

## Chapter 58 – Biopsy of Minor Salivary Glands of the Lip

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Sjögren's syndrome is a chronic autoimmune disorder characterized by the immune-mediated destruction of exocrine glands. Biopsy of the minor salivary glands of the lip has been considered the gold standard for the diagnosis of Sjögren's syndrome. Symptoms of Sjögren's syndrome are primarily related to the loss of glandular function: dry eyes due to destruction of the lacrimal glands, dry mouth due to destruction of the major and minor salivary glands, dry nose, throat, and trachea due to the destruction of the minor salivary glands, and chronic parotid swelling due to the destruction of the parotid gland.<sup>[1,2]</sup>

### PATIENT SELECTION

Biopsy of a minor salivary gland of the lip is positive for Sjögren's syndrome when one or more lymphocytic foci containing more than 50 lymphocytes adjacent to normal-appearing acini is identified per 4 mm<sup>2</sup> of glandular tissue. However, lip biopsy alone is not diagnostic; symptoms of dry eyes or dry mouth must also be present to make the diagnosis.<sup>[3]</sup> In addition to lip biopsy, the other main objective diagnostic criteria used are serum measurements of the autoantibodies SS-A (Ro) and SS-B (La). In 2002, an American-European consensus group attempted to standardize the diagnosis of Sjögren's syndrome. This group put forth a set of criteria by which Sjögren's syndrome may be diagnosed, and the criteria were shown to be approximately 95% sensitive and specific (Table 58-1).<sup>[3]</sup> The criteria do not specifically require salivary gland biopsy for the diagnosis of Sjögren's syndrome; however, either positive salivary gland biopsy or positive serum tests for SS-A or SS-B are required.

**Table 58-1 -- CLASSIFICATION CRITERIA FOR SJÖGREN'S SYNDROME**

These six criteria may be used in either of two ways to make the diagnosis. First, a diagnosis may be made if any four of the following six items is positive, provided that either the histopathology or the serum autoantibodies are positive. Alternatively, the diagnosis may be made if three of the four objective criteria are positive.

#### Subjective Criteria

1. Ocular symptoms (dry eyes)
2. Oral symptoms (dry mouth)

#### Objective Criteria

1. Ocular signs. Requires a positive result for at least one of the following objective tests:
  - a. Schirmer's test
  - b. Rose Bengal or other ocular dye score  $\geq 4$  (van Bijsterveld's scoring system)
2. Histopathology
  - a. Minor salivary gland biopsy is positive if focus score  $\geq 1$
  - b. Focus score = number of lymphocytic foci per 4 mm<sup>2</sup> of glandular tissue
  - c. Lymphocytic focus must be adjacent to normal mucous-acini and contain  $>50$  lymphocytes
3. Salivary gland involvement, considered positive if at least one of the following criteria is positive:
  - a. Unstimulated salivary flow  $\leq 1.5$  mL in 15 minutes
  - b. Parotid sialography demonstrating diffuse sialectasia but no obstruction in the large ducts
  - c. Salivary scintigraphy demonstrating delayed uptake or excretion or reduced concentration of the radioactive tracer
4. Autoantibodies. Presence in the serum of antibodies to one or both of the following antigens:
  - a. Ro (SS-A)
  - b. La (SS-B)

It has been suggested that measurement of SS-A or SS-B antibodies may be a preferable method of establishing

the diagnosis of Sjögren's syndrome.<sup>[4]</sup> However, both false-positives and false-negatives may occur with this method. SS-A is not specific for Sjögren's syndrome, but is also positive in a number of other autoimmune diseases.<sup>[2]</sup> Both SS-A and SS-B antibodies may be absent in a patient with Sjögren's syndrome diagnosed on minor salivary gland biopsy.<sup>[4]</sup> Therefore, although SS-A and SS-B testing is a reasonable option and may make the diagnosis of Sjögren's syndrome when found in association with symptoms of the disease, a negative result does not rule out Sjögren's syndrome, and in these patients, a lip biopsy is indicated. Some authors advocate routine lip biopsy in the diagnosis of Sjögren's syndrome. Four percent of patients with Sjögren's syndrome will eventually be diagnosed with lymphoma, mainly of the B-cell mucosa-associated lymphoid tissue (MALT) type. Case reports have described lymphoma being diagnosed in an otherwise asymptomatic patient on routine lip biopsy.<sup>[5]</sup>

