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## Response to: Sjögren's Syndrome and Halitosis: A Case Report☆

### *Respuesta a: Síndrome de Sjögren y halitosis: descripción de un caso clínico*

*Dear Editor*:

I read very carefully the publication of Ruiz Serrato et al.[1] in Reumatología Clínica, where the authors report a case of halitosis secondary to Sjögren's syndrome (SS). I would like to express a few considerations, which I hope will contribute to a better understanding of this association.

Sjögren's syndrome is a systemic, autoimmune disease, with a prevalence that ranges between 0.1% and 0.5%, with a predominance of women (4th and 5th decades of life).[2] Histopathological studies show it to be characterized by lymphocytic infiltration at the level of the exocrine glands.[2] This syndrome can be primary or secondary (associated with systemic lupus erythematosus, rheumatic arthritis and scleroderma).[2] The destruction of the exocrine glands leads to "sicca syndrome" (xerostomia and xerophthalmia).[2] However, SS can show extraglandular manifestations, including general, cutaneous, musculoskeletal, respiratory, urogenital, thyroid, gastrointestinal and hepatobiliary.[2] The association between halitosis and SS is multifactorial.

*First:* Parotid gland dysfunction results in xerostomia and a decrease in salivary flow that leads to periodontal diseases due to *Treponema denticola, Porphyromonas gingivalis* and *Bacteroides forsythus*, which produce mercaptan and sulfur that are associated with the level of halitosis (oral cause of halitosis).[3] Saliva has antimicrobial properties; thus, the amount and quality of saliva are essential to prevent halitosis. Therefore, in patients with SS and xerostomia, the production of saliva is reduced, increasing the possibility of generating volatile sulfur compounds (VSC), the result of the degradation of proteins with sulfur-containing amino acids from the exfoliation of human epithelial cells, leukocytes and the remains of food, and with it, oral malodor.[3] Volatile sulfur compounds are associated not only with halitosis, but can enter into a vicious circle of pathogenesis of gingivitis and periodontitis.[3]

*Second:* Extraglandular manifestations are factors that trigger halitosis in SS. Patients with SS are more predisposed to develop chronic rhinosinusitis (a perioral cause of halitosis) and bronchiectasis (an extraoral cause of halitosis). Among the gastrointestinal manifestations, they may present esophageal dysfunction, chronic gastritis, *Helicobacter pylori* infection and bacterial overgrowth, which also cause halitosis (extraoral cause). Primary biliary cirrhosis, as a hepatobiliary manifestation, is an extraoral cause of halitosis.

*Third:* Diseases associated with secondary SS play their own role. For example, gastroesophageal reflux (an extraoral cause) in SS secondary to scleroderma produces dental erosion and dysphagia that provoke halitosis.[4] Moreover, patients with SS have an elevated risk of developing non-Hodgkin's B-cell lymphoma, which can be an extraoral cause of halitosis. On the other hand, the symptomatology of halitosis in SS patients can, subjectively, be worse (not genuine), by psychosomatic halitosis, halitophobia or because the xerogenic medicine they take (antidepressant and nonsteroid anti-inflammation drugs). With respect to the case reported by Ruiz Serrato et al.,[1] as the authors, reasonably explain, it is true halitosis due to oral causes (xerostomia), with a favorable response to pilocarpine. However, we recommend follow-up, to screen for possible perioral and/or extraoral causes related to SS, in the case of therapeutic failure or recurrence. I conclude that, halitosis is a prevalent entity (up to 50% of the general population), and has been studied little in SS. Although, it is considered more a problem related to poor dental hygiene or to diseases of the oral cavity (87%), on occasions, it may be a manifestation of the disease at other levels—perioral—or even of a psychiatric or systemic disease—extraoral—(13%).[3] Therefore, an initial approximation should include a complete history (diet, drugs, poor habits and dental hygiene), a thorough examination, a complete analysis, as in screening. The therapeutic management requires a multidisciplinary evaluation, with hygienic, dietetic, pharmacological (pilocarpine hydrochloride) and/or etiological—oral, perioral, extraoral or mixed, as in the case of SS.

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☆ Please cite this article as: Qanneta R. Respuesta a: Síndrome de Sjögren y halitosis: descripción de un caso clínico. Reumatol Clin. 2016;12:357–358.

