Pediatric Anesthesia and Critical Care Journal 2022;10(1):32-36
doi:10.14587/paccj.2022.5

PACCJ

A challenging case of Francisella Tularensis: teenager's massive lymphoadenopathy caused by an uncommon infectious disease

G. Castellana[1], M. Ciuffreda[2], E. Pisello[3], U.W. Basso[3], J. Silvestri[3], M. Caimmi[2], A. Pennacchi[4], D. Galante[5], C. Piangatelli[6]

[1]Medical executive, Otorhinolaryngology Unit, ASUR Marche AV2, Fabriano, Italy.
[2]Medical executive, Anaesthesia, Resuscitation, Intensive Care and Pain Management Unit, ASUR Marche AV2, Fabriano, Italy.
[3]Specialist trainee in Anaesthesia, Resuscitation, Intensive Care and Pain Management, Università Politecnica delle Marche, Ancona, Italy.
[4]Medical Director, Otorhinolaryngology Unit, ASUR Marche AV2, Fabriano, Italy.
[5]Medical Director, Anaesthesia, Resuscitation, Intensive Care and Pain Management Unit, Cerignola, Italy.
[6]Medical Director, Anaesthesia, Resuscitation, Intensive Care and Pain Management Unit, ASUR Marche AV2, Fabriano, Italy.

Corresponding author: M. Ciuffreda; Medical executive in Anaesthesia, Resuscitation, Intensive Care and Pain Management Unit, ASUR Marche AV2, Fabriano, Italy. Email: ciuffredamat@libero.it

Keypoints

This article describes a challenging case of tularemia and its diagnostic process in a 17-year-old boy who presented to our clinic with a massive cervical left lymphadenopathy, enlargement of ipsilateral palatine tonsil and fever. Such clinical status was unresponsive to antibiotic and corticosteroid therapy.

Abstract

Tularemia is a potentially fatal, multisystemic infectious disease of humans and some animals caused by *Francisella Tularensis* bacteria. Up to six forms of clinical manifestations of tularemia have been identified, ulceroglandular tularemia being the most common form. Upper airway manifestations of tularemia include tonsillar hypertrophy and pharyngitis, accompanied by cervical lymphadenopathies. Anatomical alterations of the cervical district represent an additional risk in airways management. Between 2016 and 2019, only three cases of tularemia have been described in Italy, but some authors consider Tularemia underreported, especially in Europe. We describe a case of a 17-year-old boy who presented to our clinic with massive cervical left lymphadenopathy and enlargement of the ipsilateral palatine tonsil associated with fever. The symptoms persisted after antibiotic and corticosteroid treatment. To exclude a lymphoproliferative disease, a full body CT scan with contrast was performed, showing multiple cervical bilateral lymphadenopathies, especially on the left side and hypertrophy of the left palatine tonsil and splenomegaly. The biopsy of the left tonsil, performed under general anesthesia, demonstrated a granulomatous inflammation. A more accurate reconstruction of the patient history revealed domestic presence of rabbits. Therefore, serologic and molecular tests for *F. Tularensis* were performed, with positive results. Proper antibiotic treatment was administered with gradual and complete symptoms regression.

Keywords

Lymphadenopathy; Tularaemia; Francisella tularensis; Head and neck infection; Granulomatous disease; Pediatric infection; Tonsillar hypertrophy

Introduction

Tularemia is a potentially fatal, multisystemic infectious disease of humans and some animals caused by *Francisella Tularensis* bacteria. Ticks, biting flies and other animals such as rodents and lagomorphs are responsible

for the human transmission of the disease; other forms of transmission include water exposure, ingestion of infected food and aerosol exposure. Up to six forms of clinical manifestations of tularemia have been identified, ulceroglandular tularemia being the most common form. Oropharyngeal and gastrointestinal tularemia is characterized by pharyngotonsillitis and hypertrophy of the cervical lymph nodes[1]. Such anatomical alterations of the cervical district represent an additional risk in airways management. In paediatric surgery, the incidence of difficult intubation is 0.2-5.5%, with impossible intubations of 0.08%; instead, the prevalence of difficult OTI is 1-2%, a proportion which rises to 50% when considering the subpopulation of paediatric patients with cervical alterations[2,3]. Three quarters of all critical incidents and a third of all peri-operative cardiac arrests in paediatric anaesthesia are caused by adverse respiratory events[4]. We report a case of tularemia in a young adult with massive cervical lymphadenopathies of the neck and monolateral tonsillar hypertrophy.

Case report

A 17-year-old boy presented to our clinic with a left cervical mass associated with fever and left tonsillar hypertrophy of recent onset. The treatment with intramuscular cephalosporines and corticosteroid was ineffective. A neck ultrasound study performed at another facility described a massive cervical bilateral lymph node enlargement, the greater one on the left side with diameters of 5.0 and 2.3 cm with hypoechogenic content. Fibrolaryngoscopy showed no other mucosal lesions. To exclude a lymphoproliferative disease, the patient was hospitalized and a CT scan of the neck, thorax and abdomen with contrast was performed, showing multiple cervical bilateral lymphadenopathies (see Figure 1), especially on the left side with hypodense content and hypertrophy of the left palatine tonsil (see Figure 2), splenomegaly and minor enlargement of the mesenteric lymph nodes.

