae family is rarely associated with infection in pediatric patients and is exceptionally rare in the neonatal period. *H. alvei* is ubiquitous in the environment, causing infections in debilitated and immuno-compromised patients with few cases being reported in neonates. We report two cases of late onset sepsis in term neonates caused by *H. alvei* that were successfully treated in our unit. To the best of our knowledge, infection due to *H. alvei* has not been reported in neonates from India. *Hafnia alvei* causes infection rarely in neonates. Because it can cause nosocomial outbreaks, awareness regarding this uncommon pathogen and initiation of appropriate antibiotic therapy improves the outcome and prevents mortality.

Keywords: *Hafnia alvei*, Neonate, Sepsis

INTRODUCTION

Hafnia alvei is a Gram negative motile bacillus and facultative aerobe which rarely causes infection in infants.[1-3] In 1988, *H. alvei* infection was first reported in neonates in a 20-day old preterm (30 weeks) baby with sepsis and NEC.[4] Compared to adult population, few isolated cases of *H. alvei* infection were reported in neonates.[5,6] Two outbreaks of nosocomial *H. alvei* sepsis were reported in neonates.[7,8]

Till to date, only 17 cases of *H. alvei* sepsis were reported in neonates. We report two cases of late onset sepsis in term neonates due to *H. alvei* that were treated in our unit.

We also reviewed the literature for previously reported cases of sepsis caused by *H. alvei* in neonates. To the best of our knowledge, this is the first report of *H. alvei* causing sepsis in neonates from India.

CASE REPORT

Case 1

A term female baby weighing 2540 grams was born to an 18-year-old $G_2P_1L_1$ mother by cesarean section at 38 weeks of gestation. There was no history of maternal fever or prolonged rupture of membranes. Liquor was clear. Apgar scores were 8 and 9 at 1 and 5 minutes of age. Baby was tachypnoeic soon after birth and was admitted in NICU in the referral hospital. Tachypnoea lasted for 24 hours and feeds were started. Baby was accepting breastfeeds well. On the 4th day of life, baby had feeding intolerance and developed abdominal distension. On the 5th day of life, baby had fresh blood in stools and was referred to our unit for further care.

On examination, baby was febrile, sick looking with cold extremities and poor perfusion. Baby's temperature was 101.4°F, heart rate 162/minute, respiratory rate 54/minute and SpO_2 94% in room air. Laboratory investigations

showed Hb of 12.4 gm/dl, leucocytosis (WBC: 21700/cu.mm), thrombocytopenia (platelets: 0.83 Lakhs/cu.mm) and elevated C-reactive protein (CRP: 47.2 mg/L). Abdominal radiograph showed dilated bowel loops without pneumatosis or pneumoperitoneum. Blood culture was taken and IV antibiotics (piperacillin and amikacin) were started. Prothrombin time (PT) and activated partial thromboplastin time (APTT) were prolonged (PT: 28 seconds; APTT: 58 seconds; INR: 2.4) and baby received FFP and PRP transfusions. Cerebrospinal fluid (CSF) examination was normal.

Blood culture done on Bactec 9050 (BD Diagnostic Systems, USA) was positive at 48 hours. Gram stain showed presence of Gram negative bacilli. Subculture on Mac Conkey's agar and 5% sheep blood agar showed growth of non-lactose fermenting colonies that were catalase positive and oxidase negative. Automated bacterial identification and antimicrobial susceptibility testing were done using Microscan Autoscan 4 (Siemens, Germany). Isolate was identified as *Hafnia alvei*, which was sensitive to piperacillin-tazobactum (MIC <16 mcg/mL) and tigecycline (MIC <1 mcg/mL) and resistant to aminoglycosides, extended spectrum penicillins, cephalosporins and carbapenems. Intermediate sensitivity was reported for imipenem, meropenem and moxifloxacin.

Baby was treated with piperacillin-tazobactum and meropenem for 2 weeks and has recovered completely.

Case 2

A term female baby weighing 2980 grams was born to a 20-year-old primigravida mother by cesarean section at 39 weeks gestation. There was no history of maternal fever or prolonged rupture of membranes. Liquor was clear. Baby was vigorous at birth and was breastfed. On the 4th day of life, baby was dull and refused feeds. On the 5th day of life, baby had left focal clonic seizures and was referred to our unit. On examination, baby was afebrile and in moderate stupor. Baby's temperature was 98.6˚F, heart rate 138/minute, respiratory rate 42/ minute and SpO_2 95% in room air. Laboratory investigations showed Hb of 16.4 gm/dl, WBC 16700/cu.mm, platelets 1.93 Lakhs/cu.mm and C-reactive protein (CRP: 21.2 mg/L). Blood culture was taken and IV antibiotics (piperacillin and amikacin) were started. Head ultrasound showed cerebral edema without any intra cranial hemorrhage. CSF examination was normal. Baby had 3 episodes of focal clonic seizures over next 48 hours. Seizures were controlled with phenobarbitone and levetiracetam. Blood glucose, calcium, electrolytes, ABG, ammonia and metabolic profile were normal. EEG showed right hemsipsheric dysfunction.

