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BRIEF CLINICAL REPORT

Primary Sjögren syndrome in a 2-year-old patient: role of the dentist in diagnosis and dental management with a 6-year follow-up

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Background. Primary Sjögren syndrome is a rare autoimmune disease, especially in children, mainly affecting girls (77%), and usually diagnosed around 10 years of age. Diagnosis during childhood is difficult, especially because of the diversity of the clinical presentation and difficulty obtaining reliable history data, accounting for a higher frequency of underdiagnosed cases.

Differential conditions should be considered, especially the ones that promote xerostomia, such as diabetes, ectodermal dysplasia, rheumatoid arthritis, scleroderma, systemic lupus erythematosus, sarcoidosis, lymphoma, HIV and HTLV infection. Conditions associated with parotid enlargement should also be excluded, including juvenile recurrent parotitis (JRP), sialadenosis, sarcoidosis, lymphoma, infectious parotitis caused by streptococcal and staphylococcal infections, viral infections (paramyxovirus, Epstein–Barr virus, cytomegalovirus, and parvovirus), and diffuse infiltrative lymphocytosis syndrome (associated with HIV infection), and rare congenital conditions, such as polycystic parotid disease.

Case report. A paediatric female patient was referred to our clinic for dental treatment complaining about dry mouth, oral discomfort, and dysphagia.

The patient presented five of the required criteria to establish the diagnosis of pSS, including ocular symptoms, oral symptoms, evidence of keratoconjunctivitis sicca, focal sialadenitis confirmed by minor salivary gland biopsy, and evidence of major salivary gland involvement. Our patient did not have positive SS-A and SS-B autoantibodies. According to the literature, about 29% of individuals with pSS can present seronegativity for SS-A (anti-Ro) antibodies and about 33% can present seronegativity for SS-B (anti-La) antibodies.

Conclusion. To the best of our knowledge, this is the youngest patient reported in the scientific English literature with pSS. Primary Sjögren syndrome has a wide clinical and immunologic spectrum and may progress with increased morbidity. Clinicians must be aware of the development of pSS in such an early age and exclude all possible differential findings to provide early diagnosis and treatment.

Introduction

Sjögren syndrome (SS) is a autoimmune disease that can exist as a primary disorder, primary Sjögren syndrome (pSS), affecting the exocrine glands, or as a secondary disorder, associated with other autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus, and others[1]. Primary Sjögren syndrome is rare, especially in children, mainly affecting girls (77%), and usually diagnosed around 10 years of age. Primary SS is difficult to be diagnosed during childhood, especially because of the diversity of the clinical presentation and difficulty obtaining reliable history data, accounting for a higher frequency of underdiagnosed cases. Pathologic and laboratory findings are similar to those found in adults with pSS, including characteristic lymphocytic infiltration of exocrine glands, the presence of hypergammaglobulin-

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emia, elevated erythrocyte sedimentation rate (ESR), autoantibodies to 60-kDa Ro (SS-A) and La (SS-B), antinuclear antibody (ANA), and rheumatoid factor (RF) in the majority of the cases[1]. International diagnostic criteria for SS are based on clinical and laboratorial data and encompass six items: ocular symptoms, oral symptoms, evidence of keratoconjunctivitis sicca (KS), focal sialadenitis evidenced by biopsy of minor salivary glands, changes in major salivary glands, and presence of SS-A or SS-B autoantibodies. At least four of these characteristics must be present in pSS, and one must be histopathological evidence or autoantibodies positivity[1,2].

Primary Sjögren syndrome is unusual in children, and some differential conditions should be considered, especially the ones that promote xerostomia, such as diabetes, ectodermal dysplasia, rheumatoid arthritis, scleroderma, systemic lupus erythematosus, sarcoidosis, lymphoma, HIV and HTLV infection. Dry mouth is one of the most common SS symptoms promoting chewing, swallowing, and speaking impairment and alters the protein content of saliva decreasing IgA, amylase, and carbonic anhydrase levels and increasing lactoferrin, β_2-microglobulin, lysozyme C, and cystatin C levels, leading to a decrease in the saliva immune defence against caries and opportunistic infections. Its clinical manifestations include dry and cracked lips, mucosal sores, and tongue depapillation[3].

We report the case of a 2-year-and-7-month-old female patient who developed xerostomia with severe oral discomfort and dysphagia, dry and fissured lips, bilateral parotid swelling, xerophthalmia, photophobia, low weight, dry skin and scalp, and intense pain in upper and lower limbs and joints. Primary Sjögren syndrome has a wide clinical and immunologic spectrum and may progress with increased morbidity. Clinicians must be aware of the development of pSS in such an early age and exclude all possible differential findings to provide early diagnosis and treatment.