Recently, biopsy of a minor salivary gland of the lip has also proven useful in the diagnosis of amyloid polyneuropathy<sup>[6]</sup> and neonatal hemochromatosis.<sup>[7]</sup> In each of these cases, biopsy of the minor salivary glands of the lip represents a less invasive option for diagnosis than the gold standard of nerve biopsy or liver biopsy, respectively. In amyloid polyneuropathy, minor salivary gland biopsy also has the advantage of identifying Sjögren's syndrome, which may have an associated sensory neuropathy similar to that seen in amyloid polyneuropathy. Neonatal hemochromatosis is a rare disorder consisting of liver failure in newborns with associated extrahepatic iron deposition. The disorder is rapidly fatal if untreated, but early diagnosis and subsequent treatment with medical treatment or liver transplantation can lead to long-term survival.<sup>[7]</sup> Liver biopsy is especially dangerous in these patients, in that most have coagulopathy as a result of their liver failure. Minor salivary gland biopsy, as opposed to liver biopsy, can be performed at the bedside with very little risk even in the face of coagulopathy.<sup>[7]</sup>

It has been suggested that patients diagnosed with primary biliary cirrhosis should also be evaluated for Sjögren's syndrome. Primary biliary cirrhosis is highly correlated with Sjögren's syndrome.

## **PREOPERATIVE EVALUATION**

Other than the laboratory studies discussed above, very little preoperative evaluation is necessary. Biopsy can be performed under local anesthesia and with little risk of bleeding, even in the face of documented coagulopathy.<sup>[7]</sup>

## **SURGICAL APPROACHES**

Biopsy of a minor salivary gland is performed through an incision in the mucosal surface of the lower lip (Fig. 58-1). The procedure is performed under local anesthesia. The lower lip is everted, and 1% or 2% lidocaine with epinephrine 1:100,000 is injected (Fig. 58-2). The optimal site for biopsy is approximately 2 cm lateral to the midline, because the density of minor salivary glands is higher there than in the midline.<sup>[8]</sup> The optimal incision for glandular biopsy is debated; however, a linear or elliptical incision is standard. These minor salivary glands are superficial (Fig. 58-3) and should be easily identified with minimal dissection using scissors and forceps (Fig. 58-4). Care must be taken to avoid the neighboring branches of the mental nerve. Two to three minor salivary glands should be taken for microscopic analysis (Fig. 58-5). Alternatively, the gland may be divided and one half sent for frozen section to ensure the presence of salivary gland tissue in the biopsy specimen. Following removal of these glands, hemostasis may be achieved with electrocautery or direct pressure. The incision is then closed using silk sutures in an interrupted fashion (Fig. 58-6).

