EJ072200100293

J Microbiol Immunol Infect
2001;34:293-296

Pasteurella multocida bacteremia due to non-bite animal exposure in cirrhotic patients: report of two cases

Hsiang-Kuang Tseng, Shey-Chiang Su, Chang-Pan Liu, Chun-Ming Lee

Division of Infectious Diseases, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan, ROC

Received: January 29, 2001 Revised: February 26, 2001 Accepted: March 5, 2001

Pasteurella species are very small gram-negative coccobacilli. They are normal flora found in the oral cavity and gastrointestinal tract of many animals, and can cause various infections including septicemia and pneumonia. Human infection with *Pasteurella multocida* occurs commonly as a localized cellulitis caused by animal bites. This report described 2 rare cases of *P. multocida* bacteremia in patients with liver cirrhosis and esophageal varices. Both patients had a history of contact with sick-appearing stray dogs, but neither had been bitten. *P. multocida* bacteremia should be included in the differential diagnosis of febrile cirrhotic patients with esophageal varices who have a history of non-bite animal exposure. Avoidance of animal contact by immunocompromised patients is the most important factor in preventing pasteurellosis.

Key word: Bacteremia, liver cirrhosis, non-bite animal exposure, *Pasteurella multocida*

Pasteurella species are very small gram-negative, facultatively anaerobic, non-hemolytic, non-motile, and non-spore-forming coccobacilli measuring 1 to 2 μm in length. *Pasteurella* species, particularly *Pasteurella multocida*, have a worldwide distribution. Animals are the principal reservoirs of *P. multocida* [1-4]. Cats, dogs, and pigs have particularly high colonization rates (50%-90% in domestic cats, 50%-70% in dogs, and 50% in pigs) [2].

Pasteurellosis is a zoonotic disease [5] often caused by dog or cat bites and can results in cellulitis and/or subcutaneous abscesses [6-8]. This study reported 2 rare cases of *P. multocida* bacteremia [7] in liver cirrhosis patients with non-bite animal exposure treated at the Mackay Memorial Hospital within 1 month after a furious typhoon in northern Taiwan in early November 2000.

Case Report

Case 1

Case 1 was a 43-year-old man with a 20-year history of alcohol dependency and was a hepatitis B carrier. Liver cirrhosis had been diagnosed 3 years previously, and he had regular follow-up sessions at a gastroenterology outpatient clinic. During the follow-up period, he had been admitted many times to the hospital because of esophageal variceal (EV) bleeding and had undergone EV ligation (EVL).

He visited the emergency room because of abdominal pain on November 6, 2000, about 1 week after a serious typhoon had struck Taiwan. No specific findings were noted during the initial check-up, but he experienced sudden onset of fever and chills in the emergency room, and his body temperature was then elevated to 39.5°C. Empirical antibiotics (cephalothin and gentamicin) were given after blood sample was collected for culture. The antibiotic treatment was then changed to ceftriaxone and amikacin after blood sample was collected again for culture because of a decrease in white cell count to 1700 /mm^3 with band forms 8%, segmented neutrophils 68%, monocytes 1%, and lymphocytes 22%.

He was admitted to the hospital with a repeat white cell count of 5280 /mm^3 with band forms 15%. The fever subsided after 3 days, and the antibiotics administered were changed to cefoxitin and gentamicin. Blood cultures grew small gram-negative coccobacilli, which were identified as *P. multocida*. He was discharged in stable condition after 10 days of intravenous therapy.

The patient worked as a guard at an apartment building complex. He described that after the typhoon, the number of stray dogs around the complex had increased, with many coming into his guardhouse. He recalled that the dogs had an unpleasant odor that smelled like seminal fluid, but denied being bitten or scratched by any of the dogs.

Corresponding author: Dr. Shey-Chiang Su, Division of Infectious Disease, Department of Internal Medicine, Mackay Memorial Hospital, 92, Chung Shan North Road, Section 2, Taipei 104, Taiwan, ROC.

