Official journal of the Spanish Society of Chemotherapy

Letter to the Editor

Maria Pilar Ortega Lafont[1]
Luis Buzón Martín[2]
Ledicia Álvarez Paredes[1]
María Mora Fernández[3]
Antonio Rodríguez Pérez[3]
Miguel Ángel Morán Rodríguez[2]

Acute zoonotic total knee prosthetic joint infection due to *Pasteurella multocida* treated successfully with debridement, irrigation and antibiotics without prosthesis removal

[1]Microbiology. Hospital Universitario de Burgos, Spain.
[2]Infectious Diseases Unit, Internal Medicine. Hospital Universitario de Burgos, Spain.
[3]Traumatology and Orthopedic Surgery. Hospital Universitario de Burgos, Spain.

Article history
Received: 15 January 2019; Revision Requested: 6 February 2019; Revision Received: 19 March 2019; Accepted: 25 March 2019

Sir,

A 92-year-old woman with a total knee arthroplasty performed 10 years ago was admitted with a story of 3 days of fever, pain and joint effusion in the left knee, which ensued abruptly. Routine blood analysis showed leukocytosis (12,500 leucocytes/mm^3, 88% polymorphonuclear-PMN-), and elevated C reactive protein (202 mg/L –CRP-). Two sets of blood cultures and a urine culture were obtained. A diagnostic arthrocentesis was performed, revealing purulent effusion (40,200 leucocytes/mm^3, 94% PMN, undetectable glucose). No microorganisms were observed on gram stain.

Meropenem and vancomycin were started. The patient underwent surgery 72h after hospital admission: Capsulotomy, along with debridement and replacement of prosthetic mobile elements (tibial polyethylene and patella) with prosthesis retention, and lavage with 9 liters of sterile solution [1] were performed.

Synovial fluid and surgical samples were transported and plated immediately and [1] yielded *Pasteurella multocida* after 24h of incubation, which was identified by Matrix-associated laser desorption/ ionization-time of flight mass spectrometry (Vitek MS, BioMerieux, Database V3). Blood and urine cultures were negative. Anamnesis revealed that the patient owned a cat, which used to scratch and lick patients´ legs. An oral swab of the patient´s cat was obtained and plated.

Once *Pasteurella* was identified and susceptibility profile determined, treatment was switched to i.v ampicillin plus oral levofloxacin. CRP levels fell from 238 mg/L (normal range, 0-5 mg/L) in the day of surgery to 18 after twelve days, when she was discharged on oral levofloxacin. At the sixth week after surgery, CRP values had normalized, and the patient completed 12 weeks without remarkable side effects. There is no general agreement based on solid evidence regarding for how long should treatment after debridement and implant retention in prosthetic joint infection (PJI) caused by common microorganisms, so solid recommendations on behalf of PJI caused by rare microorganisms as in the case presented, are definitely lacking [1]. Fourteen months after withdrawing levofloxacin, there are no clinical signs of recurrence, and CRP values remain normal.

Pasteurella spp. is a genera of small gram-negative nonflagellated coccobacilli often found as part as the normal microbiota of oral and upper respiratory tracts of animals and humans. It is isolated from human infections associated to dog bites and 75% percent of cat bites. Humans acquire *P. multocida* not only through bites, but through scratches, even without skin or mucosal breakdown. Phenotypic characterization of *P.multocida* was traditionally based on morphology and biochemical characteristics, but their accuracy was low. 16S rDNA sequencing and MALDI-TOF are better for identification at the genus and species level [2-4].

Methicillin-susceptible *Staphylococcus aureus, Klebsiella oxytoca, Pantoea agglomerans, Bergeyella zoohelcum* and *Pasteurella multocida,* were isolated from cat´s sample. Why the patient´s prosthesis became infected by *P. multocida* and no by the other bacteria? Multiple virulence factors, including genes encoding capsule, lipopolysaccharide, outer membrane proteins, iron acquisition genes, thiamine metabolism genes, and the adhesion/Flp pilus assembly gene cluster (tadZABCDEFG) are present in *P. multocida*. Homologs of the tad gene locus are also present in many Pasteurellaceae, playing key roles in biofilm formation, colonization, and pathogenesis [5]. *P. multocida* can produce in vitro biofilm, although a case of PJI due to a non-biofilm-producing strain of *P. multocida* has been described [6].

In order to try to evaluate phylogenetic relationship between the patient´s *P. multocida* and the cat´s sample

Correspondence:
Maria Pilar Ortega Lafont
Microbiology. Hospital Universitario de Burgos, Spain.
Fax: 0034 947282722
E-mail: portegal@saludcastillayleon.es

Spectrometry dendrogram showing clustering of patient and cat´s isolates of *Pasteurella multocida*.

