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Tularemia: A differential diagnosis in oto-rhino-laryngology

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Abstract
Tularemia can present as an oto-rhino-laryngological disease. The clinical and radiological (CT) manifestations, diagnosis and treatment are discussed based on a case report where a patient with tonsillitis and enlarged cervical lymph nodes was admitted to the department of oto-rhino-laryngology of a hospital in Northern Norway. *Francisella tularensis* was isolated from the blood and there was a high titre of agglutinating serum antibodies to *F. tularensis*. The patient's contaminated drinking water well is the suspect source of infection.

Key words: Tularemia; Tonsillitis.

Introduction

Francisella tularensis is a small gram-negative rod, which can cause disease in both humans and animals. Rodents and hares are often found to be the reservoir of the micro-organism. Based on differences in virulence and biochemical characteristics, two biovars can be distinguished: *F. tularensis* biovar *tularensis*, and biovar *palaearctica*. Whereas biovar *palaearctica* has been isolated in Europe, North America and Asia, the more virulent biovar *tularensis* has only been isolated in North America.

F. tularensis is rarely isolated from human blood (Provenza *et al.*, 1986), and the clinician must therefore mainly rely on serological tests.

During the period 1975–1990, 105 cases of tularemia have been reported to the nationwide notification system for infectious diseases (MSIS) in Norway (Scheel *et al.*, 1992). In two cases only, the micro-organism was isolated directly from the patients' blood (Hoel *et al.*, 1991).

Clinical manifestations

The manifestations of tularemia are traditionally classified into different clinical types depending on the route of transmission: pneumonic (airborne contamination), ulceroglandular (directly through skin after contact with infected animals or after tick bites), oculoglandular (through the conjunctivae), or oropharyngeal (after ingestion of contaminated water or food). The latter manifestation often mimicks other oto-rhino-laryngological- and cervico-glandular diseases. The onset is often an episode with severe headache and tonsillitis (usually unilateral) sometimes developing to a peritonsillar abscess. After a week or two, a large, isolated, persistent cervical lymph-node appears. The diagnostic considerations include cancer, tuberculosis, or atypical mycobacterial infection, and tularemic lymph-node. The treatment is often surgical, and the enlarged persistent cervical lymph-node will usually be removed and examined histologically (Scheel *et al.*, 1992). Oropharyngeal tularemia with massive adenopathy together with correspondent CT appearance, has been reported previously by other authors (Umlas and Jaramillo, 1990).

We here present a case report presenting with a cervico-glandular picture mimicking other oto-rhino-laryngological diseases. (The case report has partially been published elsewhere (Hoel *et al.*, 1991) in another context.)

Case report

A 35-year-old woman was admitted during the winter-season to the department of medicine of a local hospital in Northern Norway. She had a four-days history of high fever, chills, headache, anorexia, limpness, photophobia and sore throat. Three days earlier she had been given oral penicillin for tonsillitis. At the time of hospitalization, she was suspected to have septicemia secondary to tonsillitis.

Physical examination at the time of admission showed bilateral tonsillitis, fur coating of the tongue, and periorbital oedema. There were no signs of neck rigidity. A 2 by 4 cm large, painful tumour, believed to be secondary to a peritonsillar abscess, was found in the right upper deep cervical area. Physical examination was otherwise normal. The patient had previously been healthy.

The temperature was 38.5°C. The leukocyte count ranged from 7.8 to 13.0 $\times$ 10^9/ml. The erythrocyte sedimentation rate (ESR) increased from 18 to 54 mm/h. She had a positive C-reactive protein test, but a test for mononucleosis (Monospot®) was negative. Serum Na^+, K^+, creatinine, LDH, SGOT, SGPT were normal. Chest X-ray,

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cerebrospinal-fluid and -pressure were also normal. Blood cultures were taken, and intravenous penicillin and cefuroxime treatment was initiated.