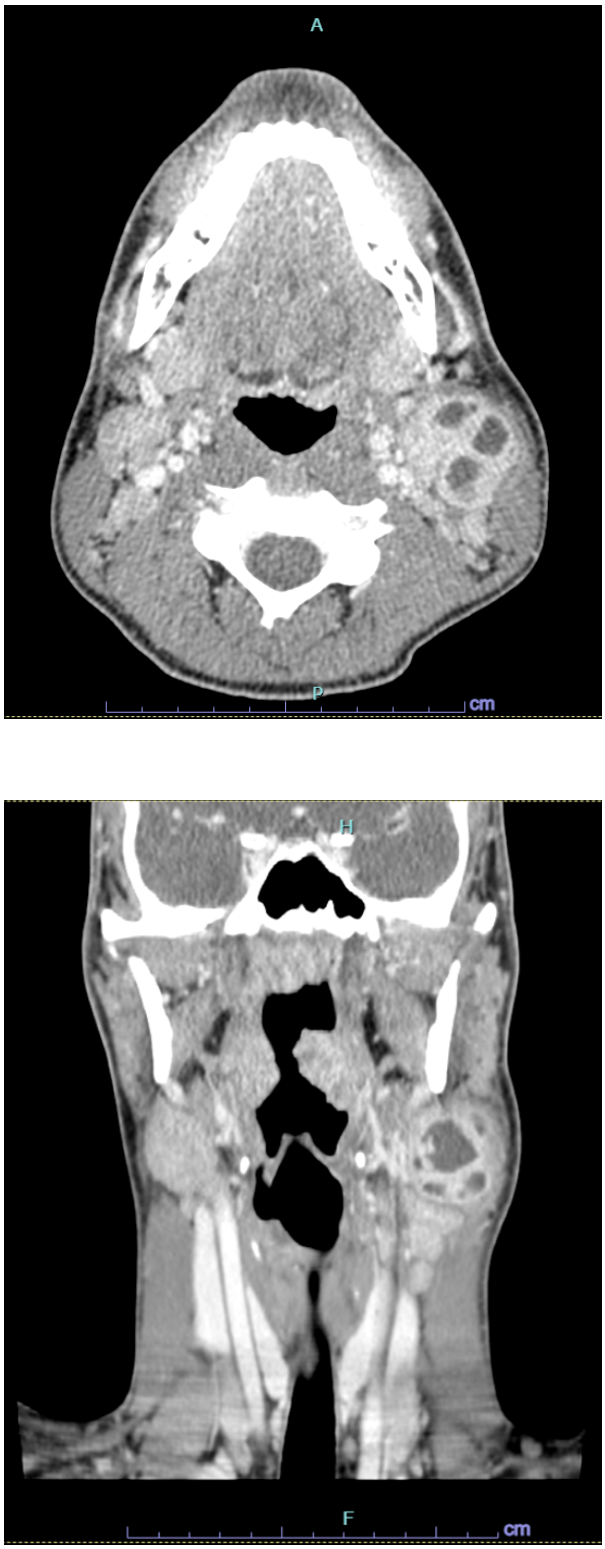

Figure 1. Axial and Coronal CT scan of the neck shows multiple left lymphadenopathies with peripherical contrast-enhancement and hypodense content, indicative of suppuration, and ipsilateral tonsillar hypertrophy.

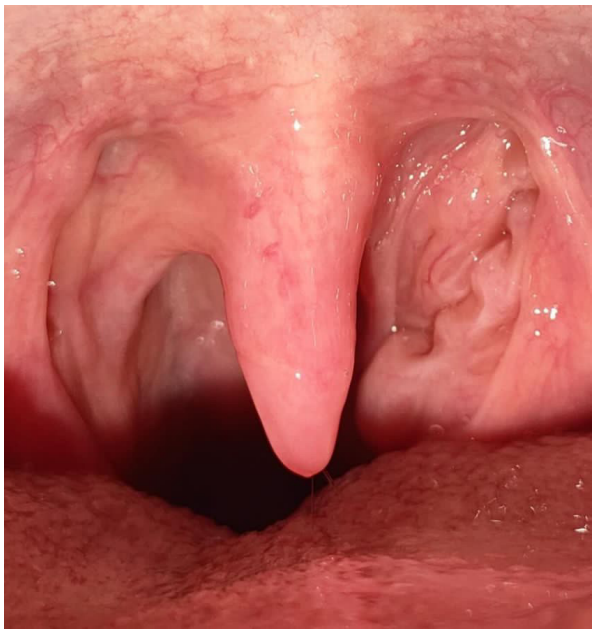

Figure 2. Bilateral tonsillar hypertrophy, with greater enlargement in the left side is evident.

