BRIEF COMMUNICATION

Yersinia enterocolitica Tonsillitis

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Abstract We present five cases of tonsillitis secondary to Yersinia enterocolitica. No response to commonly used antibiotics and continuous professional contact with pigs were common. The definitive diagnosis was established by bacteriological isolation on tonsil tissue samples. © 2010 Elsevier España, S.L. All rights reserved.

Introduction

Tonsillitis and its local complications are common in human beings because the tonsils represent the first barrier against entry of antimicrobial agents through the upper respiratory tract and their histological structure allows direct contact between lymphocyte tissue and antigen. The result is an inflammatory process with oedema, hyperaemia, congestion, suppuration and chemotaxis, almost independently of the invading microorganism. Under the clinical suspicion of bacterial infection, an empirical antibiotic treatment is usually effective in treating symptoms. However, the characteristics of some agents make them particularly resistant to this therapeutic approach.

We present a series of 5 cases with common clinical and epidemiological circumstances that led to the clinical suspicion of tonsillar infection by Yersinia enterocolitica.

Patients

Since 1999, we have treated 5 patients for acute tonsillitis in an unusual context. All attended the Emergency Service...
under conventional antibiotic treatment, with significant illness and fever syndrome resistant to antipyretic measures. All presented dysphagia with odynophagia, pharyngolalia voice, drooling without trismus (except for one case), dry irritant cough and bilateral cervical lymphadenitis.

The patients were admitted and subjected to analytical batteries in peripheral blood, pharyngeal exudate sampling and intravenous antibiotic treatment. In 2 cases, histopathological tonsil samples were obtained under local anaesthesia.

Results

Table 1 shows the characteristics of our patients. All subjects were middle-aged, and all were in almost continuous contact with animals, particularly pigs.

Two patients presented bilateral pultaceous palatine tonsillitis and 1 of them presented spontaneous emission of blood through a tonsil for 48 h. A third patient attended the service with a properly drained peritonsillar abscess. The remaining 2 were unilateral, non-ulcerating-necrotising episodes. Cervical palpation detected bilateral reactive lymphadenopathies of up to 25 mm.

The tonsils were hyperplastic and hyperaemic in all cases, with no surrounding oedema even in the case of abscesses.

The biopsies of the pharyngeal exudate and pus were ineffective. We used mainly penicillins, cephalosporins and metronidazole. The chest X-ray studies and Mantoux tests were negative. The biopsy of tonsillar tissue obtained under local anaesthesia in one case resulted definitive.

Peripheral blood contained leukocytosis of up to 22,000/mm³ with neutrophilia between 77% and 91%. There was a sharp rise in acute phase reactants, negative for heterophile antibodies. The lack of response to treatment led to tonsillectomy in 5 cases. There was relative clinical improvement, with samples being referred to Pathological Anatomy. Reports were obtained in 4 cases.

The report of the specimens was hyperplastic lymphoid tissue, containing multiple clusters of granulomatous nodules, consisting of histiocytic cells, giant cells and numerous neutrophils in central location. From the histopathological point of view, we carried out a differential diagnosis of yersiniosis, cat scratch disease and sequelae of venereal lymphogranuloma. Samples of tonsilar nucleus tissue sent to the Microbiology Service confirmed the growth of Y. enterocolitica.

Signs and symptoms disappeared between 5 and 10 days after tonsillectomy in all cases.

Discussion

Y. enterocolitica is a Gram negative coccoid member of the Enterobacteriaceae family, which is immobile at 37 °C but mobile at 25 °C by peritrich flagella. It is an asporogenous agent that grows well in ordinary media.

It is a facultative anaerobe, oxidase negative and catalase positive, which ferments glucose and sucrose with acid production. It produces a thermostable enterotoxin, similar to that of E. coli, within the intestinal epithelial cells. A total of 34 O antigens and 20 H antigens are known for it, which determine the various serotypes and may cause some cross-reactions with Brucella and Salmonella. The most abundant serotypes in Europe are O3 and O9.

In children, it causes an acute adenitis similar to appendicitis and terminal ileitis with diarrhoea. In adults, it may precede episodes of arthritis, septicaemia, and erythema nodosum. Although urinary tract infections and conjunctivitis have been described, the most common manifestation is enterocolitis with fever and abdominal pain, which can last up to 3 weeks.

The infection is acquired through the mouth and the bacterium multiplies in Peyer’s patches, from where it can spread to the rest of the intestine. It is resistant to β-lactam antibiotics and, to a lesser extent, to tetracyclines, chloramphenicol and aminoglycosides, although enterocolitis is generally treated only symptomatically. Access through foodstuffs is not exceptional and in the UK, in 1989, it exceeded food poisoning cases by Staphylococcus aureus and Bacillus spp. However, almost all food isolates are due to environmental strains. Y. enterocolitica can be isolated in soil, water, milk, poultry, fish, the intestines of small animals and especially in pork meat.

