Austin Journal of Surgery

Open Access

Austin Publishing Group

Special Article: Pancreatic Surgery

Clinical Features of Six Cases of Non-Bite or Scratch Infections by Pasteurella Multocida with the Comparison to 14 Cases with the Infections Caused by Animal Bite or Scratch

Tsubasa Asaeda, MD*; Takashi Ueda, PhD; Yasuhiro Nozaki, MD, PhD; Yasushi Murakami, MD, PhD; Mika Morosawa, MD; Kazuhiko Nakajima, MD, PhD; Hitoshi Ogasiwa; Miki Doi; Yoshio Takesue, MD, PhD

[1]Department of Respiratory Medicine, Tokoname City Hospital, 3-3-3 Asukadai, Tokoname, Aichi 479-8510, Japan

[2]Department of Infection Control and Prevention, Hyogo College of Medicine, 1-1, Mukogawa-cho, Nishinomiya 663-8501, Japan

[3]Department of Clinical Technology, Tokoname City Hospital, 3-3-3 Asukadai, Tokoname, Aichi 479-8510, Japan

[4]Department of Clinical Infectious Diseases, Tokoname City Hospital, 3-3-3 Asukadai, Tokoname 479-8510, Japan

***Corresponding author:** **Tsubasa Asaeda**
Department of Respiratory Medicine, Tokoname City Hospital, 3-3-3 Asukadai, Tokoname, Aichi 479-8510, Japan.
Email: tsubasa1127tam@gmail.com

Received: April 09, 2024
Accepted: May 03, 2024
Published: May 10, 2024

Abstract

Pasteurellosis is a popular zoonotic infection with animal bite or scratch. We reported six non-bite/scratch (B/S) infection including pneumonia (3), skin and soft tissue infection (2), and bacteremia (1). *P. multocida* was identified using MALDI-TOF mass spectrometry in all six non-B/S infections, while identification kits were used in 13 of 14 patients with B/S infections. Pneumonia occurred in two patients with underlying pulmonary disease, whereas ventilator associated pneumonia was developed in remaining one patient with cerebral infarction. *P. multocida* was isolated form blood specimen in patient with liver cirrhosis (Child-Pugh C) and diabetes. A patient with diabetes and normal pressure hydrocephalus who had toe injury with a fall and a patient with diabetes foot ulcer had cellulitis. Three of six patients with non-B/S infections did not have a pet, and there was no episode of recent animal contact. Non-B/S infections could be developed in patients with chronic pulmonary disease, those with open wound or immunocompromised hosts irrespective of the apparent animal exposure. Different from B/S infections, non-B/S infections by *P. multocida* should be assumed as opportunistic infections.

Keywords: *Pasteurella multocida;* Animal bite; Zoonotic infection; Pneumonia; Bacteremia

Introduction

Pasteurella multocida (P. multocida) is a resident microbiota in the oropharynx of cats and dogs. Skin and soft tissue pasteurellosis is a popular infection caused by animal bite or scratch [1]. In this decade, however, reports of non-bite/scratch (B/S) infections such as pneumonia, bacteremia, and meningitis have been accumulated [2-7]. Inhalation or environmental exposure with the respiratory secretions of the animal including drool could cause infections in patients with underlying pulmonary disease, chronic open wounds, or cranial trauma [8-11]. In addition, several authors addressed life-threatening infections in moderately or severe immunocompromised patients who had no episode of animal contact [3,4]. In this point, non-B/S pasteurellosis seems to be a different disease entity with B/S infections. So, we reported six cases of non-B/S infections in 20 cases of pasteurellosis.

