*Case Report*

# *Pasteurella (Mannheimia) haemolytica* septicemia in an infant: a case report

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**Abstract**

Septicemia due to *Pasteurella (Mannheimia) haemolytica* is a rare occurrence. We report a fatal case of *M. haemolytica* septicemia in a seven-month-old infant who presented with prolonged fever, sepsis, and pneumonitis without discernable preceding history of animal bites or contact. Rare cases of systemic *Mannheimia* infections are reviewed and summarized.

**Key words:** *Pasteurella; Mannheimia haemolytica;* infant; septicemia

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## Introduction

*Pasteurella* is a facultative, anaerobic Gram-negative coccobacillus commonly inhabiting the oral cavity or gastrointestinal tract of various animals. The first *Pasteurella* species was isolated in 1878 by Pasteur in fowl cholera [1]. Brugnatelli reported the first human case of *Pasteurella* infection causing puerperal sepsis in 1913 [2]. *Pasteurella multocida* is the most common species identified in human infection followed by *P. canis* and *P. dogmatis. P. haemolytica* was first reported in 1932 by Newsom and Cross as a cause of pneumonia, septicemia, and abortion in domestic animals [3]. Reports of such infections are very rare in humans. The first human case of *P. haemolytica* septicemia with endocarditis was reported in 1963 [4], followed by a case of arterial graft infection [5], a case of bacterial croup [6], and a case of septicemia associated with splenic abscess in 2003 [7]. Recent work published in 1999 on genetic analysis by Angen *et al*. has resulted in a new taxonomic classification for *P. haemolytica* which was reclassified in a new genus called *Mannheimia*, family Pasteurellaceae [8]. *Mannheimia haemolytica* infection in humans is extremely rare. Herein we report the first case of *M. haemolytica* septicemia in a child in Thailand.

## Case report

A seven-month-old male infant from a rural area of Supanburi Province, Thailand, was referred to the Children's Hospital (Queen Sirikit National Institute of Child Health/QSNICH), Bangkok, Thailand, with a history of unresolved fever for three weeks. The patient had a history of high-grade fever and pallor for six days before developing generalized tonic-clonic convulsion. No history of preceding viral syndromes or upper respiratory tract symptoms prior to the sudden high-grade fever was reported. At a community hospital, he received intravenous ampicillin before being transferred to Supanburi Provincial Hospital. Initial laboratory findings at the Provincial Hospital were as follows: Hct 24%; white blood cell count 13,800 cells/$mm^3$; neutrophils 77%; lymphocytes 7%; monocytes 3%; eosinophils 3%; platelets 250,000 cells/$mm^3$. Urinary examination revealed a white blood count of 10-20 by high power field. Chest X ray showed cardiomegaly and bilateral infiltration. Blood culture performed using an automatic BacT/Alert 3D system (bioMérieux Inc, Durham, NC, US) yielded Gram-negative bacilli of an unidentified species, susceptible to amikacin, ceftazidime, ciprofloxacin, gentamicin, imipenem, meropenem, cotrimoxazole, piperacillin, amplicillin/sulbactam. The patient was treated initially with cefotaxime for the first two days before being switched to meropenem, based on the result of the antimicrobial susceptibility pattern, due to his sustained high-grade fever. His condition did not improve after one week of meropenem treatment; azithromycin was then added. After three days of

meropenem and azithromycin combination therapy without clinical improvement, antimicrobial treatment was then changed to ciprofloxacin plus amikacin for eight days before he was referred to QSNICH in Bangkok.