Case 2

Case 2 was a 54-year-old man who had liver cirrhosis for more than 3 years with intermittent EV bleeding and repeated EVL. His cirrhosis was hepatitis C-related and was associated with a blood transfusion during a gallstone operation about 25 years ago. He also had Type II diabetes mellitus that had been well treated with oral hypoglycemic agents (metformin and glipizide) for more than 10 years.

He was admitted to the gastroenterology ward for repeat EVL therapy on October 23, 2000. His vital signs were normal at admission. Physical examination showed spider angiomata and palmar erythema. Abnormal laboratory data included a fasting glucose of 279 mg/dL (normal range, 70-120 mg/dL), albumin 2.9 g/dL (normal range, 3.5-5.3 g/dL), aspartate aminotransferase 38 U/L (normal range, 5-35 U/L), and alanine aminotransferase 43 U/L (normal range, 5-30 U/L). Chest roentgenography showed increased bilateral lung markings compatible with chronic bronchitis. He underwent EVL twice and endoscopic sclerotherapy once during hospitalization, and was scheduled to discharge on November 13, about 2 weeks after the typhoon. Nevertheless, he experienced active EV bleeding after a meal at midnight on November 12. He became hypotensive, requiring massive blood transfusion and repeat EVL. On the next day, fever occurred and a transfusion reaction was suspected. High fever (up to 39°C) and chills persisted, and the white cell count was 5180 /mm^3 with band forms 4%, segmented neutrophils 89%, monocytes 3%, and lymphocytes 4%. Two sets of blood samples were drawn and cultured separately and empirical antibiotics (cephalothin and gentamicin) were given. The fever subsided 24 h later. Both sets of blood cultures grew small gram-negative coccobacilli, which were later identified as *P. multocida*. Intravenous cephalothin and gentamicin were given for 10 days. Oral cephalexin was given for a further 5 days in the hospital, and then for 5 more days following discharge.

He reported frequent visit to his sister's house where there was a pet dog with unknown sickness recently. He had physical contact with the dog but denied being bitten or scratched. The dog had been a stray picked up by his sister 6 months before he was infected.

Microbiological methods

The isolates from Cases 1 and 2 were identified as *P. multocida* based on the following features: microaerophilic gram-negative coccobacilli (Fig. 1), nonmotile, no growth on MacConkey agar, oxidase positive, and sucrose fermentation without gas production.

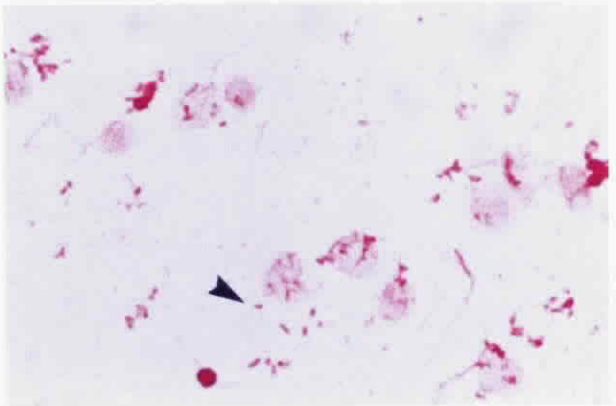

Fig. 1. *Pasteurella multocida*, small gram-negative coccobacilli, was isolated from the blood culture of a febrile cirrhotic patient with esophageal varices after a non-bite animal exposure (Gram stain with carbol-fuchsin for counterstain instead of safranin x1000).

Further biochemical characterization included being strongly indole positive; catalase, nitrate, and ornithine positive; and urea negative [4]. The API 20 E (bioMerieux sa, 69280 Marcy l'Etoile, France) revealed a numerical code of 0144524 in Case 1 and 0044524 in Case 2, confirming the identification of *P. multocida*.