Case Report

This case report was approved by the institutional review boards at Hyogo Medical University (No.). Six non-bite/scratch (B/S) pasteurellosis including pneumonia (3), skin and soft tissue infection (2), and bacteremia (1) were experienced between 2013 and 2023 in Tokoname City Hospital and Hyogo Medical University Hospital (Table 1). Fourteen B/S infections (skin and soft tissue infections [13]; and endophthalmitis by eye scratch [1]) were treated during the same period (dog bite, 3 patients; and cat bite/scratch, 11 patients). *P. multocida* was identified using MALDI-TOF mass spectrometry (MALDI Biotyper, Bruker Daltonics GmbH & Co. KG. Bremen, Germany) in all six non-B/S infections since 2018, while identification kits (ID test HN 20 rapid: Shimadzu Diagnostics Corporation, Tokyo) were used in 13 of 14 patients with B/S infections. Three of six patients with non-B/S infections did not have a pet, and there was no epi-

Citation: Asaeda T, Ueda T, Nozaki Y, Murakami Y, Morosawa M, et al. Clinical Features of Six Cases of Non-Bite or Scratch Infections by Pasteurella Multocida with the Comparison to 14 Cases with the Infections Caused by Animal Bite or Scratch. Austin J Surg. 2024; 11(1): 1321.

Table 1: Six cases of non-bite/scratch infection by *Pasteurella multocida.*

	Age	Gender	Isolated material	Identification method	Type of infection	Possible cause for the infection	Comorbidity	Admission/ ambulatory treatment	Animal contact	Scar by the injury	Other isolated organisms	Antibiotic therapy	Duration of therapy	Clinical efficacy	Mortality
1	52	Female	Sputum (M2, Geckler group 5, 107 CFU/mL)	MALDI-TOF mass spectrometry	Pneumonia	Inhalation	Chronic bronchiolitis with bronchiectasis	Outpatient setting	House dog	Both forearm (old scar)	None	Amoxicillin (per os)	10 days	Improve	Survive
2	70	Male	Sputum (P1, Geckler group 4, 107 CFU/mL)	MALDI-TOF mass spectrometry	Ventilator associated pneumonia	Endogenous infection after treatment for cerebral infarction	Chronic renal failure, Hypertension	Intensive care unit	None	None	None	Ampicillin/sulbactam	10 days	Success	Died after 59 days because of septic shock with the intestinal ischemia
3	74	Male	Sputum (P3, Geckler group 5, 106 CFU/mL)	MALDI-TOF mass spectrometry	Pneumonia, mediastinal emphysema.	Undetermined	Interstitial pneumonia (home oxygen therapy), rectal cancer, lung metastasis	Ward for respiratory surgery	No available information	None	Staphylococcus aureus	Piperacillin/Tazobactam, Ampicillin/sulbactam	10 days	Improve	Died after 54 days because of underlying cancer disease
4	54	Male	Blood, (2/2 sets), nasal swab	MALDI-TOF mass spectrometry	Bacteremia	Undetermined	Liver cirrhosis (Child-Pugh C), Diabetes (HbA1c 9.1 %)	Acute Critical Care Center, ward for hematology	House dog	None	None	Piperacillin/Tazobactam, ampicillin	14 days	Success	Survive
5	68	Female	Exudate from the wound	MALDI-TOF mass spectrometry	Cellulitis (right hand)	Trauma caused by a fall	Diabetes, Hydrocephalus (cerebrospinal fluid shunt)	Outpatient setting	None	None	Coagulase negative staphylococci	Levofloxacin (per os)	14 days	Success	Survive
6	56	Male	Exudate from the wound	MALDI-TOF mass spectrometry	Cellulitis (left foot)	Preexisting diabetes foot ulcer	Diabetes	Outpatient setting	None	None	MRSA, Streptococcus oralis	Levofloxacin (per os), minocycline (per os)	28 days	Success	Survive

sode of recent animal contact. Three of six patients with non-B/S infections and eight of 14 patients with B/S infections were elderly (>65 years old). Although patients with non-B/S infections had following comorbidity, all patients with B/S infections but one were immunocompetent. All patients with non-B/S infections were improved with antibiotic therapy. However, two patients died because of the worsening of underlying disease. Among patients with B/S infections, difficult to treat infection was experienced only in one patient with leg injure in whom multiple drainage/debridement were required and surgery was conducted under lumbar anesthesia. Antibiotic susceptibility of isolated *P. multocida* was determined according to criteria of the Clinical and Laboratory Standards Institute [13]. All isolates were susceptible to penicillin. A lot of antibiotic class except for clarithromycin can be used for the pasteurellosis (Table 2).

