Enferm Infecc Microbiol Clin. 2018;36(8):527–528

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Diagnosis at first sight

Fever of unknown origin in a laboratory worker☆

Fiebre de origen desconocido en una trabajadora de laboratorio

Irene López Ramos[a,*], Jorge Galván Fernández[b], Antonio Orduña Domingo[a]

[a] Servicio de Microbiología, Hospital Clínico Universitario de Valladolid, Valladolid, Spain
[b] Servicio de Radiología, Hospital Clínico Universitario de Valladolid, Valladolid, Spain

A 29-year-old woman, a professional microbiologist with no prior history of note, sought care for a fever which she had had for the past 10 days with night sweats, a feeling of pressure on the sternum, severe asthenia and persistent dry cough with no expectoration, chest pain or dyspnoea. A physical examination revealed only slight splenomegaly. Laboratory testing results were normal except for CRP and ESR, which were high. The patient reported having worked with live cultures of pathogenic microorganisms, including *Mycobacterium tuberculosis* and *Francisella tularensis*, though in these cases she worked in a biosafety level 3 laboratory and in a biological safety laminar flow cabinet.

A chest X-ray showed right hilar lymphadenopathy (Fig. 1).

In view of these findings, a computed tomography (CT) scan was performed. This showed paratracheal, hilar, intrapulmonary and subcarinal right lymphadenopathy of a pathological size, measuring up to 2.9 cm (Fig. 2).

Given the patient's occupational history and the fact that her condition was probably infectious in origin, a Mantoux test, an interferon gamma release assay (IGRA) and a QuantiFERON® test as well as serologies against *Brucella*, *Francisella*, CMV and EBV were performed as complementary tests.

Clinical course

The tuberculin test showed no induration after 48 h and the QuantiFERON® test was negative. The serologies against *Brucella* and CMV were negative. The serology against anti-EBNA EBV was positive; immunochromatography against *F. tularensis* was weakly positive and microagglutination was negative.

Given the patient's clinical condition and occupational history, the radiological and serological results obtained and the possibility of pulmonary tularaemia in its initial phase, a new serology against *F. tularensis* was ordered. In addition, ciprofloxacin 500 mg was prescribed for 14 days. The patient's fever remitted in the first few days and all other symptoms remitted on completion of treatment. The serology performed with the second serum obtained after 15 days showed seroconversion of microagglutination with a titre of 1/160.

Final comments

Tularaemia, an endemic zoonosis in the Spanish region of Castile and León, is mainly acquired following contact with multiple infected animal species, including hares, rodents and river crabs, or arthropods which act as vectors.[1,2] The infectious dose of *F. tularensis* is the lowest of all known pathogenic bacteria (10–50 bacteria)[3]; therefore, contamination with contaminated dust or droplets is relatively common. This means that the infectious capacity of the microorganism represents a high risk of infection for laboratory workers, despite their adoption of safety measures required for handling this type of microorganism.[4]

As a result of this occupational accident, measures were taken which consisted of retraining staff who worked with highly infectious microorganisms and revising laboratory safety protocols.

F. tularensis subspecies holarctica, the subspecies involved in this case, causes less serious clinical conditions than *F. tularensis* subspecies *tularensis*.[3,4] Transmission through tick bites and contact with animals usually results in glandular or ulceroglandular forms, with lymphadenopathy usually being the most significant symptom. When the route of acquisition is inhalation, it may present in the form of pneumonia, or more rarely typhoid (which may result from any form of acquisition) or follow a clinical course with fever and asthenia but no respiratory symptoms. In these cases, radiological findings are not always detected. When they do appear, they may vary and include hilar thickening indistinguishable from tuberculosis or lymphoma.[4,5] In routine practice, diagnostic tests for *F. tularensis* are based on serology testing, since culture is difficult and dangerous to handle and PCR techniques, despite offering faster and safer detection, are not available in all laboratories.

Anti-F. tularensis antibodies may be demonstrated through tube agglutination, haemagglutination, enzyme immunoassay, immunochromatography or microagglutination. Agglutination titres are usually negative during the first phase of the disease and serology must be repeated with a new serum sample to demonstrate seroconversion. This usually appears 2 weeks after onset of

DOI of original article: https://doi.org/10.1016/j.eimc.2017.09.006

☆ Please cite this article as: López Ramos I, Galván Fernández J, Orduña Domingo A. Fiebre de origen desconocido en una trabajadora de laboratorio. Enferm Infecc Microbiol Clin. 2018;36:527–528.

* Corresponding author.
E-mail address: irenelora@hotmail.com (I. López Ramos).