Case report

A 2-year-and-7-month-old female patient was referred for dental treatment complaining about dry mouth, oral discomfort, and dysphagia. Clinical examination revealed low weight, dry skin and scalp, xerophthalmia, photophobia, dry and fissured lips, and bilateral parotid glands' enlargement (Fig. 1). The patient reported intense pain in upper and lower limbs and joints (pain score of 7; Faces Pain Scale-Revised 0–10). The parents of the patient gave their signed informed consent for the publication of the pictures.

Serum tests were performed to detect the presence of anti-SS-A and anti-SS-B antibodies (enzyme-linked immunosorbent assay), antinuclear antibodies (indirect immunofluorescence using Hep-2 cell lines), and rheumatoid factor (nephelometric method). Serum tests revealed positive markings for ANA (titulation 1 : 1280) and RF (27.60 IU/mL) and negative markings for SS-A and SS-B. Antibodies against

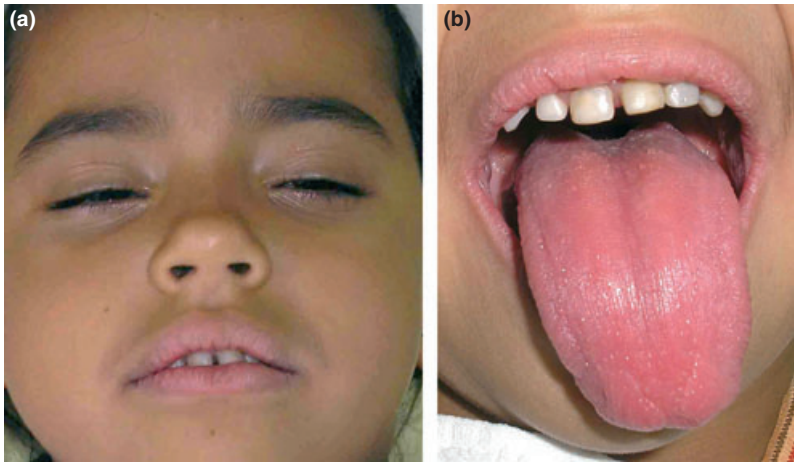

Fig. 1. Clinical features of the patient. (a) Dry and fissured lips with remarkable xerophthalmia and photophobia; (b) Depapilated tongue associated with dry lips and mucosa. Total stimulated saliva measurement revealed a 0 mL/min flow.