Case 1 (pneumonia): A 52 years old woman presented to the outpatient office with a recent worsening of productive cough, dyspnea on exertion, and fever elevation (transcutaneous oxygen saturation 96%, white blood cell count [WBC] 11600/mm^2, and C-reactive protein [CRP] 4.91 mg/dL). She had been treated as cough variant asthma using budesonide–formoterol for four years. She owed a 12 years old dog kept in door. Sometimes she kissed the dog and shared foods. A Computed Tomography (CT) scan of the thorax revealed bilateral bronchiectasis in the middle lobe/lingular segment, and micronodule shadow especially in the right lower lobe. Isolates showed smooth fluorescent grayish-white colonies with 3–5 mm diameter on blood agar (trypticase soy aga with 5 sheep blood, Nippon Becton Dickinson CO.LTD, Japan). Commercially available identification kits were used for biochemical examination. MALDI-TOF mass spectrometry was also performed to identify *P. multocida. As differential diagnosis, Mycobacterium avium-intracellulare* Complex was ruled out by biological tests. After amoxicillin therapy for 10 days, *P. multocida* in sputum was eradicated. Her symptoms were improved. WBC decreased to 6400/mm^2 and CRP was 0.61 mg/dL seven days after completion of antibiotic therapy. The radiological abnormal findins in the right lower lobe was also improved. Four weeks later, productive cough was recurred. Maintenance therapy with a low-dose macrolide therapy was started for the exacerbation of pre-existing chronic bronchiolitis with bronchiectasis.

Case 2 (pneumonia): A 70 years old man with chronic renal

Table 2: Antibiotic susceptibility in *Pasteurella multocida.*

No.	Minimum inhibitory concentration (μg/mL)											
	Penicillin G	Ampicillin	amoxicillin-clavulanate	ceftriaxone	cefepime	Cefpodoxime Proxetil	meropenem	levofloxacin	clarithromycin	azithromycin	minocycline	Sulfamethoxazole/trimethoprim
1	0.12	0.25	≤0.25	≤0.25	≤0.25	–	≤0.06	≤1	2	0.5	≤1	≤0.12
2	0.12	0.25	≤0.12	≤0.12	≤0.12	≤0.12	≤0.06	≤0.03	8	0.5	≤0.25	≤0.12
3	0.12	0.25	≤0.12	≤0.12	≤0.12	≤0.12	≤0.06	≤0.03	8	0.5	≤0.25	≤0.12
4	0.12	0.25	≤0.12	≤0.12	≤0.12	≤0.12	≤0.06	≤0.03	8	1	≤0.25	≤0.12
5	≤0.06	0.25	≤0.12	≤0.12	≤0.12	≤0.12	≤0.06	≤0.03	8	0.5	≤0.25	≤0.12
6	0.12	0.25	≤0.12	≤0.12	≤0.12	≤0.12	≤0.06	≤0.03	8	0.5	≤0.25	≤0.12

failure (eGFR 31 mL/min/1.73 m^2 on admission). He lost consciousness and collapsed at his house. He was transported to the critical care department, and diagnosed as cerebral infarction with the occlusion of basilar artery. He underwent the intravascular catheter treatment, and ventilator management was required. Although no abnormal finding was demonstrated by chest X-ray examination on admission, Ventilator Associated Pneumonia (VAP) was developed on day 3 (blood temperature 39.0°C, WBC 15470/mm^2, and CRP was 2.18 mg/dL). *P. multocida* was isolated from the sputum. Ampicillin/sulbactam was administered for 10 days, and infection was resolved. He owed no pet in his house, and no injury lesion was detected on his extremities. Although the cause of *P. multocida* infection was unclear, endogenous infection secondary to preceding respiratory tract colonization was suspected.