Documentation is sparse with regard to pharyngotonsillar involvement. Outbreaks of yersiniosis appear more related to faecal-oral transmission than to direct person-to-person contact. Its pathogenesis is determined by adhesins and invasins, proteins encoded by plasmids. Cherchi describes a case of tonsillitis from Y. enterocolitica in a thalassemic child and in another healthy patient within a group of 100 control subjects.

It is recognised that pigs are the reservoir of Y. enterocolitica. Although the original source is identified, transmission control is impractical since it requires the systematic evisceration of the animals. However, a significant decrease in the transmission of yersiniosis has been demonstrated through the removal of the tongue and tonsils. Thus, bacterial risk varies with food preferences.

The affinity of Y. enterocolitica for lymphatic tissue is extraordinary and its adherence to intestinal Peyer’s patches is very high. At the top of the latter, there are M cells that transport macromolecules and microorganisms from the intestinal lumen into the patches by pinocytosis, with the antigen accessing the lymphoid tissue. In childhood, these patches show a predominance of T cells in 80%. M cells partially inactivate the bacteria. Neighbouring macrophages process their antigens and present them to T cells to produce cytokines, which promote the mechanisms of intestinal inflammation.

This action is carried out due to the synthesis of plasmid invasins, especially Ail (attachment invasion locus) and YadA (Yersinia adhesion). The intestinal epithelium possesses integrins, which are β1 chain receptors for these invasins. Generally, intestinal integrins are of β4 chains and are not adhesive, but at 37 °C and with a pH less than 7, the integrins become strong recruiters of Y. enterocolitica. This acidification of focal pH enhances highly reactive Peyer’s patches in individuals younger than 14 years.

The bacterial plasmid also produces Yersinia outer proteins (Yops). These are highly virulent proteins if they access lymphatic tissue adhered to Yersinia, although they do not generate any effect whatsoever when exogenously injected into cell cultures. Yops have protein kinase activity,
transducing signals from the host cell and altering their ability to attract antigen-presenting cells and phagocytes.\textsuperscript{7,8} This culminates in aggressive oxidative stress of their lysosomal content, with complete consumption of antioxidant titres, enhancing tonsillar damage.\textsuperscript{9} Furthermore, Yops inhibit platelet aggregability and cytokine release from this source, so the defence mechanisms of the tonsil are overthrown. The focal clinical expression is a hyperplastic palatine tonsil, hyperaemic, suppurrative and without oedematous reactions in its vicinity.\textsuperscript{8}

Additionally, YaDA invasin shows a strong resistance to the bactecial reaction of serum, inducible at 37 °C, degrading the C3b complement factor and cancelling its cascade.

Lastly, there is evidence that iron in the host enhances the virulence of \textit{Y. enterocolitica} through its accessibility. This is done by generating a siderophore known as yersiniabactin, a protein of 482 D capable of sustaining a weak but consistent binding with iron of ferritin, transferrin and lactoferrin in the subject.\textsuperscript{4,10}

These powers of adhesion, interference to phagocytosis and resistance to the bactecial action of serum are enhanced by \textit{Y. enterocolitica} in Peyer’s patches based on proximity to M cells. Tonsillar yersiniosis seems to be more related to sustained contact of the agent with a surrounding environment of the patient’s aerodigestive tract, because the bacteria present mucoid fimbriae—\textit{Myf} (mucoid \textit{Yersinia} factor) and PsA (pH 6 antigen adhesin)—which predispose them towards the formation of tonsillar phagosomes in situations of pH 5–6.

Changes in the pH of the tonsillar area are not generally sudden unless there is a previous infectious trigger or a repetition of bacterial contact with the subject. It seems evident that an environment contaminated by \textit{Y. enterocolitica} predisposes the tonsils towards its incubation. These environments are relatively rare and are restricted to stocks of pigs. An anamnesis directed in this regard and the finding of unusual tonsillitis—inflammatory asymmetries, unilateral tonsillitis, abscesses—with torpid response to conventional antibiotic therapy, should lead diagnostic suspicion towards this agent.

Serological diagnosis is difficult due to the variability of serotypes, but enterobacteria are easy to isolate in simple culture media, such as MacConkey or peptone water with 5% salt, unless an antibiotic protocol has been previously initiated. This is common and delays filiation of the case. Capacity for serum autoagglutination at 37 °C and for Congo red stain uptake of infected histological samples should guide the process. However, the limitation in bacterial isolates and the fact that antibiotic sensitivity requires unusual chemotherapeutic agents, such as aminoglycosides or chloramphenicol, make tonsillectomy advisable in the previously discussed epidemiological circumstances.

### Conflict of Interests

The authors have no conflicts of interest to declare.

### References

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