Francisella tularensis bacteraemia causing multi-organ failure

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Abstract

Tularemia is a zoonosis caused by the gram-negative coccobacillus Francisella tularensis. The bacterium can be transmitted in several ways including direct contact with animal reservoirs, ingestion, inhalation and bites, and typical clinical symptoms are headache, fever, diarrhea and dyspnea. Francisella tularensis has two predominant subspecies (ssp), namely ssp. tularensis and ssp. holarctica. Ssp. holarctica is less virulent and does usually not cause fatal disease. We here present a 51-year-old male with sepsis and multi-organ failure caused by F. tularensis ssp. holarctica infection suggesting that atypical agents including F. tularensis should be considered in patients presenting symptoms of infections without response to standard treatments.

INTRODUCTION

Tularemia is a rare zoonotic disease caused by the gram-negative coccobacillus Francisella tularensis. It is mainly transmitted by direct contact with animal reservoirs, ingestion, inhalation, contaminated water or tick bites. Clinical manifestations and treatment outcomes differ between subspecies. In Europe, the F. tularensis subspecies (ssp.) holarctica is most frequently associated with human disease and typically causes mild clinical symptoms. However, the pathogen is rarely isolated in Norway. We here present a case of multi-organ failure due to F. tularensis infection in a patient with alcoholic liver cirrhosis.

CASE REPORT

A 51-year-old male living in a rural part of western Norway was hospitalized after 2 weeks of influenza-like symptoms including fever, mild headache and a reduced general condition. During the last week before hospitalization, his wife had noted abdominal distention. Otherwise, no focal symptoms were noted. Two days prior to admittance, he started oral penicillin because of bacterial sinusitis. Previous medical history was significant for alcohol abuse, pancreatitis and alcoholic liver cirrhosis.

At admittance, he had memory and orientation impairment. Physical examination revealed blood pressure 133/85 mmHg, heart rate 107 beats per minute, temperature 40.3°C, respiratory rate 24 per minute and oxygen saturation 97%. He had scleral icterus and the abdomen was significantly distended although he denied abdominal pain. Laboratory tests showed leukocytes 8.8 × 10⁹/l (references: 4.3–10 × 10⁹/l), platelet count 26 × 10⁹/l (references: 145–348 × 10⁹/l), hemoglobin 13.8 g/dl (references: 13.4–17.0 g/dl), international normalized ratio (INR) 1.1 (references: <1.1), activated partial thromboplastin time 41 s (references: 28–48 s), sodium 133 mmol/l (references: 137–145 mmol/l), potassium 3.2 mmol/l (references: 3.5–5.0 mmol/l), magnesium 0.56 mmol/l (references: 0.71–0.94 mmol/l), creatinine 58 μmol/l (references: 60–105 μmol/l), alanine aminotransferase 59 U/l
Typhoidal Unknown
Respiratory Inhaling contaminated dust or as a secondary
Oropharyngeal Ingesting infected food or water

failure, CRP increased to 200 mg/l, bilirubin to 159
prophylaxis against Wernicke
tous bacterial peritonitis. In addition, he was given thiamine
taxime was prescribed for his sinusitis and a potential spontan-
detected. Computer tomography (CT) of the skull and brain

Table 1: An overview of the clinical types of Tularemia [5, 6].

| Form                | Route of acquisition                      |
|---------------------|------------------------------------------|
| Ulceroglandular or | Vectorborne or touching material or animals|
| glandular          | infected with F. tularensis              |
| Oculoglandular     | Contaminated material on the eye (from    |
|                    | fingers or infected dust)                |
| Oropharyngeal      | Inhaling infected food or water          |
| Respiratory        | Inhaling contaminated dust or as a secondary|
|                    | manifestation from the oropharyngeal or   |
| Typhoidal          | Unknown                                  |

The bacterium can be transmitted via direct contact with infected animals, arthropod bites, and by ingestion or inhalation. Rodents like hares and rabbits, mosquitoes and ticks are typically reservoirs. Contaminated water or soil may cause human infections [2] and also laboratory-acquired tularemia has been reported [3]. In our case, the source of infection was most likely the patient’s private well for drinking water, which according to his family was contaminated with surface water.

