The Role of Parotid Biopsy in the Diagnosis of Pediatric Sjögren Syndrome

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Objectives: To describe our experience with primary and secondary Sjögren syndrome (SS) in the pediatric population and to evaluate the effectiveness of parotid gland biopsy in the diagnosis of pediatric SS.

Design: Case series review of 6 pediatric patients evaluated during a 4-year period with varied head and neck manifestations of SS.

Setting: Tertiary care children’s hospital.

Patients: Six children (4 boys and 2 girls) ranging in age from 6 to 12 years, who were diagnosed as having primary or secondary SS.

Intervention: Six minor salivary gland and 4 parotid gland biopsies for pathologic examination.

Main Outcome Measures: Pathologic examination of salivary tissue consistent with SS.

Results: All 6 patients underwent minor salivary gland biopsy, 2 (33%) were consistent with SS, while the remaining 4 (67%) were nondiagnostic. The 4 patients with nondiagnostic minor salivary gland biopsy results went on to have parotid biopsies, of which all 4 had histologic findings consistent with SS. No complications were encountered.

Conclusion: Parotid gland biopsy is an effective and safe means of obtaining salivary gland tissue for histologic evaluation of SS in the pediatric population.


Sjögren syndrome (SS) is an autoimmune disorder characterized by chronic lymphocytic infiltration of the lacrimal and salivary glands that is relatively rare in the pediatric population. Only about 200 pediatric cases of primary SS (SS without an associated connective tissue disorder) and secondary SS (SS in association with a connective tissue disorder) have been reported in the literature.1-3 The chronic lymphocytic infiltration eventually leads to the clinical findings of keratoconjunctivitis sicca and xerostomia. Early diagnosis is important to prevent both the immediate complications (ie, corneal desiccation and dental caries) and the late sequelae associated with SS. While adult-onset SS has a definite set of diagnostic criteria, no specific diagnostic criteria have been established for SS in childhood because of the relatively rare incidence.3 Currently, pediatric SS is a clinical diagnosis based on findings from physical examination, clinical history, and laboratory data, with histologic findings of lymphocytic or plasmacytic infiltration of involved salivary glands helping to confirm a suspected diagnosis of SS. In adults, Biasi et al4 have shown that parotid gland biopsy is an effective means of obtaining histologic evidence of SS. However, to our knowledge, no study has shown the effectiveness of parotid biopsy in obtaining histologic evidence of SS in the pediatric population. Therefore, we reviewed our experience with pediatric SS and the role of parotid gland biopsy.

METHODS

Between 1993 and 2000, 6 pediatric patients with the diagnosis of primary or secondary SS were identified, who had been seen at the Wake Forest University Baptist Medical Center, Winston-Salem, NC. A retrospective medical record review was then performed to determine the clinical presentation, diagnostic tests, radiographic imaging, and pathologic condition in each patient.

Presenting symptoms and history included parotid swelling, xerostomia, xerophthalmia, oral and/or lip ulcers, or family history of connective tissue disorders. Laboratory evaluation included erythrocyte sedimentation rate,
antinuclear antibody, rheumatoid factor, a complete blood cell count, lupus inhibitor, anti–SS-A/anti–SS-B antibodies, Epstein-Barr virus, and quantitative immunoglobulin studies. All patients underwent either minor salivary gland biopsy (lip) or parotid biopsy for pathologic confirmation of SS.

All surgical procedures and biopsies were performed by the senior author (W.M.). Minor salivary gland biopsies were performed through a lower lip incision with removal of salivary gland tissue. Parotid biopsies were performed as initially described by Kraaijenhagen5 in 1975 and more recently by Marx et al6 in 1988 through a small 1- to 2-cm incision just below the earlobe near the posterior angle of the mandible. A No. 15 blade is used to sharply incise the skin, and the parotid capsule is exposed by blunt dissection. The capsule is then incised using scissors, and a small amount of superficial parotid tissue is removed for pathologic examination. Skin closure is obtained using subcutaneous absorbable sutures. Care is taken to remain superficial with the initial skin incision as well as with removal of parotid tissue once the capsule is incised because the facial nerve has a more superficial location in children. Specimens were collected and sent to the pathology department for examination. Follow-up was maintained for a mean of 3 years.

**RESULTS**

Six patients (4 boys and 2 girls) with a mean age of 7 years (range, 6-12 years) were identified as having a diagnosis of primary or secondary SS. Patient examination, laboratory, and pathologic results are presented in the **Table**.

