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# Recurrent Parotitis as a Presentation of Primary Pediatric Sjögren Syndrome

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**KEY WORDS**

parotitis, Sjögren syndrome

**ABBREVIATIONS**

ANA—antinuclear antibody  
ESR—erythrocyte sedimentation rate  
RF—rheumatoid factor  
SLE—systemic lupus erythematosus  
SS—Sjögren syndrome

Drs Baszis, Toib, Cooper, French, and White made substantial contributions to this manuscript and were involved in conception and design, critical appraisal and revision, and final approval of the manuscript.

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## abstract

Parotitis is a common condition seen in the pediatric population, usually as an isolated occurrence associated with viral or bacterial infection. The differential diagnosis expands when recurrent parotitis is encountered. One etiology is primary pediatric Sjögren syndrome (SS), an autoimmune condition typically associated with dryness of the eyes and mouth in adults. Pediatric patients often present with isolated recurrent bilateral parotitis, however, and we describe 4 such cases in children aged 9 to 17 years at presentation. Despite lack of ocular complaints, 3 of these patients had ocular findings on ophthalmologic exam. Our patients also exhibited classic laboratory abnormalities, including positive antinuclear antibody, SS A, and SS B antibodies; presence of rheumatoid factor; and hypergammaglobulinemia. Consideration of SS in the child with recurrent parotitis is important for timely and appropriate referral and treatment. We review the differential diagnosis of parotitis in children as well as the salient features of pediatric SS. *Pediatrics* 2012;129:e179–e182

Parotitis is encountered relatively frequently in the pediatric population. It is typically acute and self-limiting and usually represents viral (mumps, Epstein-Barr virus, adenovirus, coxsackievirus, influenza, HIV, cytomegalovirus) or bacterial (*Staphylococcus aureus*) infection. Less common etiologies include juvenile recurrent parotitis or pneumoparotid or anatomic abnormalities, such as calculi or tumors. Even less frequent etiologies include autoimmune diseases such as Sjögren syndrome (SS) or sarcoidosis; however, a high level of suspicion for an autoimmune disorder should be maintained when a child presents with recurrent parotitis, particularly with bilateral involvement.

SS is an autoimmune disorder characterized by dryness of the eyes (keratoconjunctivitis sicca or xerophthalmia) and mouth (xerostomia) and associated with autoantibodies to the nuclear antigens SS-A/Ro and SS-B/La. It is defined as primary disease, which is rare in children, or secondary, when it is associated with another autoimmune disease, such as systemic lupus erythematosus (SLE). Classification criteria exist for adults,<sup>1,2</sup> but children rarely fulfill these diagnostic criteria because of differences in clinical presentation. Pediatric patients rarely have sicca symptoms at presentation but often present with parotitis.<sup>3</sup> Timely recognition of this disorder is important to facilitate treatment and screening for complications. We describe 4 pediatric patients who were diagnosed with primary Sjögren disease after presenting with recurrent parotitis and classic laboratory abnormalities.

## PATIENT PRESENTATION

Patient 1, a 9-year-old girl, presented with a history of 7 episodes of bilateral parotitis in the preceding 2 years, each lasting from several days up to 2 weeks. She denied xerophthalmia and xerostomia. Laboratory evaluation revealed a positive antinuclear antibody

(ANA) with a titer of 1:1280, positive SS-A and SS-B autoantibodies, positive rheumatoid factor (RF), and hypergammaglobulinemia (Table 1). She had evidence of tear film insufficiency and keratoconjunctivitis sicca on ophthalmologic examination, and she was treated with hydroxychloroquine and artificial tears. During the next 2 years, she had difficulties with dental caries and 4 episodes of parotitis, 2 of which occurred after she stopped taking hydroxychloroquine.