Case 3 (pneumonia): A 74 years old man with rectal cancer and lung metastasis and on the home oxygen therapy because of interstitial pneumonia. mediastinal emphysema was detected based on a CT scan examination, and ground-glass appearance was worsened compared with the finding of CT conducted before 30 days. Piperacillin/tazobactam was started, and after confirmation of isolated organisms from the sputum (*P. multocida* and methicillin-sensitive *Staphylococcus aureus*), antibiotics was changed to ampicillin/sulbactam. Totally antibiotics was used for 10 days. WBC and CRP were improved from 16830/mm^2 and 9.74 mg/dL to 9430/mm^2 and 1.11 mg/dL, respectively. He died on day 54 because of underlying cancer disease. There was no record whether he had pets or not.

Case 4 (bacteremia): A 54 years old man with diabetes (HbA1c 9.1%), and liver cirrhosis (Child-Pugh C). He experienced hepatic encephalopathy and hematopoietic stem cell infusion was performed for liver cirrhosis. Because of septic shock and diabetic ketoacidosis (Lactate 15.0 mmol/L), he was transported to the critical care department (BT 39.3°C, WBC 20610/mm^2, CRP 9.79 mg/dL, total bilirubin 1.7 mg/dL, AST/ALT 234/99 IU/L). On the CT scan, no apparent focus for sepsis including pneumonia was identified. He owed a dog. Although, there was no recent episode of the bite, the dog licked his eye a few days ago. *P. multocida* was isolated form the blood and nasal swab. Negative culture for *P. multocida* was conformed in the specimen from sputum, urine and tear from the eye. Piperacillin/tazobactam was used as initial empiric therapy, and changed to ampicillin/sulbactam after identification of *P. multocida* in the blood culture, and totally antibiotics was used for 14 days. Clinical course was good and patient discharged on day 19. Although nasal colonization of *P. multocida* was demonstrated, the source of bacteremia was undetermined.

Case 5 (cellulitis occurred from the diabetes foot ulcer): A 56 years old man with diabetes foot ulcer on the second toe presented to the emergency department (BT 37.2°C, WBC 7130/mm^2, CRP 4.24 mg/dL). He complained the worsening of the ulcer with pain and swelling. He bumped the site against the desk several days before. *P. multocida*, methicillin-resistant *Staphylococcus aureus* and *Streptococcus oralis* were isolated from the wound. He did not have pet and there was no episode of animal exposure. Levofloxacin followed by minocycline was administered for 14 days. Wound infection was resolved without the development of osteomyelitis.

Case 6 (cellulitis on the right hand): A 68 years old woman with diabetes and normal pressure hydrocephalus (cerebrospinal fluid shunt). She injured on her thumb of right hand with a fall on the road. Although the open wound was small, the wound worsened with purulent discharge and pain and swelling She consulted on day 3 (BT 37.3°C; WBC 13020/mm^2: and CRP 7.4 mg/dL). *P. multocida,* Methicillin-resistant *Staphylococcus aureus, and Streptococcus oralis* were isolated from the wound. She had no pet, and there was no episode of animal contact including B/S. Wound was irrigated and levofloxacin followed by minocycline was administered for 28 days totally.

Discussion

We reported six non-B/S infections by *P. multocida*. *Pasteurella* pneumonia was developed in two patients with chronic pulmonary disease and in one patient with chronic renal failure who were managed by ventilator after the attack of cerebral infarction. Bacteremia was occurred in a patient with liver cirrhosis (Child-Pugh C) and diabetes. Although nasal colonization of *P. multocida* was demonstrated, the source of bacteremia was not determined. In addition, a patient with diabetes and normal pressure hydrocephalus who had toe injury with a fall, and a patient with diabetes foot ulcer had cellulitis.