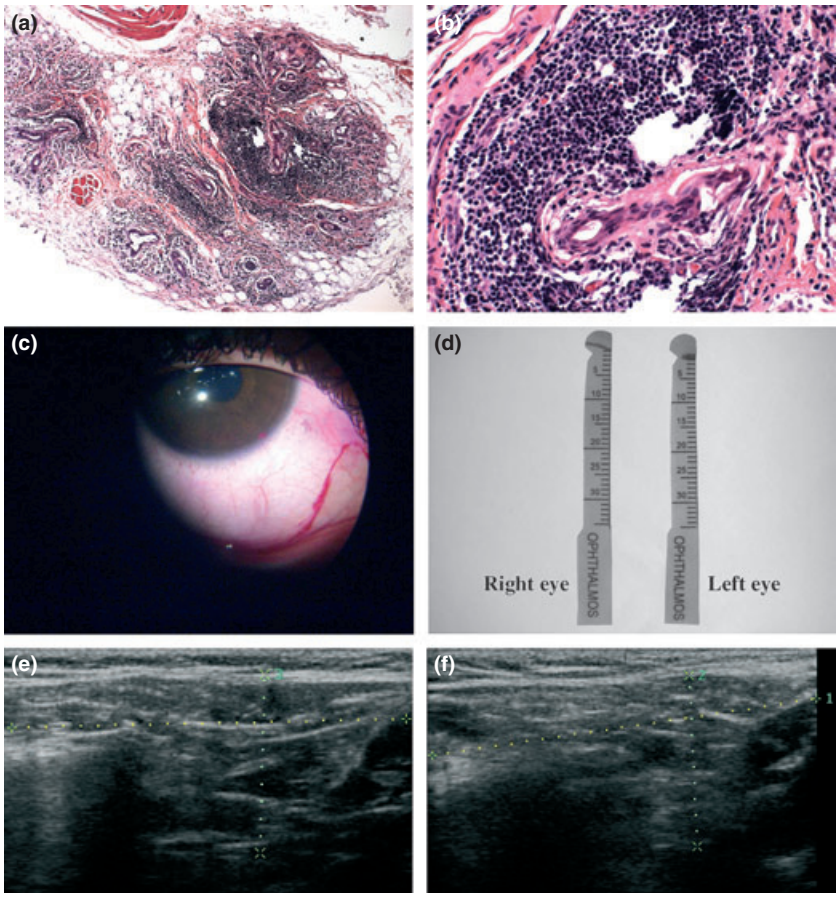

Fig. 2. Histopathological features, keratoconjunctivitis sicca confirmation, and ultrasound features. (a) Histopathologic appearance of minor salivary gland biopsy revealing focal chronic sialadenitis characterized by intense lymphocytic inflammatory infiltrate associated with acinar structures destruction (hematoxylin–eosin, original magnification 40×); (b) Higher magnification showing intense focal periductal lymphocytic infiltrates (hematoxylin–eosin, original magnification 400×); (c,d) Ophthalmological criteria were confirmed by positive Rose Bengal test (07+/09+ right eye and 06+/09+ left eye) and Schirmer's test revealing decreased tears' production (<01 mm right eye and <01 mm left eye); [e (left parotid gland) and f (right parotid gland)] Parotid ultrasound revealed an increase in the size of the parotid glands and parenchymal inhomogeneity with multiple hypo-echoic focal areas and bulging contours.

HIV, HTLV, cytomegalovirus, Epstein–Barr virus, and hepatitis B and C in the serum were not detected, and diabetes was excluded (blood glucose; 79 mg/dL). No other autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus, and systemic scleroderma, were recognized.

With a diagnostic hypothesis of SS, a minor salivary gland biopsy was performed. Histopathological analysis of the minor salivary gland biopsy revealed focal chronic sialadenitis characterized by intense lymphocytic inflammatory infiltrate (focus score > 1; >50 lymphocytes/4 mm^2 of glandular tissue; Fig. 1). Ophthalmological criteria were confirmed by Schirmer's test (<01 mm right eye and <01 mm left eye) and Rose Bengal test (07+/09+ right eye and 06+/09+ left eye; Fig. 2). Periodical ultrasound images of parotid glands revealed bilateral increase in size and parenchymal inhomogeneity with multiple hypo-echoic focal areas and bulging contours (Fig. 3).

Based on the American-European Consensus Group classification criteria for SS, a diagnosis of pSS was established. The patient was referred to the rheumatologist, who prescribed methylprednisolone 9 mg every 48 h and methotrexate 2.5 mg (once per week) owing to myalgia and arthralgia.

Intraoral examination revealed cavities and loss of pulp vitality on the upper right pri-

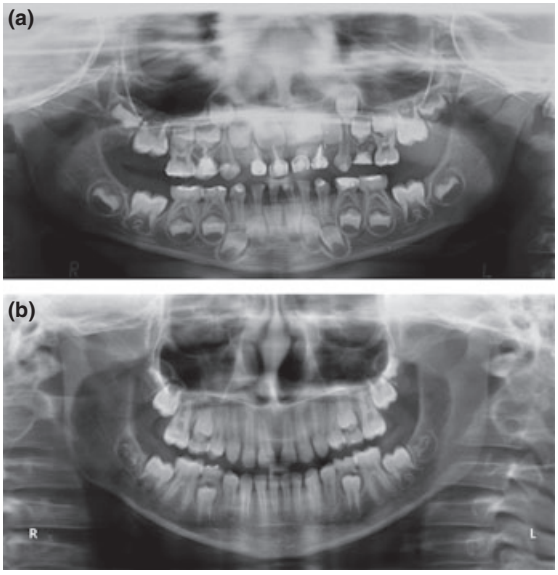

Fig. 3. (a) Panoramic radiography taken after complete oral rehabilitation when the patient completed 4 years; (b) Panoramic radiography showing early eruption of canines, permanent molars, and premolars. At the age of 8, she already presented upper and lower canines in position.

mary first molar and upper lateral and central incisors, which were endodontically treated. All cavities were subsequently restored with glass ionomer cement (Fuji IX GP®; GC Int. Corp., Tokyo, Japan). The mucosa and gingiva were red and dry as well as the tongue that was also depapilated (Fig. 1). Total whole stimulated salivary flow collected by spitting for 10 min while chewing on a block of paraffin wax revealed a flow of 0 mL/min. The patient's parents were instructed to apply an oral lubricant (Oral Balance Mouth Moisturizing Gel®; Laclede, Inc., CA, USA) five times a day to decrease mouth discomfort.