Significant past medical history included low birth weight (2,370 grams) and epilepsy diagnosed at three months of age at QSNICH. The first and second convulsive episodes were generalized tonic-clonic seizures, which occurred when the patient was two and three months of age, respectively. There was no postictal neurological deficit. A lumbar puncture and a brain computed tomography (CT) scan were performed with no abnormality detected. The electroencephalogram had not been performed yet prior to this current illness episode. His seizure was brought under control after treatment with oral phenytoin and phenobarbital. Additionally, he had been diagnosed with pneumonia four times but had not yet been investigated for an underlying cause. Physical examination on admission at QSNICH showed an axillary temperature of 39.4°C; respiratory rate of 48/minute; blood pressure of 107/77 mmHg; body weight of 5.4 Kg with length of 61 cm and head circumference of 40 cm; and oxygen saturation of 92%. Chest auscultation showed bilateral rhonchi and systolic ejection murmur grade 2/6 in the left upper parasternal border. Liver was palpable at 5 cm below the right costal margin, with a firm, smooth surface. The spleen was palpable at 5 cm below the left costal margin. The rest of the physical examination was unremarkable. Laboratory tests showed leukocytosis of 35,800 cell/$mm^3$ with 70% neutrophils and 34.5% hematocrit. Electrolyte, liver and renal function tests were within normal limits except for hyponatremia (Na 131). Chest radiograph showed bilateral parenchymal infiltration. The initial antimicrobial regimen was ceftazidime plus amikacyinn. Three days later, no signs of improvement the antibiotic regimen was changed to cefoperazone/sulbactam (80 mg/kg/day since there was no sign of improvement. All other investigations including urinary analysis, stool examination and culture, stool for acid-fast bacilli stain, urine metabolic screening, Epstein Barr viral capsid antigen, melioid titer, anti-human immunodeficiency virus antibody, leptospirosis titer, rapid test for influenza, tuberculin skin test, lumbar puncture, bone marrow examination, bone survey, and echocardiography were negative. Blood culture done on admission at QSNICH was also negative. On day 5 of hospitalization, the patient developed a high-grade fever with progressive abdominal distension without any other signs of peritonitis. Abdominal radiography show generalized bowel ileus, and metronidazole was added to the regimen. On day 11 of the hospitalization, the patient's condition deteriorated with a spiked fever of 40°C and progressive abdominal distension. An ultrasound of the abdomen revealed intra-abdominal fluid collections. CT abdomen performed on the following day revealed bilateral pneumonia in the lower lobes with minimal bilateral pleural effusion, hepatosplenomegaly without space-occupying lesion, bowel ileus with questionable bowel edema or small amount of ascites. Vancomycin was added to the regimen due to concurrent phlebitis. On day 18 of admission, the patient developed progressive dyspnea requiring mechanical ventilation. Chest radiograph showed bilateral alveolar infiltration. Antimicrobial therapy was continued with cefoperazone/sulbactam (80 mg/kg/day), vancomycin (60 mg/kg/day) and metronidazole (30 mg/kg/day). Two days into the mechanical ventilation, the patient's condition progressively deteriorated, resulting in death on day 20 of admission. Post-mortem heart blood culture identified an elongated hyphal structure indicative of mold infection. However, the attending physician during that time did not request further investigations which would require sending the specimen to the Department of Medical Science, Ministry of Public Health, to identify the type of that particular fungus. The result of the initial blood culture done at Supanburi Provincial Hospital prior to referral to QSNICH was completed two days after the patient died. According to the report by the National Laboratory Center of the Department of Medical Sciences based on manual biochemical tests, the causative agent was identified as *Mannheimia haemolytica* biotype A *(Pasteurella haemolytica)*. The biochemical characteristics of this pathogen are shown in Table 1.

## Discussion

*Pasteurella (Mannheimia)* species, especially *M. haemolytica*, rarely causes infection in humans. *Pasteurella (Mannheimia) multocida* is among the most common species in the Genus Mannheimia identified as a human pathogen [1]. The most common manifestation is localized cellulitis in the area bitten or scratched by animals. Other and less frequent manifestations include septicemia, meningitis, respiratory tract infections, appendicitis, liver abscess, peritonitis, and urinary tract infections [1].

**Table 1.** Biochemical characteristics of the isolated organism

| Characteristic | Result | Base:Ent/OF/CTA/ASS | Result |
|---|---|---|---|
| Gram stain | negative rod | Glucose/gas | positive/negative |
| Hemolysis | ß-hemolysis | Lactose | negative |
| Growth on MacConkey | small mucoid pink colonies | Maltose | negative |
| TSI | A/N<br>gas negative | Mannitol | positive |
| $H_2S$ | negative | D-Xylose | positive |
| Catalase | positive | Rhamnose | negative |
| Oxidase | positive | Sucrose | negative |
| Motility | negative | Adonitol | negative |
| Indole | negative | L-Arabinose | positive |
| Citrate | negative | Inositol | negative |
| Urease | negative | Sorbitol | negative |
| Nitrate | positive | Trehalose | negative |
| $N_2$ gas | negative | Salicin | negative |
| Esculin | negative | | |
| Malonate | positive | | |
| VP | negative | | |
| LDA | negative | | |
| Lysine | not change | | |
| Arginine | not change | | |
| Ornithine | not change | | |