Parotid swelling was present in all 6 patients; however, xerostomia and xerophthalmia was present in only 3 (50%) of 6 patients. Oral and lip ulcers were present in 3 of (50%) 6 patients. All 6 patients had elevated antinuclear antibody and immunoglobulin levels. Only 2 of 6 minor salivary gland biopsy results were consistent with SS on pathologic examination. The remaining 4 patients with negative minor salivary gland biopsy results underwent a parotid biopsy for pathologic confirmation. All 4 patients who underwent a parotid biopsy had pathologic examination findings consistent with SS. No complications were encountered (ie, facial nerve injury, wound infection, hematoma, or fistula) in all 6 patients.

Sjögren syndrome is a relatively rare pediatric autoimmune disease characterized by chronic lymphocytic infiltration of exocrine glands leading to xerostomia and xerophthalmia. Systemic manifestations of SS include vasculitis, cryoglobulinemia, autoimmune hepatitis, alveolitis, neuropathy, central nervous system involvement, renal tubular acidosis, and, rarely, malignant B-cell lymphoma.1,2,7 While adult SS has a well-defined set of diagnostic criteria, pediatric SS has no specific diagnostic criteria.2 Diagnosis is based on clinical findings (ie, history, physical examination, and laboratory abnormalities), with lymphocytic infiltration of involved salivary gland tissue providing histologic evidence of SS. Our clinical experience with pediatric SS is consistent with the reported literature in that parotid swelling was the most common symptom noted (6 of 6 patients).1,8 Only 3 (50%) of our patients had xerostomia and 2 (33%) had xerophthalmia, clinically. Two patients developed oral ulcerations (lip and buccal), both of which underwent biopsy and found to be consistent with SS. A 2-to-1 male-female predominance and a white-black ratio of 2 to 1 were noted. These findings differ from the literature, which reports a significant female-male ratio, but this may be

**COMMENT**

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related to our small sample size. Two children were thought to have primary SS, while the remaining 4 children had secondary SS in association with juvenile rheumatoid arthritis. Laboratory data revealed that all 6 patients had an elevated erythrocyte sedimentation rate, polyclonal hypergammaglobulinemia, and were positive for antinuclear antibodies; however, only 4 of 6 patients were positive for anti-SS-A and anti-SS-B antibodies.

Minor salivary gland biopsy has become a widely used diagnostic tool in the evaluation of patients with suspected SS. The most typical change is represented by periductal lymphocytic infiltration (Figure). However, minor salivary gland biopsy has been shown to be poorly sensitive and frequently provides inadequate salivary tissue for histopathologic confirmation of SS. Marx et al confirmed the diagnosis of SS in 58% of their adult patients with minor salivary gland biopsy, while Biaisi et al have shown parotid biopsy to be accurate and safe in the diagnosis of adult SS, with all 32 of their study patients having histologic findings consistent with SS. In our pediatric population, minor salivary gland biopsy results were consistent with SS in only 2 (33%) of 6 patients; the remaining 4 patients with nondiagnostic minor salivary gland biopsy results went on to have parotid biopsies, the results of which were all consistent with SS. No complications were encountered with parotid biopsy—specifically, wound infection, facial nerve injury, fistula, or hematoma. To our knowledge, no other study of parotid biopsy for the diagnosis of pediatric SS has been described.

Once the diagnosis of SS has been established, treatment should be directed at preventing the sequelae of keratoconjunctivitis sicca (ie, corneal desiccation, ulceration, and dental caries) as well as long-term follow-up for systemic involvement. Four of our 6 patients required systemic corticosteroids and antibiotics for their symptomatic parotid swelling. None of our patients have developed non-Hodgkin lymphoma despite the reported increase in risk; however, further long-term follow-up is needed.

CONCLUSIONS

Although SS is a rare entity in the pediatric population, it is an important diagnosis to consider in the presence of salivary gland enlargement, even in the absence of xerophthalmia and xerostomia. While pediatric SS is currently a clinical diagnosis, pathologic involvement of salivary tissue provides histologic data to support suspected cases. In patients with clinical suspicion of SS and a negative minor salivary gland biopsy result, our experience has been that parotid gland biopsy is a safe and effective means of establishing histopathologic evidence for the diagnosis of SS.

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REFERENCES