The 2 isolates were sensitive *in vitro* to ampicillin, chloramphenicol, cephalothin, cefoxitin, lomefloxacin, co-trimoxazole, amoxicillin-clavulanic acid, cefmetazole, cefuroxime, gentamicin, and tobramycin by the disc diffusion method [9].

Discussion

Pasteurellosis is a rare zoonotic disease. Brugnatelli [1] described the first human case of *Pasteurella* infection, a case of puerperal sepsis, in 1913. *Pasteurella* organisms usually cause cellulitis associated with animal bites. The infection is sometimes deep enough to cause tenosynovitis, septic arthritis, and osteomyelitis [6]. However, neither of the 2 cases reported here has been bitten.

The 5 species or subspecies that cause the majority of pasteurellosis are *P. multocida* subspecies *multocida*, *P. multocida* subspecies *septica*, *Pasteurella canis*, *Pasteurella stomatis*, and *Pasteurella dagmatis* [1,2]. In the 2 patients in this study, further identification of subspecies (dulcitol negative and sorbitol positive [4]) revealed *P. multocida* subspecies *multocida*.

P. multocida causes a wide spectrum of disease, including bacteremia, respiratory tract infections, abdominal and pelvic infections, endocarditis, meningitis, and endophthalmitis [6-8]. Reports of *P. multocida* bacteremia had been relatively infrequent. Raffi *et al* [7] reported 13 cases over a 12-year period

(1974-1985) and 10 (77%) of the patients had liver cirrhosis. Liver dysfunction has been reported to be a major factor associated with *P. multocida* bacteremia because of the impaired reticuloendothelial function in the patient [10,11]. Liver diseases reported to increase the risk of *P. multocida* bacteremia included cirrhosis of any etiology, hepatitis, and infiltrating tumors. Case 1 in this study had a history of cirrhosis associated with hepatitis B and alcohol dependence, and Case 2 had a history of cirrhosis associated with hepatitis C.

The virulence of *P. multocida* is associated with the degree of encapsulation [1,2]. Large capsules are more resistant *in vivo* to phagocytosis and intracellular killing by neutrophils [1,2]. There are 4 capsular types (A, B, D, and E) and 11 somatic antigens. Most human strains belong to capsular type A, and the remainders are mostly type D [1-3]. However, capsular typing is not routinely done in most clinical microbiology laboratories.

Most cases of pasteurellosis result from direct inoculation via bites. Infections following animal exposure in the absence of bites probably stem from contact with animal secretions [6]. However, a culture from the dogs in question was not obtained in either case of this study. Colonization of *P. multocida* is more commonly found in the tonsil of young male dogs, especially in the cold seasons [3].

Only some indirect associative evidences of stray dog transmission were available in both cases, and whether the transmission has resulted in the infection remains speculative. The stray dogs that colonized *P. multocida* may have become ill during stressful situations, for example the furious typhoon. The typhoon may have resulted in greater exposure of drinking water and food to animal secretions. On the other hand, nasopharyngeal colonization by *P. multocida* can occur in humans with a history of household animal contact, especially in patients with underlying respiratory tract disease, including sinusitis and bronchiectasis [1,8]. Case 2 had chronic bronchitis and a history of domestic animal contact. The active EV bleeding episode in this case may have led to the subsequent bacteremia. Nasopharyngeal culture of this patient, however, is lacking to prove this.

Diagnosis of zoonotic *Pasteurella* infections demands precision in eliciting a detailed travel, occupational, and animal exposure history [5]. The family *Pasteurellaceae* encompasses the genera *Pasteurella*, *Actinobacillus*, and *Haemophilus*, and *Pasteurella* species can thus easily be mistaken for *Haemophilus*, *Moraxella*, *Neisseria*, or *Acinetobacter* species on Gram stain [8]. A 10-U penicillin disc may help with identification [4]. *Pasteurella* species are typically penicillin-susceptible, yielding a zone of inhibition of ≥15 mm when tested with a McFarland 0.5 inoculum suspension on a Muller-Hinton agar plate [4]. The unpleasant odor from the dogs described in Case 1 smelled like seminal fluid [12], which might be caused by the strong indole formation of the infecting organisms from diseased animals [4]. A history of such an odor should increase the index of suspicion for pasteurellosis [12].