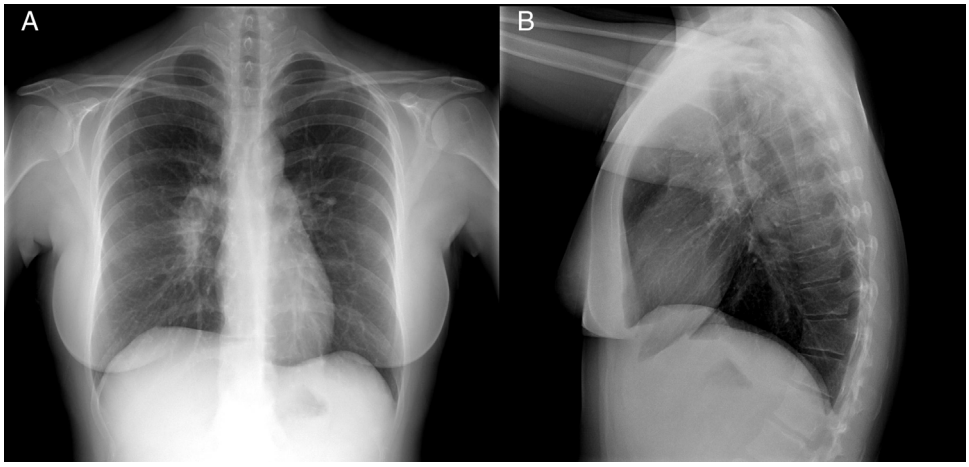

Fig. 1. (A) Posteroanterior chest X-ray. (B) Lateral chest X-ray. Right hilar enlargement related to lymphadenopathy.

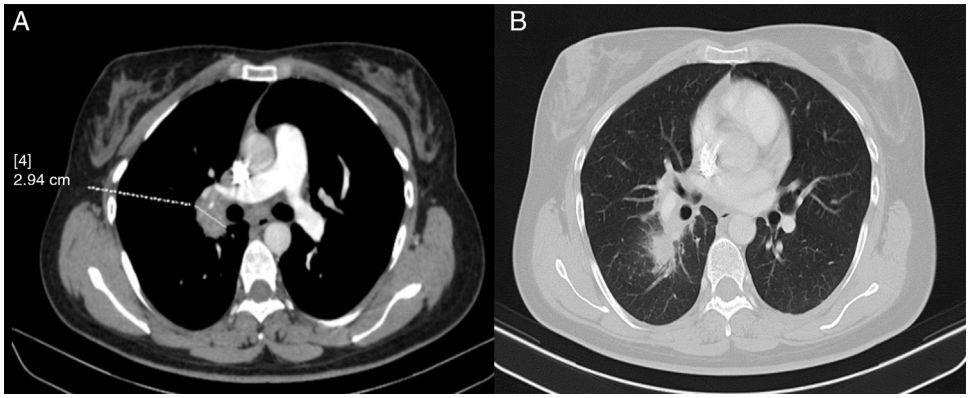

Fig. 2. Axial images from chest CT scan with intravenous contrast. (A) Mediastinal window. (B) Lung window showing paratracheal, hilar, intrapulmonary and subcarinal right lymphadenopathy of a pathological size, measuring up to 2.9 cm.

symptoms and shows a peak titre after 4–5 weeks. Titres greater than or equal to 1/160 are considered positive.[6] Antibodies may show cross-reaction with *Brucella* spp., *Yersinia enterocolitica* O:3 and O:9 and *Proteus* OX19; however, in these cases, titres against *F. tularensis* are almost always higher.[7]

References

1. Ariza-Miguel J, Johansson A, Fernández-Natal MI, Martínez- Nistal C, Orduña A, Rodríguez-Ferri EF, et al. Molecular investigation of tularemia outbreaks, Spain, 1997–2008. Emerg Infect Dis. 2014;20:754–61.
2. Anda P, Segura del Pozo J, García J, Escudero R, Peña F, Velasco M, et al. Waterborne outbreak of tularemia associated with crayfish fishing. Emerg Infect Dis. 2001;7:575–82.
3. Penn RL. *Francisella tularensis* (Tularemia). In: Mandell GL, Bennett JE, Dolin R, editors. Principles and practice of infectious diseases. Philadelphia, PA: Elsevier, Churchill Livingstone; 2015. p. 2590–602.
4. In: Tärnvik A, editor. WHO guidelines on tularaemia WHO; 2007.
5. Tärnvik A, Berglund L. Tularaemia. Eur Respir J. 2003;21:361–73.
6. Kiliç S, Çelebi B, Yesilyurt M. Evaluation of a commercial immunochromatographic assay for the serologic diagnosis of tularemia. Diagn Microbiol Infect Dis. 2012;74:1–5.
7. Dueñas A.I., Ortega M, Garrote I, de Frutos M, Gutiérrez P, García-Pascual A, et al. Laboratory diagnosis and serologic course in patients with tularemia. Med Clin (Barc). 2000;114:407–10.