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LETTER TO THE EDITOR

Acute submandibular sialadenitis in a patient with Crohn's disease being treated with infliximab☆

Submaxilitis aguda en paciente con enfermedad de Crohn en tratamiento con infliximab

Dear Editor:

Submandibular sialadenitis is inflammation of the submaxillary salivary glands. The most common cause is sialolithiasis, the formation of stones which block the ducts that drain the gland. The second most common cause is infection, mainly by viruses with a special tropism for the salivary glands (cytomegalovirus [CMV], varicella zoster virus [VZV], Epstein–Barr, herpes 6 virus, influenza virus, parainfluenza virus, respiratory syncytial virus, coronavirus, rhinovirus and mumps virus),[1] with bacterial infections being less common. Infections of this type are very often associated with underlying immunosuppression. A third group consists of cases associated with diseases of the immune system, primarily Sjögren's syndrome, or in the context of hyper-IgG4 syndrome. There are other aetiologies, such as transient submandibular sialadenitis after endoscopic procedures of the gastrointestinal or upper respiratory tract, and in relation to orotracheal intubation.

There is also a small group of drugs (doxycycline, nitrofurantoin, methimazole, nifedipine and captopril) with which a correlation has been suggested, although no clear mechanism has been established.[2,3] Worth noting is the publication of cases associated with azathioprine,[4] infliximab and adalimumab,[5] and tocilizumab,[6] although here it should be considered whether or not the origin might be more related to immunosuppression.

In this context, we present the case of a 72-year-old man who developed ileal Crohn's disease in 2016. He was started on treatment with azathioprine in February 2018 due to evidence of disease progression, but was unable to tolerate it. As a result, in May 2018 he was switched to mercaptopurine, but only took that for a few weeks. The patient made his own decision to stop all treatment.

He was admitted with a new flare-up in July 2019. Computed tomography (CT) showed a fistulous tract between two small bowel loops and another from the right colon (immediately cranial to the ileocaecal valve) to an ileal loop. He was started on infliximab. Six weeks after starting treatment, he was readmitted with painful oedema in the submandibular area of his neck and symptoms of diffuse abdominal pain, with CT now showing progression of the already documented fistulous tracts. Infliximab levels were not determined. The patient was prescribed antimicrobial therapy with intravenous metronidazole and ciprofloxacin and also intravenous methylprednisolone 1 mg/kg/day. While in hospital he was assessed by the Ear, Nose and Throat (ENT) Department and a neck ultrasound was ordered, showing bilateral submandibular sialadenitis. There was no evidence of obstruction or suppuration of the salivary ducts. Twenty-four hours after steroid treatment was started, a marked decrease in the patient's neck inflammation was seen. The study was completed with IgG4, antinuclear antibody (ANA), anti-Ro and anti-La levels and IgG and IgM serology for CMV, Epstein–Barr and VZV; these were negative.

A literature review found no direct relationship between submandibular sialadenitis and Crohn's disease. When we analysed the drugs used in Crohn's disease that have been associated with submandibular sialadenitis, we found it highly doubtful that the drug was directly responsible for the toxic effect on the gland. The mechanism suggested in other cases of submandibular sialadenitis associated with infliximab, adalimumab[5] and tocilizumab[6] is the immunosuppression induced by these drugs, which makes patients more susceptible to either the formation of abscesses, in this case unilateral, or the reactivation of latent viruses. In our case, we cannot establish a pathophysiological mechanism by which infliximab acts directly on the salivary glands, and although we were unable to determine the microorganism responsible, the most feasible hypothesis for the origin of the patient's submandibular sialadenitis is the reactivation of a virus with special tropism for the salivary glands.

In the case reported by Guerra et al.,[4] in which submandibular sialadenitis was associated with azathioprine, the fact that the condition reappeared after the treatment was reintroduced does not necessarily point to direct toxic effect. Both in this case and in all other cases, the possibility that the submandibular sialadenitis was due to reactivation

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of the virus in immunosuppressed patients cannot be ruled out.

Treatment in these cases consists of anti-inflammatories (mainly prednisone or methylprednisolone) and concomitant reduction of immunosuppression to enable the immune system to control the viral infection.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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