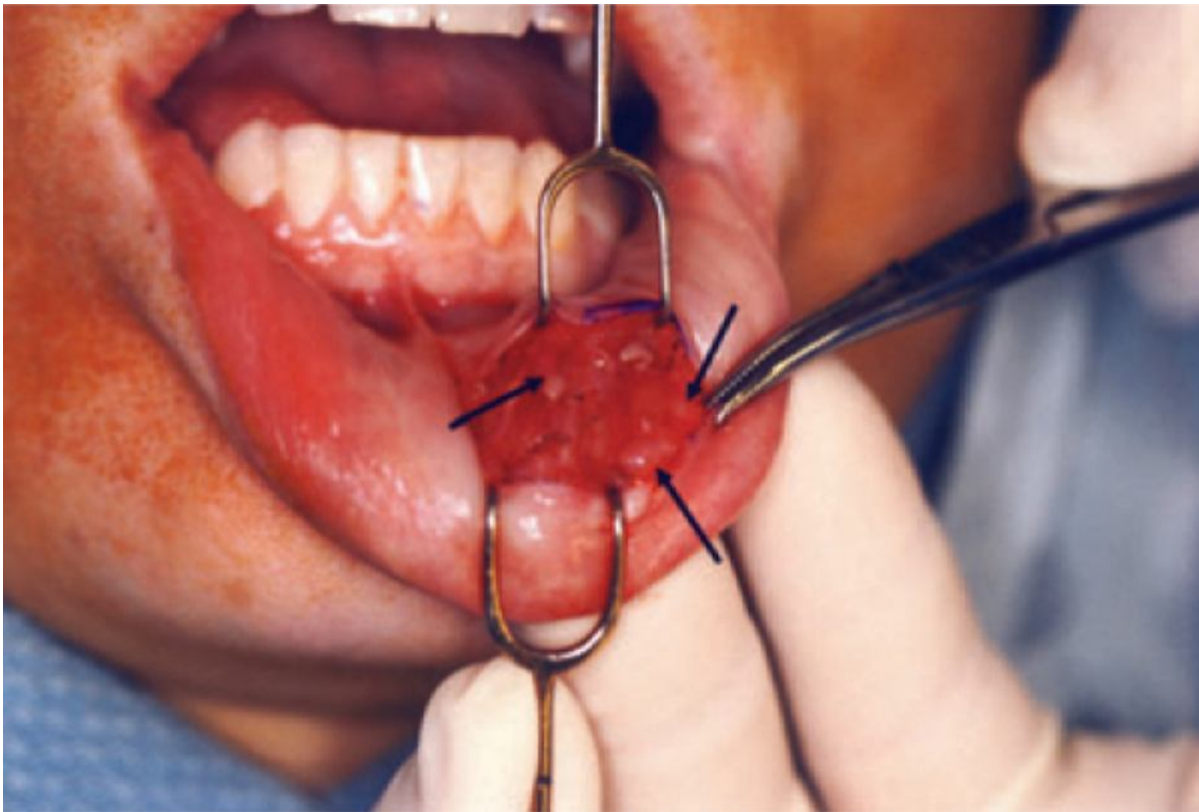


**Figure 58-1** Line of incision drawn on mucosal surface of the lip.



**Figure 58-2** Local anesthesia is infiltrated into the lip along the line of the proposed incision.





**Figure 58-3** Once the incision is made through the mucosa, the minor salivary glands immediately become apparent (*arrows*).



**Figure 58-4** The minor salivary gland is gently grasped and bluntly dissected out and removed.



**Figure 58-5** Multiple minor salivary glands are removed for pathologic analysis.



**Figure 58-6** The incision is closed with 4-0 silk suture.

Variations on the above method have been suggested. One group reports that the use of a chalazion forceps allows good retraction of the lower lip and also helps evert the minor salivary glands and helps eliminate bleeding.<sup>[9]</sup> A second group suggests that minor salivary glands be labeled individually with a marking pen as they are seen through the buccal mucosa before the incision. Glands are then removed individually through stab

incisions made in the form of an X directly overlying the gland. In this method, sutures are not necessary due to the small size of each individual incision.[10]

## **POSTOPERATIVE MANAGEMENT**

Postoperative management is minimal. The patient will likely not notice more than temporary pain at the incision site, which should be controlled with acetaminophen. Healing is rapid, and the patient can return to a normal diet and normal activity level the same day as the procedure. Antibiotics (perioperative or postoperative) are not required for biopsy of the minor salivary glands.

Branches of the mental nerve exist in close proximity to the labial salivary glands. Even with careful dissection, small branches may be transected. An oblique incision made in an inferior-lateral direction approximately 1.5 cm lateral to the midline may minimize this risk; however, patients should be cautioned preoperatively about the risk of postoperative numbness of the lip.[8]

### **PEARLS**

- Biopsy should be performed through a transoral incision to ensure good healing.
- Two or three glands should be removed for analysis.
- A chalazion forceps may assist in lip eversion and hemostasis.

### **PITFALLS**

- Inadvertent injury to the mental nerve can be avoided by an oblique incision parallel to the nerve.
- Hemostasis can be a problem in patients who are anticoagulated despite the small size of the incision.

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