P. multocida was identified exclusively using MALDI-TOF mass spectrometry in all six non-B/S infections, while identification kits were used in 13 of 14 patients with B/S infections. In addition, non-B/S infections were found only in the recent five years over 10-years study period. Kormondi et al. [3] found that the number of isolates and human pasteurellosis cases has increased from year to year. Considering that pathogenicity or antibiotic susceptibility have not been changed in *P. multocida* [14], possible explanation for the increasing tendency is the development of microbiological methods for identification, such as use of MALDI-TOF mass spectrometry and molecular methods. Although earlier automated identification systems provided adequate identification of *Pasteurella* strains, pasteurellosis might have been overlooked in the absence of animal B/S especially in patients who did not have a household animal.

Although non-B/S infections could be associated with licks, inhalation leading to respiratory tract colonization, contamination of open wounds, contamination of food with pet saliva by the sharing, and incidental pet exposure, the possible cause was not determined in a considerable number of patients [2]. In our

series, three of six patients did not owe a pet and there was no apparent animal exposure (case 2, 5, and 6). Respiratory tract can be colonized by *P. multocida* with above-mentioned deep animal contact. VAP by *P. multocida* was developed in patient underwent therapy for cerebral infarction (case 2). Endogenous infections secondary to preceding respiratory tract colonization was suspected in this case. Although the source was not determined, bacteremia was developed in a patient with nasal colonization (case 4).

Patients with open wound is vulnerable to non-B/S pasteurellosis. We experienced two patients in whom cellulitis was developed because of the contamination of the wound except for B/S. Pet owners with open wounds must protect them from infection from the pet saliva either with the direct licking or the contaminated environment such as carpet. Non-B/S infection is more serious than B/S infections. Giodarno et al. [4] reported that four patients were died and 7 patients admitted intensive care unit among 19 patients with non-B/S infections. Patients with non-B/S infections were more frequently bacteremic, hospitalized more often, and frequently had comorbidities than those with B/S infections [2]. Although patients with animal bite are treated early by a physician, non-B/S infections are diagnosed and treated after the patients become sick, and the culture reports were available.

Although pneumonia by *P. multocida* could be developed in patients with chronic obstructive pulmonary disease who are otherwise-immunocompetence [9,16], non-B/S infections such as bacteremia [17], meningitis [11], intraabdominal infections [12,18] occur exclusively in immunocompromised hosts. Chatelier et al. [17] reviewed 119 proven cases of P. multocida bacteremia. The most common comorbidities were cirrhosis, immunosuppressive therapy, and malignant diseases. Kobayaa et al. [19] reported 2 newborns developing meningitis after incidental pet exposure. There are several reports of peritonitis in patients with peritoneal dialysis [2,18]. In conclusion, Pasteurella pneumonia in patients with underlying pulmonary disease, and Pasteurella skin and soft tissue infections in patients who have chronic open wounds should be ruled out as differential diagnosis, if the patient owes household pets. Moreover, clinicians should not overlook pasteurellosis in immunocompromised hosts even if patients deny having animal contact. Different from B/S infections, non-B/S infections by *P. multocida* should be assumed as opportunistic infections.