A/N: Acid/Neutral; Ent/OF/CTA/ASS: Enterobacteriaceae sugar base/Oxidation-fermentation basal medium/ Cystine tryptic agar/Ammonium salt sugar base; $H_2S$: Hydrogen sulfide; LDA: Lysine decarboxlase agar; $N_2$: Nitrogen gas; TSI : Triple Sugar Iron; VP: Voges-Proskauer

*M. haemolytica* infection in humans was reported for the first time in 1962 from the United States in a 54-year-old female patient presenting with diarrhea and fever for two weeks. No previous history of animal bite or scratch was identified. Investigations revealed evidence of endocarditis with blood culture positive for *M. haemolytica.* Despite the *in vitro* susceptibility to penicillin and chloramphenical, the patient had a relatively large vegetation and associated leaflet perforation and died on day 6 after hospitalization [4]. In 1991 Yaneza and colleagues reported the case of a 40-year-old male with fatal *P. haemolytica* endocarditis from Saudi Arabia [9]. The patient had neither underlying disease nor history of animal exposure. All four blood culture specimens yielded *P. haemolytica* susceptible to ampicillin, gentamicin, and ceftriaxone. Although the patient responded well initially to antimicrobial treatment, he developed intractable cardiac failure and died during the second week of hospitalization. In 1994, Rivera *et al*. reported another case with *M. haemolytica* infection in a 50-year-old male who underwent aortic bypass graft presenting with fever, abdominal, and back pain for three weeks [5]. A CT scan of the abdomen revealed pus collection at the aortic graft area. Pus culture grew *M. haemolytica* and group C beta-hemolytic streptococcus. After being treated with intravenous ampicillin for six weeks, the patient's condition improved significantly and eventually returned to normal. In 1998, the first case of *M. haemolytica* localized infection in children was reported from Japan in a nine-month-old infant with bacterial croup [6]. The patient presented with acute respiratory distress and deterioration of consciousness. Tracheal secretion culture on the day of admission grew *M. haemolytica* exclusively. The patient responded well to intravenous cefpirome and had an uneventful recovery. In 2003, Takeda *et al*. reported *M. haemolytica* sepsis in a 26-year-old male with asymptomatic mitral valve abnormality presenting with fever, pallor, and hepatosplenomegaly [7]. Magnetic resonance imaging of the abdomen revealed splenic abscess. No evidence of endocarditis was detected on the echocardiogram. *M. haemolytica* was isolated from the blood culture. The patient was treated with intravenous isepamicin and recovered after three weeks of antimicrobial therapy.

We report a case with pneumonia and septicemia from *M. haemolytica* biotype A unresponsive to antimicrobial therapy despite *in vitro* susceptibility data. No apparent history of prior animal contact or exposure was identified. Although we are not certain

that a history of animal bites was specifically investigated during the clinical evaluation, no pet was reported. In addition, the patient's age indicated exposure to an animal outside his home to be unlikely, making it unclear as to how he acquired this infection. However, existing literature indicates that it is possible for systemic *Pasteurella (Mannheimia)* infection to occur without any history of animal contact. Given the severity of the illness, the previous history of recurrent pneumonia, and early onset seizure disorder, we suspected that the patient might have had an underlying condition impairing his host defense mechanism. As the patient had received blood components prior to hospitalization at QSNICH, additional investigation was not feasible at that time.

The described case exemplifies the fatal outcome of *M. haemolytica* infection in an infant with a likely impaired host defense mechanism. To our knowledge, this is the first reported case of *M. haemolytica* septicemia in the pediatric population.

Invasive *M. haemolytica* infection is a rare clinical entity especially among the pediatric population. Significant and fatal complications may be associated with this infection despite *in vitro* antimicrobial susceptibility data. Risk factors of this condition remain to be elucidated.

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