Patient 2, a 9-year-old boy, presented with a 4-year history of recurrent bilateral parotitis. He had laboratory evidence of a positive ANA (1:640), SS-A, SS-B, and RF, and hypergammaglobulinemia. Despite a lack of ocular symptoms, he had an epithelial erosion of his left eye and was started on nocturnal ocular lubrication, as well as hydroxychloroquine. In the subsequent year of follow-up, he experienced 2 episodes of unilateral parotitis (the first occurred 1 week after diagnosis), which were responsive to short courses of oral steroids. His hypergammaglobulinemia nearly resolved. Patient 3, a 13-year-old girl, presented with a 4-year history of recurrent painful bilateral facial/neck swelling, increasing in frequency to once or twice monthly over the preceding year. At the time of diagnosis, she acutely presented with fever and headache and was evaluated for meningitis. During her hospitalization, she developed bilateral painful parotitis and polyarthrititis. Testing revealed a positive ANA (>1:5120), SS-A, SS-B, and RF; hypergammaglobulinemia; elevated acute-phase reactants (erythrocyte sedimentation rate [ESR]) 124 (normal 0–20);

C-reactive protein 70.4 mg/L (normal 0–10); lymphopenia (absolute lymphocyte count 1200–1400); and Coombs'-positive anemia. Anti-double stranded DNA, anti-Smith, and antiphospholipid antibodies were negative. Urinalysis showed no signs of nephritis, and C3 and C4 were normal. She lacked other clinical features of SLE. Ocular exam showed punctate keratopathy, despite a lack of sicca symptoms. She rapidly improved after starting oral prednisone and hydroxychloroquine.

Patient 4, a 17-year-old girl, presented with a single episode of unilateral parotitis, associated with fever and an erythematous, tender papular rash. She had no ocular symptoms. Laboratory evaluation was significant for a positive ANA (>1:5120), SS-A, SS-B, and RF; hypergammaglobulinemia; ESR of 80; and lymphopenia. She was started on hydroxychloroquine. She developed a second episode of parotitis shortly after diagnosis. She had not yet seen an ophthalmologist at time of last follow-up.

Infectious workup was negative in all 4 patients, and all had complete immunization histories.

## DISCUSSION

We report on 4 pediatric patients, ages 9 to 17, who presented with recurrent parotitis as the initial manifestation of primary SS. Three of these 4 cases had bilateral parotid involvement. Although SS is rare in children, it should be considered in the child with recurrent parotitis after more common etiologies, such as infection, juvenile recurrent parotitis, and anatomic abnormalities, have been excluded.

**TABLE 1** Characteristics of Patients With Primary SS at Disease Presentation

| Patient | Age | Gender | ANA    | SS-A | SS-B | RF, IU/mL | IgG, mg/dL | ESR | Duration follow-up, mo |
|---------|-----|--------|--------|------|------|-----------|------------|-----|------------------------|
| 1       | 9   | F      | 1:1280 | +    | +    | 148       | 1758       | 28  | 25                     |
| 2       | 9   | M      | 1:640  | +    | +    | 75        | 2430       | 19  | 26                     |
| 3       | 13  | F      | 1:5120 | +    | +    | 99        | 2517       | 124 | 10                     |
| 4       | 17  | F      | 1:5120 | +    | +    | 34        | 2005       | 21  | 10                     |

Age indicates age at diagnosis. Normal ESR is 0–20. F, female; IgG, immunoglobulin G (normal 750–1600); M, male.

Infection remains the most common etiology of parotitis. Besides rare outbreaks of mumps, viral pathogens include Epstein-Barr virus, coxsackievirus, influenza, parainfluenza, adenovirus, HIV, and human herpesvirus 6. In one study, 601 Finnish children with acute mumps-like illness who had negative mumps serology underwent screening for alternate viruses. Eighty-four (14%) of these children had antibodies to Epstein-Barr virus, parainfluenza viruses 1 to 3, and adenovirus. Of the 114 tested for human herpesvirus 6, 5 (4%) had evidence of antibodies.<sup>4</sup> Bacterial pathogens include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus viridans*, *Haemophilus influenzae*, and *Bacteroides* species. Fungal and mycobacterial infections are rare and typically associated with an immunocompromised state.