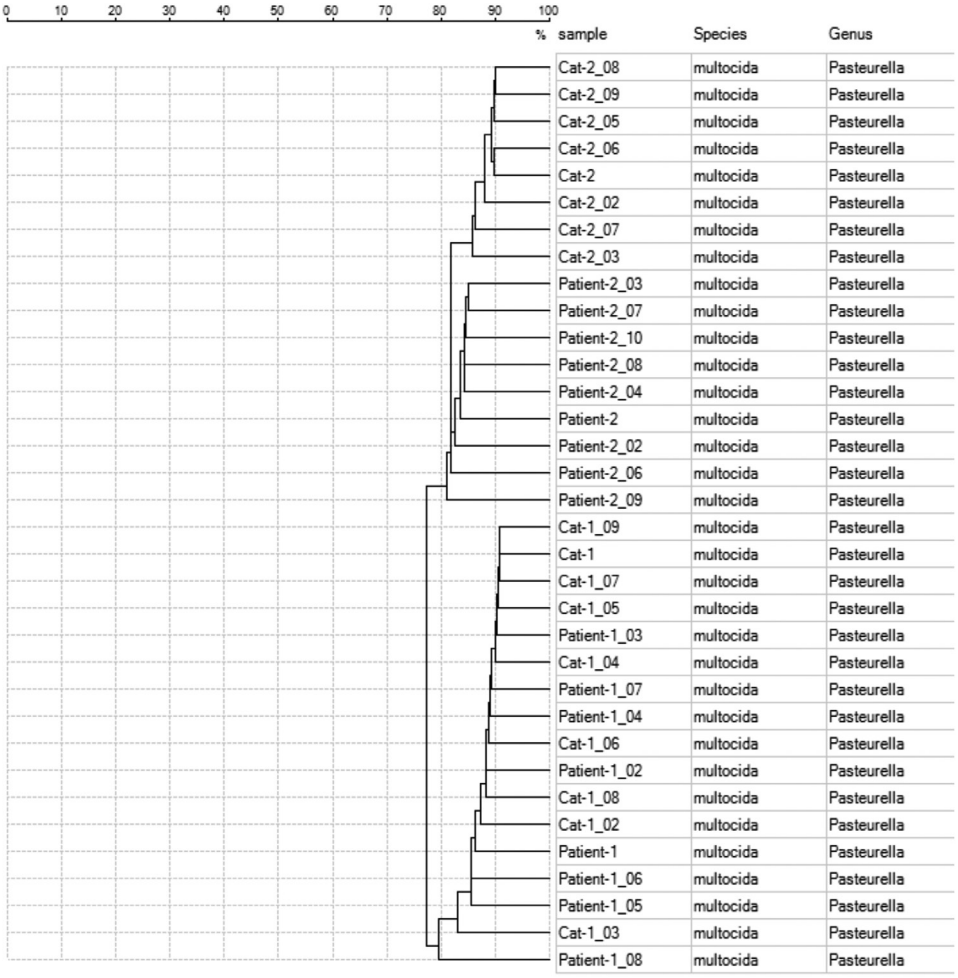

Figure1 **Relationship of Pasteurella multocida isolated from the case patient (patient 1), patient's cat (cat 1) and another unrelated strains (patient 2 and cat 2) by matrix-assisted laser desorption/ionization-time of flight mass spectrometry dendrograms and clustering (mass/ charge)**

isolate, samples from another cat not related to the index case and samples from another patient with *P. multocida* infection were collected, and MALDI-TOF was used (RUO database). In order to avoid biases, each isolate was analyzed under identical experimental conditions [7]. Main spectrum projection showed that patient's and her cat´s isolates were very similar, and differed from the unrelated isolates, pointing to a possible ethiopathogenical link between the infected patient´s prosthesis and her cat´s oral flora. Nevertheless, the mass distance between all of them, related and unrelated samples, was close (figure 1).

Since 1975, only 32 cases of PJI due to *P. multocida* have been reported. Almost every case diagnosed share some common features: abrupt late onset infections with a median time of 7.6 years after implantation, absence of documented bacteremia in most cases, very intense inflammatory reaction, easy recovery from joint effusion samples and a relationship with close contact with dogs or cats. The case presented represents, therefore, an archetypal example [8].

In these 32 cases, about half were treated with prosthesis removal. This series suggests that surgical lavage, debridement and prosthesis retention combined with optimal targeted antimicrobial therapy is enough, thus avoiding two steps exchange procedure, an impression supported by the case presented. All of the cases, whatever the surgical approach performed, were successfully cured [8]. Penicillins and doxycycline were the drugs most commonly used followed by fluoroquinolones. Our experience, along with previously reported data, suggests that monotherapy along with appropriate surgical drainage is enough for treating acute periprosthetic infections caused by *P. multocida* in most cases.

FUNDING

None to declare

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest

REFERENCES

1 Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and management of prosthetic joint infection: Clinical Practice Guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2013; 56(1): e1-25. PMID: 23223583

2. Wilson BA, Ho M. *Pasteurella multocida:* from zoonosis to cellular microbiology. Clin Microbiol Rev 2013; 26(3): 631-55. PMID: 23824375

3. Zangenah S, Güleryüz G, Boräng S, Ullberg M, Bergman A et al. Identification of clinical Pasteurella isolates by MALDI-TOF -- a comparison with VITEK 2 and conventional microbiological methods. Diagn Microbiol Infect Dis 2013; 77(2):96-8. PMID: 23824375.

4. Dewhirst FE, Paster BJ, Olsen I, Fraser GJ. Phylogeny of 54 representative strains of species in the family Pasteurellaceae as determined by comparison of 16S rRNA sequences. J Bacteriol 1992; 174(6): 2002-13. PMID: 23886788.

5. Harper M, Boyce JD, and Adler B. *Pasteurella multocida* pathogenesis: 125 years after Pasteur. FEMS Microbiol Lett 2006; 265(1):1-10. PMID: 1548238.

6. Romanò CL, De Vecchi E, Vassena C, Manzi G, Drago L. A case of a late and atypical knee prosthetic infection by no-biofilm producer *Pasteurella multocida* strain identified by pyrosequencing. Pol J Microbiol 2013; 62:435–8. PMID: 17101417.

7. Culebrasa E, Álvarez-Buyllab A, Artacho Reinoso MJ, Lepe A. Studies of bacterial typing with MALDI-TOF. Enferm Infecc Microbiol Clin 2016; 34(Supl 2):42-6. PMID: 24730139.

8. Honnorat E, Seng P, Savini H, Pinelli PO, Simon F, Stein A. Prosthetic joint infection caused by *Pasteurella multocida*: a case series and review of literature. BMC Infect Dis 2016; 16(1):435. PMID: 27544345.