Blood culture turned positive at 48 hours and the isolate was identified as *Hafnia alvei.* The antibiotic susceptibility pattern was exactly similar to the previous case. Baby's sensorium improved from 5th day of admission without recurrence of seizures.

Baby was treated with piperacillin-tazobactum and meropenem for 2 weeks and has recovered completely. Both the babies had normal growth and development at follow-up.

DISCUSSION

Hafnia alvei, a Gram negative motile bacillus and facultative aerobe that belongs to the family *Enterobacteriaceae* is a part of the human gastrointestinal flora and environmental habitats such as surface water, soil and sewage.[1] In 1954, Möller first described this genus and suggested the name *Hafnia alvei*.[2] The genus name *Hafnia* is the historical name (Havn) for the city of Copenhagen, Denmark and the species name *alvei* (derived from Latin) means "of a beehive".[1,3] Literature search of Pubmed, Embase, Medline and Google scholar were done using the words: neonate, sepsis and *Hafnia alvei*. Infants ≤4 weeks of age and those reported as new-born or neonate were included in the review.

Once thought to be a simple commensal of the gastrointestinal tract, recent findings suggest that it is a rare but significant pathogen causing opportunistic infections in man.[3,9,10] Till to date, 17 cases of *H. alvei* sepsis were reported in neonates, of which 15 were preterm (88% of cases) and the mortality was 17.6% (3 deaths) (Table 1).

Table 1: Characteristics of *H. alvei* sepsis reported in neonates.

Author and year	No. of cases	Age of onset	Isolated from	Outcome
Ginsberg, Goldsmith[4]	1	20 days	Blood	Survived
Amil Pérez et al[7]	4	7, 21, 30 and 35 days	Blood, vascular catheter (2 cases)	1 died, 3 survived
Casanova-Román[5]	1	8 days	Blood	Survived
Rodríguez-Guardado et al[8]	10	26 days	Blood, vascular catheter (2 cases), tracheal aspirate (3 cases)	1 died, 9 survived
Claudia Moreno et al[6]	1	3 days	Blood	Died
Present case	2	5 days	Blood	Survived

In 1988, *H. alvei* infection was first reported in neonates in a 20 day old preterm (30 weeks) baby with sepsis and NEC.[4] In 2004, a nosocomial outbreak of *H. alvei* sepsis was reported in 4 preterm babies (24-31 weeks) by Pérez A et al from Spain.[7] In the same year, another case of late onset neonatal sepsis with *H. alvei* was reported in an 8 day old neonate.[5] A retrospective study by Rodríguez-Guardado et al identified 10 cases of *H. alvei* sepsis in preterm neonates.[8] Four cases of *H. alvei* sepsis in a cardiac surgical unit were reported by Moreno C et al from Chile, of which 1 patient was a neonate.[6] *H. alvei*, though considered rarely pathogenic, has been reported to cause gastroenteritis, meningitis, pneumonia, septicemia and abscesses.[9,10]

Though still uncommon in NICUs, infection with *H. alvei* is worrisome because of intrinsic resistance to commonly used antibiotics including ampicillin, aminoglycosides, first generation cephalosporins and carbapenems. It is usually susceptible to II and III generation cephalosporins and quinolones but resistance to these antibiotics is reported due to β-lactamases.[1,3] Both the cases of *H. alvei* sepsis admitted to our unit exhibited similar drug sensitivity patterns, though they were referred from different hospitals. They were sensitive to piperacillin-tazobactum and tigecycline, resistant to aminoglycosides, extended spectrum penicillins, cephalosporins and carbapenems and intermediately sensitive to imipenem, meropenem and moxifloxacin.

Both the cases presented on the 5th day of life and it was presumed that infection is perinatal in origin, acquired either from mother or postnatally in the referral hospitals. Maternal swabs, blood culture and environmental sampling were not done, and the source of infection was not identified.

H. alvei infection is usually associated with prolonged hospital stay, long duration of antibiotic therapy, mechanical ventilation and presence of central venous catheter.[6,9] None of these risk factors were present in our patients.

CONCLUSION

This case report highlights that *H. alvei* is isolated for the first time in India and there is a need for epidemiological surveillance in hospitals to identify the source of this uncommon pathogen. *H. alvei* infection, though uncommon can cause outbreaks with high mortality because of innate resistance to ampicillin and first generation cephalosporins. Awareness of this uncommon pathogen and initiation of appropriate antibiotic therapy improves the outcome and prevents mortality.

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