IgM antibodies. Often, there will be chorioretinal scars, and reactivation can occur on the edge of a previous lesion, making diagnosis easier. However, the active area can cover a scar, particularly if it is small, making it difficult to see the original scar. Rising titers of IgG do not occur with ocular reactivation. There is increasing evidence that patients acquire this infection postnatally rather than by congenital transmission [18], and it is not yet known whether the most common source of infection is undercooked infected meat [19] or cats [20].

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Clinical microbiological case: sore throat and painful bilateral lymph nodes

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Please refer to the article on pages 637–638 of this issue to view the questions to which these answers refer.

1. Oropharyngeal tularemia. This clinical case may be confused with other infectious and non-infectious diseases affecting cervical lymph nodes, such as streptococcal angina, infectious mononucleosis, tuberculosis and lymphoma [1].

2. Oropharyngeal tularemia results from ingestion of potentially infected animals or fruits (hare, strawberries); however, sometimes there is no risk factor present (68.5%) [1,2]. In our case, the patient and his mother had no previous history of tick bite, and the possible routes were direct contact (skinning by hand) and inhalation. Both of them had skinned a wild boar, but the incubation period was too long for this to be the cause, and neither of them had had wounds or ulcers on their hands. They also denied having eaten other wild animals, river crabs or wild fruits, or having drunk water from springs. The similarity of the clinical picture in the patient and his mother suggested a common source of infection, but its etiology could not be established.

3. The laboratory diagnosis is generally based on the positivity of agglutinating antibodies to *Francisella tularensis*. Our patient developed seroconversion with a maximum titer of $1:2560$. Another microbiological technique for the diagnosis of tularemia is PCR [3]. In this case, a sample of the fluid obtained was positive for *F. tularensis* by PCR (performed by Dr Pedro Anda, Instituto Carlos III, Spain).

4. Because *F. tularensis* antibodies may cross-react with *Brucella* sp., as well as with other microorganisms such as *Proteus* OX19 and *Yersinia* sp. [2,4].

5. Treatment is usually empirical. Streptomycin is the drug of choice, although the percentage of cure of tularemia with streptomycin and gentamicin is similar [5]. Therapy must be continued for 10–14 days, but the duration of the fever is the best indicator of response [2,5]. Because our patient declined therapy with intramuscular streptomycin, treatment with intravenous gentamicin was started (6 mg/kg per day, divided every 8 h, for 14 days).

DISCUSSION

Tularemia is caused by *F. tularensis,* a small, Gram-negative coccobacillus. Two main types of *F. tularensis* have been described, type A and type B, which have differences in their epidemiology and virulence. Type A is the predominant biovar found in North America; type B, a less virulent biovar, occurs in Europe, Asia and North America [6]. In Spain, this is a rare illness with sporadic reports, with the exception of a recent epidemic tularemia outbreak in Valladolid [7].

The most important reservoirs are hares and ticks, although other wild animal can be reservoirs of this illness. It is transmitted to human by tick bite, direct contact with infected animals (skinning of dead animals), and inhalation and ingestion of contaminated water or food [1,2,8]. A bimodal distribution of cases has been described. Tick-associated disease occurs from May to September, whereas rabbit-associated disease is most common from November to February [2].

The clinical presentation depends on the route of inoculation and the lymphadenopathy is used to determine the site and mode of inoculation. After mammal exposure, 65% of lymphadenopathy occurred in the axilla; but after tick bite, 64% of lymphadenopathy occurred in the inguinal area. Because there was no previous tick bite history in our patient, the possible routes were skinning and inhalation. Oropharyngeal tularemia is due to ingestion of potentially infected animals or fruits (hare, strawberries) or contaminated water ingestion; however, sometimes there is no risk factor present (68.5%) [1,2,8].

Six classical forms of tularemia have been described in humans, based on clinical presentation of the illness: ulceroglandular, glandular, oculoglandular, oropharyngeal, typhoideal and pneumonic [2,9]. The most common clinical form of tularemia is ulceroglandular, with a primary ulcer on the skin and corresponding regional lymphadenopathy. Glandular tularemia, in which no primary ulcer is seen, is less common [1,2,7]. Among all the clinical pictures of tularemia, oropharyngeal tularemia appears to represent about 3% [1]. It is possible that this type of tularemia, without other manifestations, could remain undiagnosed, and its diagnosis is more a fortuitous finding than a primary suspicion [8]. In Spain, during the report of the first 65 cases of an epidemic tularemia outbreak in Valladolid, no cases of oropharyngeal tularemia were diagnosed [7].

The usual incubation period is 3–5 days (range, 1–21 days). Tularemia usually begins abruptly. Fever, chills, headache, malaise, anorexia and fatigue are quite common. Persistent lymphadenopathy could be present for a long time, even years, without appropriate treatment [1,2]. About 50% of patients have a history of sore throat, but, on examination, this is not clinically infected. These patients are often referred to a specialist, because the symptoms do not subside with β-lactam antibiotics [1].

Laboratory parameters are unremarkable [2]. The laboratory diagnosis is generally based on the positivity of agglutinating antibodies to *F. tularensis.* A fourfold increase in titer between two determinations is considered to be diagnostic, but a single titer of 1 : 160 or higher in a patient suspected of tularemia is very suggestive. Because of the infectious risk for laboratory workers, routine culture of *F. tularensis* is not indicated. When there is a suspicion of tularemia, laboratory workers should be notified. Another useful microbiological technique for the diagnosis of tularemia is PCR [3], but this is not available in all laboratories.

F. tularensis antibodies may cross-react with *Brucella* sp., *Proteus* OX19 and *Yersinia* sp. [2,4]. In patients with tularemia, slide tests for heterophilic antibodies (Monotest) may be positive. Therefore, cases of oropharyngeal tularemia may be misdiagnosed as mononucleosis if the tularemia agglutination titer is not determined [1,2].

If a biopsy specimen (node or abscess) shows a combination of abscess and caseous type of necrosis with an infiltration of numerous polymorphonuclear leukocytes, tularemia should be considered [1].

Treatment is usually empirical. Streptomycin is the drug of choice (1 g every 12 h IM for 7–14 days). The percentages of cure of tularemia with streptomycin and gentamicin are 97% and 86%, respectively. Additional factors could have contributed to failure in gentamicin therapy (i.e. inclusion of severe illness or presence of underlying diseases), so the efficacies of streptomycin and gentamicin are similar against tularemia [5]. The therapy must be continued for 10–14 days, but the duration of the fever is the best indicator of response [2,5]. During pregnancy and when the use of streptomycin is not possible, gentamicin is an effective alternative. The use of once-daily gentamicin for the treatment of tularemia has been suggested, but there is little evidence available, so further studies will be necessary to determine its efficacy. Other alternative regimens are doxycycline, quinolones (ciprofloxacin), and even imipenem–cilastatin [5,7].

In areas where tularemia has been described, this should be included among differential diagnoses of oropharyngeal infection when β-lactam antibiotics are not successful [1,8].

Chemoprophylaxis for risk groups is not recommended, and antibiotic prophylaxis after tick bite is not indicated. Avoiding exposure to the microorganism is the best way to prevent

tularemia (not skinning or dressing the animal without gloves, mask and glasses, avoiding tick bites, and removing ticks as quickly as possible with tweezers) [2].

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