After discussion with the patient and his parents, a biopsy of the left tonsil under general anesthesia was proposed, in order to grant a stable and safe airway. Anesthesiology management started form a detailed preoperative evaluation of patient's past, recent and family medical history, which showed anything relevant; physical examination revealed a left bigger cervical mass and many other little cervical masses on the right side; anthropometric anesthesiology assessment showed a normal BMI (< 30), neck circumference of 39 cm and an El Ganzouri Index <4, which is predictive of a non-difficult intubation. Induction of anaesthesia started from adequate preoxygenation, followed by the administration of Fentanyl, Propofol and Rocuronium (the latter chosen among other neuromuscular blockers because of Sugammadex's availability). The intubation was performed using videolaryngoscopy, the main technique to facilitate tracheal intubation and reduce its complications[5], routine practice in our operating block since November 2021. An armored tracheal tube of size 7,5 was used. Videolaryngoscopy showed a full glottic view according to the Fremantle classification; intubation was performed at first attempt, with no need for additional devices. Maintenance of general anesthesia was achieved using Sevoflurane under bispectral index (BIS) depth monitoring; protective ventilation was administered. Extubation at the end of anesthesia was performed under neuromuscular monitoring (NMT) and after Sugammadex administration. Histologic examination demonstrated a granulomatous inflammation and hypertrophy of the lymphatic component, without signs of neoplastic tissue. A more accurate examination of the patient history revealed recent contact with rabbits. Molecular tests for mycobacterial infection were negative. Serologic and molecular tests for *F. Tularensis* showed positive results. Proper antibiotic treatment was administered with gradual and complete resolution of the symptoms.

Discussion

Tularemia is a rare zoonotic disease that can be transmitted to humans from arthropods, rodents and lagomorphs. Human cases of tularemia are more frequent in late summer and fall and predominates in the northern hemisphere[1]. The granulomatous inflammation of lymph nodes and upper airways is a non-specific sign of the infection. The differential diagnosis of granulomatous inflammation of the head and neck region includes infectious causes, chronic inflammatory and autoimmune diseases. Tuberculosis, atypical mycobacterial infection and cat scratch disease are associated with presence of granulomas of the head and neck. Moreover, the involvement of the upper airways and cervical lymph nodes is described in inflammatory diseases such as sarcoidosis and Chron's disease as well[6]. Autoimmune diseases such as granulomatosis with polyangiitis (GPA) and eosinophilic granulomatosis with polyangiitis (EGPA) can present with inflammation of the sinonasal and oral mucosa[7]. Once a neoplastic disease has been ruled out through a histological exam of the lymph node or of the mucosa, differential diagnosis often requires further microbiologic, serologic and imaging exams to reach a conclusion. Importantly, an accurate preoperative evaluation is essential when performing general anesthesia in pediatric patients presenting with cervical anatomical alterations, as the risk of difficult intubation in this population is much

higher[2,3]. In some patients it's not possible to find a definite cause. Diagnostic exams must be oriented in accordance with epidemiological factors such as the TB's prevalence in that geographical area and the patient's age; in fact, some authors highlight that the incidence of atypical mycobacteria is higher in children[6]. Finally, anamnestic informations are of utmost relevance, as history of contact with animals and hunting could be an indicator of a zoonotic infection. Between 2016 and 2019, only three cases of tularemia have been described in Italy[8], but some authors consider Tularemia underreported, especially in Europe[9]. In the case reported, a detailed investigation of the patient history, conducted after the histological report, revealed a recent contact with rabbits, raising suspicion for *F. Tularensis* infection. According to the patient's symptoms and presentation, oropharyngeal form of tularemia can be assumed, although ulceroglandular and glandular forms are reported most frequently in children and adults[9]. The previous antibiotic treatment with cephalosporines was ineffective, leading to the suspicion of a lymphoproliferative disease, which was excluded through an oropharyngeal biopsy. General anesthesia and intubation using videolaryngoscopy presented no complications of any kind. *F. Tularensis* is frequently resistant to beta-lactams and its eradication requires therapy with aminoglycosides and ciprofloxacin[10]. The fatality rate of tularemia can be as high as 5% if untreated[1]; suppuration, abscess formation and skin manifestations such as erythema nodosum, erythema multiforme or papular lesions are possible complications[11]. Prevention of tularemia mainly consists in measures of behavioral strategies to avoid or reduce exposure to the most common local transmission routes such as proper clothing to prevent insect bites and prompt removal of ticks[12].

Conclusions

To bring things to a close, the presence of a granulomatous inflammation in the head and neck region should raise the suspicion of a zoonotic infection; patient's history should always be well known to reveal any risk factor for F. Tularensis infection. Early identification of the pathogen is essential to administrate a proper treatment and avoid complications.

Disclosures

The approval of the regional ethical committee is not requested for case reports. Authors declare no funding for the production and publication of this article and no conflict of interest.

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