The patient did not respond to this antibiotic treatment. Therefore, three days later, she was transferred to the department of oto-rhino-laryngology at a larger hospital, where she was given ampicillin and metronidazole intravenously. On admission, there was no sign of a true peritonsillar abscess, but there was a hypertrophy of the right infected tonsil. She had a temperature of 39.5°C. The lymphadenitis on the right side of the neck had increased to 4 by 6 cm. It was punctured, but no fluid was obtained. Cytology showed nonspecific infection. Ultrasound examination indicated that the tumour consisted of multiple enlarged lymph nodes. Normal bacterial flora was found by throat swabbing.

Seven days after her first admission to hospital *F. tularensis* was isolated from the blood cultures. The treatment was immediately changed to erythromycin, since the resistance pattern showed susceptibility to erythromycin, doxycycline, tobramycin and chloramphenicol, but resistance to all beta-lactams. The temperature quickly returned to normal and on the 20th day of hospitalization the tumour had decreased to 3 by 5 cm, and the patient was discharged in good condition. At a follow-up examination, agglutinating serum antibodies to *F. tularensis* was demonstrated at a titre of 1:1,000.

The tumour did not disappear; two months after discharge from hospital the patient was readmitted to the department of oto-rhino-laryngology with a growing tumour in the neck. She experienced problems with swallowing and CT-scan showed lymphadenitis with a central necrotic abscess of 2 cm (Fig. 1). The abscess was punctured and four ml of brownish fluid was aspirated. The fluid showed no bacterial growth. All laboratory tests including leukocyte-count and ESR, were normal. She underwent an uncomplicated tonsillectomy and the abscess was drained. Histology of the tonsils showed reactive changes representing chronic infection. Shortly afterwards, she was discharged from the hospital and received a two weeks treatment of oral oxytetracycline.

In the follow up period of the second hospital stay, the patient did not present any symptoms of infection, but a small tumour persisted on the right side of the neck. This tumour disappeared two to three months later.

Four years after the acute infection, there was no clinical or laboratory pathological findings, except for an antibody titre to *F. tularensis* of 1:200.

Discussion

Shortly after the patient's first admission to the department of oto-rhino-laryngology, a possible tularemia infection was suspected. This suspicion was verified, when three out of six blood cultures grew *F. tularensis*. This underlines the importance of taking blood cultures as an early diagnostic step when suspecting a tularemia infection. The positive serological test result was not obtained until much later, after discharge from the hospital following successful treatment. Retrospectively, the typical CT-scan (Fig. 1) showing massive lymphadenopathy in the right side of the neck with central necrosis, might have underlined our suspicion of oropharyngeal tularemia (Umlas and Jaramillo, 1990).

The patient and her household shared a private groundwater drinking water well together with two other households. This well was poorly secured at the top with a wooden cover.

After the patient was discharged, a boy from one of the other two households sharing the same source of drinking water, developed tonsillitis. Serum samples from the boy and all 20 other household members, were taken. The boy's serum agglutinated antigen derived from the strain isolated from our patient, to a titre of 1:10,000. Eight other household members also had agglutinating titres ranging from 1:200–1,000.

These findings led to a closer examination of the well. A dead ground vole (Arvicola terrestris) was found on the ice covering the well. Later, in the spring, remnants of seven other voles were found at the bottom of the well. Since water samples also showed contamination with thermostable coliform bacteria, the well was emptied for cleaning shortly after. Unfortunately, the dead voles and the water were not tested for *F. tularensis*. However, the high number of seropositive persons among those using the same well, and the fact that two of them had symptoms of oropharyngeal tularemia, suggest the well as the source of infection. Other sources of oropharyngeal tularemia can be discussed, such as infected meat of other wild animals. There is, however, no information that any family-members had been hunting or eaten such meat during the actual period of time. Other routes of infection seem unlikely as we are dealing with an oropharyngeal form of the disease and the risk of insect- and tick-bites is very small during the winter season in Northern Norway.