Parents were given proper guidance regarding the potential functional difficulties of the child in relation to the syndrome, including feeding and swallowing impairment, along with the increased risk of caries because of xerostomia. Topical application of 1% neutral sodium fluoride has been carried out every 3 months since the diagnosis. The patient exhibited early eruption of permanent teeth (Fig. 3). After 6-year follow-up, the patient has controlled oral health, without new cavities, periodontal disease, pain or discomfort in the mouth. Her food intake improved significantly after the dental rehabilitation and use of oral lubricants.

Discussion

As far as we know, this is the youngest patient with pSS in the English scientific literature. Early diagnosis is difficult, not only because it is a rare condition with several differential diagnoses, but also because of the difficulty of a child being able to express her complains. In this case, diagnosis was made by the dentist, which reinforces the important role that oral healthcare provider plays in the diagnosis of nonoral diseases by observing oral signs and physical symptoms and analysing specific laboratorial findings.

Primary SS is very rare in children. Our patient presented five of the required criteria to establish the diagnosis, including ocular symptoms, oral symptoms, evidence of keratoconjunctivitis sicca, focal sialadenitis confirmed by minor salivary gland biopsy, and evidence of major salivary gland involvement. Our patient did not have positive SS-A and SS-B autoantibodies. According to the literature, about 29% of individuals with pSS can present seronegativity for SS-A (anti-Ro) antibodies and about 33% can present seronegativity for SS-B (anti-La) antibodies[4].

Despite the patient has fulfilled the criteria for pSS diagnosis, it was important to exclude conditions with similar clinical manifestation. Bilateral parotid swelling is the most common clinical manifestation of pSS, besides other diseases in children, such as juvenile recurrent parotitis (JRP), sialadenosis, sarcoidosis, lymphoma, infectious parotitis caused by streptococcal and staphylococcal infections, viral infections (paramyxovirus, Epstein–Barr virus, cytomegalovirus, and parvovirus), diffuse infiltrative lymphocytosis syndrome (associated with HIV infection), and rare congenital conditions, such as polycystic parotid disease. Clinical features associated with periodic ultrasonography examinations and negative serology rejected those hypotheses. The ultrasound features of parotid lymphoma are variable, usually involving nodes presenting a 'pseudocystic' appearance, even though a micronodular pattern and large masses may also occur. In acute inflammation, the gland enlarges and appears hypoechoic and of

heterogeneous echotexture, with abscess formation in severe cases[5].

The treatment of pSS requires the use of anti-inflammatory and immunosuppressive drugs, especially when the patient has muscle and joint pain, besides dental and eye palliative topical care[1]. In this case, the patient has been using methotrexate for 6 years owing to the presence of important myalgia and arthralgia. Implementation of oral functions is an important component of health at this age. Salivary flow and salivary composition changes in SS predispose to dental caries, dysgeusia, and opportunistic infections. Dental treatment is usually symptomatic and supportive, including the use of moisturizing mouthwashes, salivary substitutes, good hydration, strict control of oral health through optimal hygiene, diet control, topical fluoride application, and oral cholinergic stimulators. Ultrasound of salivary glands provides a complimentary view of the status of the glandular parenchyma and must be used periodically to monitor patients with SS for lymphoma development to which they are prone.

What this case report adds

- To the best of our knowledge, this is the youngest patient reported in the scientific English literature with primary Sjögren syndrome.
- Rationale for diagnosis was presented.
- The importance of the dental team follow-up was to provide comfort, prevention of caries and periodontal disease and to monitor for possible lymphoma development.

Why this case report is important to paediatric dentists

- Paediatric dentists have to consider the occurrence of primary Sjögren syndrome in children because this professional can provide early diagnosis and consequently better prognosis to the patient.
- This manuscript provides guidance on the diagnosis and dental management of patients with primary Sjögren syndrome to dentists.
- The dentist must be aware of the diagnostic possibilities offered by complementary examinations described in this case report.

References

1 Civilibal M, Canpolat N, Yurt A *et al.* A child with primary Sjögren syndrome and a review of the literature. *Clin Pediatr (Phila)* 2007; **46**: 738–742.
2 Vitali C, Bombardieri S, Jonsson R *et al.* Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Ann Rheum Dis* 2002; **61**: 554–558.
3 Mathews S, Kurien B, Scofield R. Oral manifestations of Sjögren's syndrome. *J Dent Res* 2008; **87**: 308–318.
4 Hammi AR, Al-Hashimi IH, Nunn ME, Zipp M. Assessment of SS-A and SS-B in parotid saliva of patients with Sjögren's syndrome. *J Oral Pathol Med* 2005; **34**: 198–203.
5 Howlett DC. High resolution ultrasound assessment of the parotid gland. *Br J Radiol* 2003; **76**: 271–277.