References

1. Talan DA, Citron DM, Abrahamian FM, Moran GJ, Goldstein EJ. Bacteriologic analysis of infected dog and cat bites. Emergency Medicine Animal Bite Infection Study Group. N Engl J Med. 1999; 340: 85–92.
2. Kannangara DW, Dhyanesh Pandya D, Patel P. Pasteurella multocida Infections with Unusual Modes of Transmission from Animals to Humans: A Study of 79 Cases with 34 Nonbite Transmissions. Vector-Borne Zoonotic Dis. 2020; 20: 637-651.
3. Körmöndi S, Terhes G, Pál Z, Varga E, Harmati M, Buzás K, Urbán E. Human Pasteurellosis Health Risk for Elderly Persons Living with Companion Animals. Emerg Infect Dis. 2019; 25: 229-235.
4. Giordano A, Dincman T, Clyburn BE, Steed LL, Rockey DC. Clinical features and outcomes of Pasteurella multocida infection. Medicine (Baltimore). 2015; 94: e1285.
5. Christenson ES, Ahmed HM, Durand CM. Pasteurella multocida infection in solid organ transplantation. Lancet Infect Dis. 2015; 15: 235–40.
6. Nollet V, Souply L, Rosolen B, Mohseni-Zadeh M, Martinot M. Risk factors for invasive pasteurellosis: a retrospective case study. Eur J Clin Microbiol Infec Dis. 2016; 35: 1975–81.
7. Branch J, Kakutani T, Kuroda S, Shiba Y, Kitagawa I. Pasteurella multocida infective endocarditis: a possible link with primary upper respiratory tract infection. Intern Med. 2015; 54: 3225–31.
8. Lee WS, Chen FL, Wang CH, Ou TY, Lin YH, Jean SS. Community-acquired bacteremic pneumonia due to Pasteurella multocida subspecies multocida in a patient with poor-control diabetes mellitus. J Microbiol Immunol Infect. 2019; 52: 163-164.
9. Myers EM, Ward SL, Myers JP Life-threatening respiratory pasteurellosis associated with palliative pet care. Clin Infect Dis. 2012; 54: e55-7.
10. Yu GV, Boike AM, Hladik JR. An unusual case of diabetic cellulitis due to Pasturella multocida. J Foot Ankle Surg. 1995; 34: 91-5.
11. Kumar A, Devlin HR, Vellend H. Pasteurella multocida meningitis in an adult: case report and review. Rev Infect Dis. 1990; 12: 440–8.
12. Rueda Prada L, Cardozo M, Hudson A, McDermott M, Urbina Verjel DC, Dumic I. Disseminated Pasteurella multocida in a patient with liver cirrhosis and spontaneous bacterial peritonitis - The role of cirrhosis-associated immune dysfunction. IDCases. 2022; 29: e01542.
13. M100: Performance Standards for Antimicrobial Susceptibility Testing, 30th Edition. 2022.
14. Smith E, Miller E, Aguayo JM, Figueroa CF, Nezworski J, Studniski M, Wileman B, Johnson T: Genomic diversity and molecular epidemiology of Pasteurella multocida. PLoS One. 2021 Apr 6;16(4):e0249138.
15. Arashima Y, Kumasaka K, Okuyama K, Kawabata M, Tsuchiya T, Kawano K, et al. Clinicobacteriological study of Pasteurella multocida as a zoonosis (1). Condition of dog and cat carriers of Pasteurella, and the influence for human carrier rate by kiss with the pets. Kansenshogaku Zasshi. 1992a; 66: 221–224
16. Hubbert WT, Rosen MN. Pasteurella multocida infections. II. Pasteurella multocida infection in man unrelated to animal bite. Am J Public Health Nations Health. 1970; 60: 1109-17.
17. Chatelier E, Mahieu R, Hamel JF, Chenouard R, Lozac'h P, Sallé A, et al. Pasteurella bacteraemia: Impact of comorbidities on outcome, based on a case series and literature review. .Int J Infect Dis. 2020;92:89-96.
18. Antony SJ, Oglesby KA. Peritonitis associated with Pasteurella multocida in peritoneal dialysis patients--case report and review of the literature. Clin Nephrol. 2007; 68: 52-6.
19. Kobayaa H, Souki, RR, Trust S, Domachowske JB. Pasteurella multocida meningitis in newborns after incidental animal exposure. Pediatr Infect Dis J 2009; 28: 928-9.