A four-fold antibody titre rise is seen with current infection, but a single titre of $\geq 1/160$ is also considered diagnostic of past or current infection (Boyce, 1990). This titre level is usually reached in the third or fourth week of infection. In addition to serology, blood cultures should be taken to verify the diagnosis.

F. tularensis is resistant to most beta-lactam antibiotics,

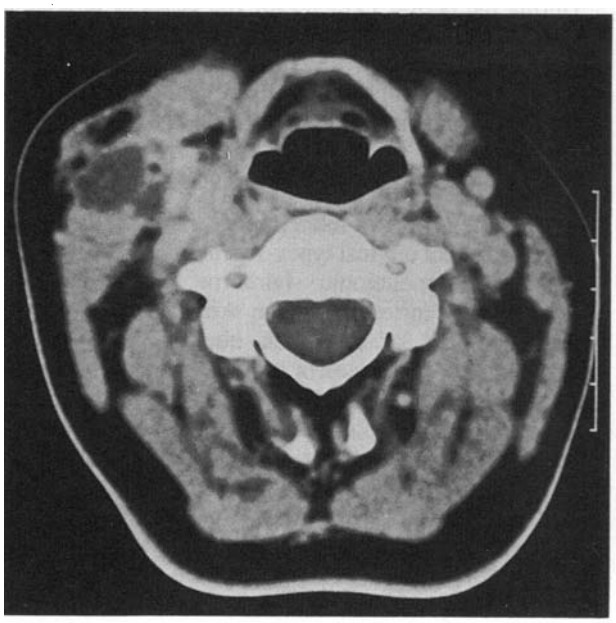

FIG. 1

Transverse contrast enhanced CT-scan through the level of the valleculae showing enlarged lymph nodes of the right side of the neck with central necrosis typical of oropharyngeal tularemia.

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including all penicillins (Scheel *et al.*, 1992). The treatment of choice with our patient was erythromycin. Other authors have also reported successful treatment with erythromycin (Harrell and Simmons, 1990). Quinolones can also be used if resistance is seen with erythromycin. Relapses are often seen after tetracycline treatment, unless it is administered for extended periods (Evans *et al.*, 1985).

In conclusion, tularemia should be thought of in unclear upper respiratory tract infections with cervical lymphadenitis, especially with no response after regular penicillin treatment.

References

Boyce, J. M. (1990) *Francisella tularensis* (tularemia). In *Principles and practice of infectious diseases.* (Mandell, G. L., Douglas, R. G., Bennett, J. E., eds.) Churchill Livingstone, New York, p. 1742–1746.

Evans, M., Gregory, D., Schaffner, W., McGee, Z. A. (1985) Tularemia: A 30-year experience with 88 cases. *Medicine*, **64:** 251–269.

Harrell, R. E., Simmons, H. F. (1990) Pleuropulmonary tularemia: successful treatment with erythromycin. *Southern Medical Journal*, **83:** 1363–1364.

Hoel, T., Scheel, O., Nordahl, S. H. G., Sandvik, T. (1991) Water- and airborne *Francisella tularensis* biovar palaearctica isolated from human blood. *Infection*, **19** no. 5: 348–350.

Provenza, J. M., Klotz, S. A., Penn, R. L. (1986) Isolation of *Francisella tularensis* from blood. *Journal of Clinical Microbiology*, **24:** 453–455.

Scheel, O., Sandvik, T., Hoel, T., Aasen, S. (1992) Tularemi i Norge. *Tidsskrift for Den norske lægeforening*, **5:** 635–637.

Scheel, O., Reiersen, R., Hoel, T. (1992) Treatment of tularemia with ciprofloxacin. *European Journal of Clinical Microbiology and Infectious Diseases*, **11** (5): 447–448.

Umlas, S. L., Jaramillo, D. (1990) Massive adenopathy in oropharyngeal tularemia: CT demonstration. *Pediatric Radiology*, **20:** 483–484.

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