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Review Article

Pediatric primary Sjögren syndrome presenting with bilateral ranulas: A case report and systematic review of the literature

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ABSTRACT

Context: Primary Sjögren syndrome is uncommon in children, and the standard clinical criteria used in diagnosis of adult Sjögren syndrome will miss many children with the disease. Floor of mouth ranulas have not been described in Sjögren syndrome.
Objective: This study aims to describe a novel presentation of juvenile primary Sjögren syndrome, and to present a comprehensive systematic review of the literature regarding the presentation and diagnosis of Sjögren syndrome in children.
Data sources: Ovid MEDLINE.
Study selection: A MEDLINE literature search was performed using the following search terms: primary, Sjögren, disease, and children. Results were limited to human subjects and articles written in English between 1981 and 2014. Applicable articles were reviewed and qualitatively summarized.
Data extraction: Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRIMA).
Results: Initial MEDLINE search yielded 146 articles, 80 of which were excluded as not clinically pertaining to Sjögren syndrome. An additional 25 were excluded due to lack of pediatric-specific data. Systematic review of the literature revealed no reports of ranula in association with Sjögren syndrome. 6 papers were manually included from review of reference lists of included articles. Our review indicated that recurrent parotitis is the most commonly reported presenting symptom in children, followed by ocular and oral symptoms, musculoskeletal, and renal symptoms. Compared to adults, children are less likely to present with dry eyes and mouth.
Limitations: All studies were retrospective chart reviews, case series or case reports.
Conclusion: This is the first report of a child presenting with floor of mouth ranulas in association with Sjögren syndrome. While recurrent parotitis is the most common presentation in children, other salivary gland and extra-salivary manifestations may be seen, and the clinician must maintain a high index of suspicion for underlying Sjögren syndrome.

Contents

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1. Introduction

Sjögren syndrome is a chronic lymphocytic inflammatory condition characterized by a spectrum of oral, ocular, and systemic symptoms, and remains a difficult entity to accurately diagnose. This diagnosis is particularly challenging in children, who may not be able to communicate their symptoms clearly. Despite the challenges of diagnosis, early identification is important in preventing complications and sequelae of the disease.

Common clinical manifestations are related to autoimmune exocrinopathy, with decreased salivation leading to xerostomia, dental caries, glossitis, candidiasis, angular cheilitis, dysgeusia, periodontitis, dysphagia, and failure to thrive, and decreased lacrimation leading to keratoconjunctivitis sicca. Salivary gland enlargement, particularly of the parotid glands, is frequently noted, particularly in children [1].

The disease is stratified into primary and secondary categories. Primary Sjögren syndrome describes patients with no associated connective tissue disease. Secondary Sjögren syndrome requires a connective tissue disorder to be present, including scleroderma, systemic lupus erythematosus, rheumatoid arthritis, mixed connective tissue disease, inflammatory muscle disease, and autoimmune liver or thyroid disease.

Many diagnostic criteria exist, and controversy remains as to which diagnostic criteria is most accurate, particularly in children. These criteria typically require a patient to display a combination of ocular and oral symptoms, objective measures for dry eyes and salivary dysfunction, histologic diagnosis with salivary gland biopsy, and positive autoantibody titers. The most widely accepted set of criteria for adults is the is the American-European Consensus Group (AECG) classification criteria (Table 1) [2].

Based on the AECG classification, a patient must demonstrate either a positive salivary gland biopsy or positive SS-A and/or SS-B antibodies, and satisfy 4 of the 6 items from the AECG classification scheme for the syndrome to be diagnosed.

Bartunkova, *et al* proposed a novel schema for the diagnosis of Sjögren syndrome in children, adapting the AECG classification to include additional qualifying oral and ocular symptoms, systemic symptoms, and other mucosal symptoms (Table 2) [3]. Further, additional laboratory abnormalities were added, in addition to renal tubular acidosis. Houghton, *et al* followed this study, analyzing 128 patients in an attempt to validate the sensitivity of these criteria. They found that the inclusion of recurrent parotitis increases the sensitivity of the pediatric criteria, identifying 76% of patients with primary Sjögren syndrome; in comparison, only 39% of children with primary Sjögren syndrome fulfilled the AECG primary Sjögren syndrome criteria [4]. The conclusion of Houghton, *et al*, however, was that neither the adult nor proposed pediatric diagnostic criteria were sensitive enough to be used as a diagnostic tool, and that clinical acumen should remain the gold standard in diagnosis [4].

Given the limitations of criterion-based diagnosis for this disease, we sought to systematically review the literature published on the presentation of Sjögren syndrome in children, in order to provide a comprehensive assessment of the range of clinical manifestations of this disease in children. We also present a case from the senior author's clinical practice of a child presenting with bilateral floor of mouth ranulas in association with Sjögren syndrome. This is the first report of ranulas associated with this disease.

2. Case report

A 10-year-old otherwise healthy male presented to our Pediatric Otolaryngology clinic with a history of bilateral recurrent parotitis of childhood, as well as bilateral floor-of-mouth ranulas.

Prior to presentation at our clinic, he had been treated elsewhere. He initially presented at age 6 with recurrent left floor of mouth swelling that had been present for one year. An MRI was obtained that showed a 2.5 cm × 1.2 cm x 2.2 cm T1 hypointense,

Table 1
American-European Consensus Group criteria for the classification of primary Sjögren syndrome (adults).

Ocular symptoms	A positive response to at least one of the following questions: 1. Have you had daily, persistent, troublesome dry eyes for more than 3 months? 2. Do you have recurrent sensation of sand or gravel in the eyes? 3. Do you use tear substitutes more than 3 times a day?
Oral symptoms	A positive response to at least one of the following questions: 1. Have you had a daily feeling of dry mouth for more than 3 months? 2. Have you had recurrent or persistently swollen salivary glands as an adult? 3. Do you frequently drink liquids to aid in swallowing dry foods?
Ocular signs	Objective evidence of ocular involvement defined as a positive result for at least one of the following two tests: 1. Schirmer test, without anesthesia (<5 mm in 5 min) 2. Rose-Bengal score or other ocular dye score (>4 according to the van Bijsterveld scoring system
Histopathological features	Focus score ≥1, defined as a number of lymphocytic foci (which are adjacent to normal-appearing mucous acini and contain more than 50 lymphocytes) per 4 square mm of glandular tissue
Salivary gland involvement	Objective evidence of salivary gland involvement defined by a positive result for at least one of the following diagnostic tests: 1. Unstimulated whole salivary flow (≤1.5 ml in 15 min) 2. Parotid sialography showing the presence of diffuse sialectasias (punctate, cavitary or destructive pattern), without evidence of obstruction in the major ducts 3. Salivary scintigraphy showing delayed uptake, reduced concentration and/or delayed excretion of tracer
Autoantibodies	Autoantibodies: presence in the serum of the following autoantibodies: 1. Antibodies to Ro(SSA) or La(SSB) antigens, or both
For primary SS	The presence of any 4 of the 6 items as long as either serology or histopatology is positive