Typically, two ssp. of F. tularensis are dominating in human infections. F. tularensis ssp. tularensis (type A) strains are mainly found in Canada and USA and F. tularensis ssp. holarctica (type B) strains are found throughout the Northern Hemisphere, including Europe [4]. The ssp. tularensis can cause severe invasive diseases such as pneumonia and bacteremia whereas ssp. holarctica usually causes mild symptoms and have a low mortality rate (0.99%) [2, 4]. Tularemia is a rare disorder in the western parts of Norway with only 78 cases reported over the last 40 years, only 15 from our region [5]. Our patient probably suffered from F. tularensis ssp. holarctica since ssp. tularensis was excluded with the PCR assay. Although not performed in our case, a subspecies specific PCR analysis targeting the region of difference-1 (RD1) could probably identify the exact subspecies.

Tularemia can present with a variety of clinical symptoms and six different clinical forms are described (Table 1) [6, 7]. In our case report the patient developed multi-organ failure with pneumonia and bacteremia. Bacteremia is associated with underlying conditions such as diabetes mellitus, high age, alcohol abuse and immunosuppression [8]. Isolation of F. tularensis in blood culture is exceedingly rare and has only been reported infrequently in Europe [8]. However, our isolation of the strain was probably due to prolonged bacteremia in the patient as well as an extended incubation period of the samples.

First line treatment for severe F. tularensis, which requires hospitalization, is parenteral administration of an aminoglycoside. Aminoglycosides usually display a low minimal inhibitory concentration, have a bactericidal effect and a lower treatment failure rate compared to doxycycline [9]. In less severe cases fluoroquinolones, doxycycline and chloramphenicol are suggested [10, 11]. Notably, F. tularensis is resistant to all betalactam antibiotics including the carbapenems. Initially, we did not suspect tularemia in our patient and adequate antimicrobial treatment was therefore delayed. Aminoglycosides was anyhow not given to our patient because of crucial contraindications.

CONCLUSION

We here report a patient presenting severe sepsis and multi-organ failure caused by the low virulence F. tularensis. We therefore suggest that tularemia should be considered in patients at risk of infection with atypical microbes not responding to regular treatment. A high index of suspicion is needed to establish the correct diagnosis and prolonged incubation of blood cultures and microbiological samples should be considered for detection of fastidious bacteria.

ACKNOWLEDGEMENTS

We would like to thank Reidar Hjetland, Anne Grete Wågø and Jan Egil Afset for their valuable contributions.

CONFICT OF INTEREST STATEMENT

None declared.
FUNDING
No funding.

ETHICAL APPROVAL
No approval is required.

CONSENT
The patient’s relatives gave written informed consent for publication of this case report.

GUARANTOR
Bent-Are Hansen and Øyvind Bruserud.

REFERENCES
1. Su TY, Shie SS, Chia JH, Huang CT. Case report of low virulence francisella tularensis presented as severe bacteremic pneumonia. Medicine 2016;95:e3390.
2. Sigaloff KCE, Chung PK, Koopmans J, Notermans DW, van Rijckevorsel GGC, Koene M, et al. First case of severe pneumonic tularemia in an immunocompetent patient in the Netherlands. Neth J Med 2017;75:301–3.
3. Roberts RR, Hota B, Ahmad I, Scott RD 2nd, Foster SD, Abbasi F, et al. Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: implications for antibiotic stewardship. Clin Infect Dis 2009;49:1175–84.
4. Maurin M, Gyuranecz M. Tularaemia: clinical aspects in Europe. Lancet Infect Dis 2016;16:113–24.
5. https://www.fhi.no/en/hn/health-registries/msis/ (1 March 2018, date last accessed).
6. Thomas LD, Schaffner W. Tularaemia pneumonia. Infect Dis Clin North Am 2010;24:43–55.
7. Maurin M, Pelloux I, Brion JP, Del Bano JN, Picard A. Human tularemia in France, 2006–2010. Clin Infect Dis 2011;53:e133–141.
8. Karagoz S, Kilic S, Berk E, Uzel A, Celebi B, Comoglu S, et al. Francisella tularensis bacteremia: report of two cases and review of the literature. New Microbiol 2013;36:315–23.
9. Caspar Y, Hennebique A, Maurin M. Antibiotic susceptibility of Francisella tularensis subsp. holarctica strains isolated from tularaemia patients in France between 2006 and 2016. J Antimicrob Chemother 2018;73:687–91.
10. https://www.cdc.gov/tularemia/resources/whotularemiamanual.pdf (15 June 2018, date last accessed).
11. Perez-Castrillon JL, Bachiller-Luque P, Martin-Luquero M, Mena-Martin FJ, Herreros V. Tularemia epidemic in northwestern Spain: clinical description and therapeutic response. Clin Infect Dis 2001;33:573–6.