Juvenile recurrent parotitis is an entity characterized by nonobstructive inflammation of the parotid gland. The cause is unknown. Affected children are typically febrile and develop painful swelling of 1 (more common) or both parotids every 3 to 4 months.<sup>5</sup> It most often manifests between 3 and 6 years of age and is more common in boys. Symptoms may completely resolve following puberty. Treatment regimens vary from conservative observation and supportive therapy to administration of antibiotics; prophylactic regimens are largely unsuccessful.<sup>4</sup> One group had therapeutic success with sialography and sialoendoscopy with lavage, dilation, and hydrocortisone injection. Only 2 of 26 children had recurrent symptoms, both affecting the contralateral parotid gland.<sup>6</sup>

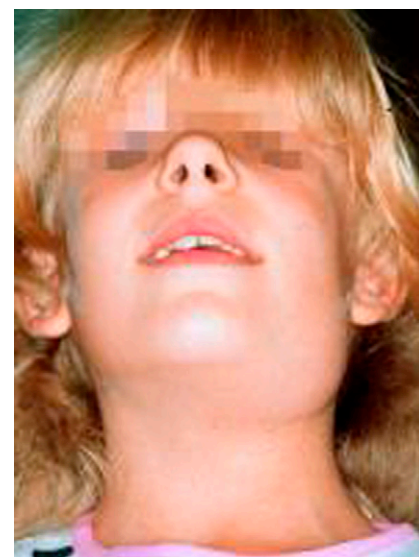
Pneumoparotid, or air insufflation of the parotid gland, has only rarely been reported in pediatric patients.<sup>7,8</sup> It has been associated with wind-instrument players, rapid decompression during diving, anesthesia, dental instrumentation, during pulmonary function testing,

the Valsalva maneuver in chronic lung disease (cystic fibrosis), and voluntary or involuntary blowing out of the cheeks. Malnutrition can be associated with noninflammatory enlargement of the parotid glands and can be accompanied by bulimia, anorexia nervosa, diabetes, beriberi, or pellagra. Sialolithiasis and parotid tumors, including lymphoma, are rare in pediatrics but should be considered in the differential diagnosis. SS in childhood is classified as primary if it occurs in isolation, or secondary if it coexists with another connective tissue disease, such as SLE, juvenile idiopathic arthritis, systemic sclerosis, or mixed connective tissue disease. Prevalence of primary SS in adults is estimated at 0.5%<sup>9</sup>; pediatric data are limited owing to rarity.<sup>10</sup> A multicenter report of 40 pediatric patients noted a 7:1 female predominance and a mean age of presentation of 10.7 years.<sup>3</sup> Classically, adults present with xerophthalmia and xerostomia, and adult diagnostic criteria for SS reflect this.<sup>12</sup> Criteria for adults include the presence of 4 of 6 of the following: ocular symptoms, oral symptoms, objective evidence of dry eyes and salivary gland involvement, laboratory abnormalities (presence of positive ANA, SS-A, SS-B, or RF), and minor salivary gland biopsy demonstrating sialoadenitis and lymphocytic infiltration. Pediatric criteria are not standardized, and many pediatric patients would not fulfill adult criteria<sup>11</sup> because of the relatively infrequent presence of sicca symptoms at presentation and tendency to avoid salivary gland biopsy in cases where the diagnosis is clear. Sicca symptoms and objective findings of lacrimal/salivary gland involvement develop over time, because of chronic inflammation and damage to glands. Preliminary pediatric criteria were proposed in 1999, but these have not been validated or adopted in subsequent studies.<sup>10</sup> These proposed criteria took

into account the frequent absence of oral and ocular signs in children owing to short duration of disease. Modifications included presence of recurrent parotitis (Fig 1) or conjunctivitis, the addition of recurrent vaginitis and systemic symptoms (fever, arthralgias, hypokalemic paralysis, abdominal pain), and the addition of other laboratory values (elevated serum amylases, leukopenia, elevated ESR, polyclonal hypergammaglobulinemia, and renal tubular acidosis).<sup>10</sup> It has been noted that the inclusion of recurrent parotitis increases the sensitivity of the pediatric over the adult criteria.<sup>11</sup>