Penicillin is the recommended antimicrobial agent for the treatment of all forms of *Pasteurella* infection [1,2]. Many cephalosporins demonstrate *in vitro* activity against *P. multocida* [1]. Empiric use of cephalosporins plus aminoglycosides in the patients of this report resulted in a favorable outcome. β-lactamase-producing *P. multocida* strains have been reported by Rosenau *et al* [1]. Antibacterial susceptibility testing for *Pasteurella* species, however, has not been standardized by the National Committee for Clinical Laboratory Standards [13].

In summary, 2 cases of liver cirrhosis and EV bleeding in patients who had *P. multocida* bacteremia in association with non-bite animal exposure were reported. Avoidance of animal contact [2] by immuno-compromised patients, especially those with liver cirrhosis and EV, is important in the prevention of this infection. Sick stray animals that are found should be dealt with carefully.

References

1. Zurlo JJ. *Pasteurella* species. In: Mandell GL, Bennett JE, Dolin R, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 5th ed. Philadelphia: Churchill Livingstone; 2000:2402-6.
2. Slack MPE. Gram-negative coccobacilli. In: Armstrong D, Cohen J, eds. Infectious Diseases. London: Mosby; 1999:20. 10,20.15.
3. Gutman LT, Willett HP. *Pasteurella* and miscellaneous Gram-negative bacilli. In: Joklik WK, Willet HP, Amos DB, Wilfert CM, eds. Zinsser Microbiology. 19th ed. Norwalk: Appleton & Lange;1988:506-7.
4. Holmes B, Pickett MJ, Hollis DG. Pasteurella. In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH, eds. Manual of Clinical Microbiology. 7th ed. Washington, DC: American Society for Microbiology Press; 1999:632-7.
5. Weinberg AN. Zoonoses. In: Mandell GL, Bennett JE, Dolin R, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 5th ed. Philadelphia: Churchill Livingstone; 2000:3239-45.
6. Weber DJ, Wolfson JS, Swartz MN, Hooper DC. *Pasteurella multocida* infections: report of 34 cases and review of the literature. Medicine 1984;63:133-54.
7. Raffi F, Barrier J, Baron D, Drugeon HB, Nicolas F, Courtieu AL. *Pasteurella multocida* bacteremia: report of thirteen cases over twelve years and review of the literature. Scand J Infect Dis 1987;19:385-93.

8. Klein NC, Cunha BA. *Pasteurella multocida* pneumonia. Semin Respir Infect 1997;12:54-6.
9. Jorgensen JH, Turnidge JD, Washington JA. Antibacterial susceptibility test: dilution and disk diffusion methods. In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH, eds. Manual of Clinical Microbiology. 7th ed. Washington, DC: American Society for Microbiology Press; 1999:1526-43.
10. Patton F, Dumas M, Cannon NJ. *Pasteurella multocida* septicemia and peritonitis in a cirrhotic cock trainer with a pet pig. N Engl J Med 1980;6:1126-7.
11. Fernandez-Esparrach G, Mascaro J, Rota R, Valerio L. Septicemia, peritonitis, and empyema due to *Pasteurella multocida* in a cirrhotic patient. Clin Infect Dis 1994;18:486.
12. Arashima Y, Kumasaka K, Tutchiya T, Yanai M, Kawano K. Two cases of pasteurellosis accompanied by exudate with semen-like odor from the wound. Kansenshogaku Zasshi [J Jpn Assoc Infect Dis] 1999;73:623-5.
13. National Committee for Clinical Laboratory Standards. Performance standards for antimicrobial disk susceptibility test. Approved standards. 7th ed. NCCLS document M2-A7. NCCLS: Wayne, PA: National Committee for Clinical Laboratory Standards; 2000.