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## New Drugs in Takayasu Arteritis, Role of Tocilizumab☆

### *Nuevos fármacos en la arteritis de Takayasu, papel del tocilizumab*

*Dear Editor:*

Evaluating Takayasu arteritis (TA), one of the so-called rare diseases, we should know that this is a granulomatous vasculitis that affects large vessels, especially the aorta and its major branches, especially in young women.[1] Given the infrequency of this disease, there are no controlled randomized studies. Thus, its treatment is based on retrospective observational studies.[1] In patients who are refractory to conventional treatment, a marked effect by biological therapies like tocilizumab was recently reported.[1,2]

We describe the case of a 63-year-old woman who had a 4-year-history of TA. She initially presented with left suboccipital headache associated with ipsilateral episcleritis, an increase in acute-phase reactants, and physical examination showed differences in systolic arterial blood pressure of her two arms of more than 10 mmHg, as well as, weakness in her temporal, carotid and radial pulses of her left side. The diagnostic study found relevant analytical data, including her positivity for rheumatoid factor, high C-reactive protein and erythrocyte sedimentation rate, and her testing positive for anti-Sp100 and negative for: antinuclear antibodies, extractable nuclear antigen, anti-cyclic citrullinated protein antibodies, human leukocyte antigens B7 and B52 and anti-smooth muscle antibody. She underwent magnetic resonance angiography (MRA) of supraaortic arteries with the following findings: 50% stenosis of right internal carotid artery, insignificant stenoses of left internal carotid artery, left external carotid artery and partially assessed subclavian arteries. Aside from MRA of aorta, which indicated stenosis proximal to the right subclavian and, with a filiform and irregular trajectory, and left subclavian stenosis. On the other hand, whole-body positron emission tomography indicated inflammatory activity at the level of the ascending aorta, aortic arch and abdominal aorta, with no evidence of involvement at other sites. Initially the patient was treated with prednisone (initial dose was 15 mg/24 h) for 2 years and azathioprine was incorporated (50 mg a day), to be discontinued because of an increase in her transaminases. Then, after only 1 year of corticosteroid therapy, mycophenolate mofetil was introduced at 1 g/12 h. She continued 1 year later in remission, but it was necessary to increase mycophenolate mofetil to 2.5 g daily. Seven months later, treatment with tocilizumab was begun, which achieved the disappearance of her clinical manifestations, together with a decrease in the prednisone dose to 10 mg/day.

The treatment of choice in TA is corticosteroids, although they induce an initial remission in 90% of the patients. It is estimated that approximately half of the effects will be resistant to them, and it will be necessary to add immunosuppressive agents (azathioprine, methotrexate or mycophenolate mofetil).[2,3] Moreover, we should not forget the secondary toxicity of long-term corticosteroid therapy.[4] The use of immunosuppressive drugs will help to decrease the corticosteroid dose to the minimum necessary.[4] However, their effectiveness will not be completely demonstrated by randomized studies, taking into account that an estimated 33% of the patients treated will have relapses.[5] The pathogenesis of TA involves the secretion of proinflammatory cytokines (tumor necrosis factor, interleukin [IL] 6), and it has been demonstrated that serum IL-6 levels are markers of the its own activity.[4] For this reason, tocilizumab (a monoclonal antibody that blocks IL-6 receptor) is an effective option for the treatment of refractory TA.

One of the largest long-term studies, which deals with biological therapy in TA, indicates that, whether corticosteroid-resistant or dependent, the association with immunosuppressive agents can improve the control of the disease, and even, reduces the corticosteroid dose to the minimum necessary.[2] However, relapses and the progression of vascular involvement persist. The use of tocilizumab in refractory TA is safe and effective. The clinical response is good (improvement in 83%), and it even enables reduction of the corticosteroid dose (up to 50%).[2,4] Nevertheless, when the drug is discontinued, there is a reactivation of the disease, a fact that points to the need for a maintenance therapy.

Despite the good results observed with tocilizumab, studies performed to date reveal limitations. As they are retrospective, the sample size is small, and they are carried out without a control group.[3,5] However, we can consider it an alternative to be studied in patients with TA that is difficult to control. In conclusion, this is a good therapeutic option, even in patients who are easy to manage. Nonetheless, multicenter randomized studies must be performed to confirm these findings.

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☆ Please cite this article as: Martín Guillén S, Álvarez de Cienfuegos A, Hurtado García R. Nuevos fármacos en la arteritis de Takayasu, papel del tocilizumab. Reumatol Clin. 2016;12:358–359.