All of our patients exhibited classic laboratory and autoantibody profiles typical of adult SS, with positive ANA, RF, SS-A, and SS-B, and hypergammaglobulinemia (Table 1). In previous cohorts of pediatric patients with SS, these laboratory findings were not universal but were found in most patients and were included in the proposed pediatric criteria.<sup>3,10,12</sup>

Extraglandular involvement is also unusual in children, but can include fever, renal tubular acidosis, arthritis, pancreatitis, interstitial lung disease,



**FIGURE 1** Left parotid swelling in a child (Image reprinted with permission from Medscape.com, 2011. Available at: <http://emedicine.medscape.com/article/882461-overview>.)

pericarditis, neuropathy or central nervous system involvement, autoimmune hepatitis, cytopenias, and cryoglobulinemia with or without vasculitis and rash. The increased risk of lymphoma is well documented in adults<sup>9</sup> but is exceedingly rare in children. One of our patients had evidence of arthritis and 2 had cytopenias at presentation, but the remainder had no signs of extraglandular involvement.

In the child with recurrent parotitis, laboratory evaluation may be very helpful. A combination of positive ANA, RF, SS-A, and SS-B; hypergammaglobulinemia; elevated amylase (parotid or pancreatic); and elevated ESR is suspicious for SS; however, the presence of anti-double-stranded DNA antibodies or hypocomplementemia raises the concern for other systemic autoimmune disorders, such as SLE or another connective tissue disease.

When there is clinical or laboratory evidence concerning for SS, prompt referral to a rheumatologist, ophthalmologist, and dentist is recommended, in addition to otolaryngology

as indicated. Even in the absence of xerophthalmia, objective testing may be able to document evidence of subclinical disease. These include the Schirmer test (wetting of filter paper strip to quantify tear production, abnormal being less than 5 mm in 5 minutes) and rose bengal or fluorescein staining to identify corneal erosions. In unclear cases, parotid ultrasound, sialography, or biopsy of a minor salivary gland (sublingual) may be useful.

Therapy for symptomatic relief can be very helpful, including artificial tears, nasal saline douches, sialogogues (lemon drops), and parasympathomimetics such as pilocarpine. Treatment under the care of a rheumatologist may include nonsteroidal anti-inflammatory drugs for symptomatic relief of parotitis or corticosteroids for systemic inflammation or extraglandular involvement.<sup>9</sup> Long-term therapy with immunomodulating agents, such as hydroxychloroquine, methotrexate, mycophenolate mofetil, or cyclophosphamide, is often helpful and may be necessary, depending on the extent

and severity of organ involvement.<sup>9</sup> The available adult studies on the use of hydroxychloroquine in SS have demonstrated more improvement in laboratory parameters (ESR, C-reactive protein, hypergammaglobulinemia) than in clinical symptoms,<sup>13–15</sup> although a small retrospective study showed significant increases in saliva and tear production.<sup>16</sup> Of note, all 4 of our patients were treated with hydroxychloroquine, and through the available period of follow-up (although brief), none have developed features of another autoimmune disease, such as SLE. In summary, parotitis is a frequently encountered pediatric problem. Although infection, recurrent juvenile parotitis, and anatomic abnormalities are more common etiologies, primary pediatric SS should be considered when encountering a patient with recurrent parotitis. These patients typically exhibit a distinctive laboratory and autoantibody profile and will benefit from early referral to a pediatric rheumatologist for treatment and monitoring for disease complications.

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