

Histopathological Sample Preparation with Unique Biopsy Forceps in The Diagnosis of Sjögren's Syndrome

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Abstract

Histopathological sample preparation for light microscopic examinations from the lower lip is the easiest way to obtain exocrine glandular tissue for the diagnosis of Sjögren's syndrome (SS), since labial glands show typical autoimmune inflammation markers after simple haematoxylin-eosin staining. It is however, an invasive intervention with possible minor mucosal complications.

Authors' aim with this report was to show a recently introduced and successfully used forceps in the lower lip biopsy of SS patients. The instrument is a specially modified Desmarres-Chalazion forceps used in ophthalmology, which was adapted by changing its handle's angulation in a slight curve for being able to conform the lower lip surface. The modified angle is 40° to the horizontal plane which can highly aid the biopsy procedure. This method might be successful in increasing the speed of the procedure by providing better access to the operative field and, reduce the risk for further mucosal tissue complications.

Keywords: Sjögren's-syndrome; Diagnosis; Autoimmune; Biopsy; Lower lip biopsy; Histology; Biopsy forceps

Introduction

Sjögren's syndrome (SS) is a slowly developing disease of unknown origin. Its main symptom is autoimmune epithelitis: mainly T-cell infiltration of the exocrine glands and epithelial histologic structure [1]. As a consequence exocrinopathy develops, resulting in xerostomia and keratoconjunctivitis sicca (15). In its primary form, the disease manifests independently, while in case of its presence together with another autoimmune systemic disease the diagnosis is secondary SS. Fifteen to thirty-six percent of the cases are accompanied with systemic lupus erythematosus (SLE), 20-32% with rheumatoid arthritis (RA) and 11-24% with progressive systemic sclerosis (PSS); in smaller percentages it is associated with autoimmune hepatitis and thyroiditis [2]. In the progress of autoimmune epithelitis the main role is played by the glandular epithelial cells as well as the existence of circulating anti-Ro/SSA and anti-La/SSB autoantibodies. The incidence and the severity of the symptoms vary by individual [1].

Main symptoms of the disease are dry mouth and dry eyes with decreased saliva production, causing irritating sensation during speaking and chewing. Patients report a burning, stinging feeling and foreign body sensation in the eye. Diagnosis of SS is difficult as there are no available and well circumscribed diagnostic factors. Patients try to treat their different symptoms with the general practitioner, dentist, ophthalmologist and several years pass until the accurate clinical diagnosis and the appropriate treatment begins [2].

From 2016, the diagnosis of SS is based on the classification criteria of the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) Executive Committee [3]. Five differently weighed objective signs are considered: 1.) anti SSA/Ro positivity; 2.) focal lymphocytic sialadenitis (FS); each counts as 3; 3.) abnormal ocular staining score (OSS); 4.) positive Schirmer's test and 5.) hyposalivation: unstimulated whole saliva flow rate (UWS) ≤ 0.1 ml/min count as 1. If the sum of the scores, nearby the "suggestive" SS-symptoms, is equal to-, or higher than 4, Sjögren's syndrome is diagnosed.

Minor salivary gland biopsy and focus score

As focal lymphocytic sialadenitis is a chief diagnostic sign, its diagnostic method has principal importance and can be evidenced by Minor Salivary Gland Biopsy (MSGB) (6) followed by a hematoxylin eosin staining and a light microscopic histopathological evaluation. The method was suggested by Daniels in 1984. Positive focus score is considered if the glandular tissue shows cell groups at least one "focus" of more than 50 lymphocytes /4 mm² of tissue on the light microscopic field [4].

Sample preparation

Histopathological section preparation for light microscopic examinations from the lower lip is easy [5]. Minor salivary glands are distributed in the submucosa of the oral cavity, e.g. palatal and buccal mucosa and in the lips, and they are named after their localization [5]. Histological alterations of the minor salivary glands are correspondent with those of the major glands, additionally, they are superficial under the mucosa; therefore, they are suitable for sampling with the least possible tissue damage. Findings might show focal periductal or perivascular lymphocytic infiltration in the form of dense aggregates [6,7].

MSGB was introduced by Chisholm and Mason in 1968 in the diagnosis of Sjögren's syndrome while others later modified the basic technique [5]. Currently, the sample is taken from the lower lip.

It must be noted, that MSGB is an invasive painful uncomfortable intervention to the patient, so it is essential to reduce the patient's discomfort and the duration of the procedure.. Most common immediate intra- and postoperative complication is bleeding, most frequent mediate complications are haematoma development, wound infection, swelling, pain, inflammation, suture dehiscence and cheloid scars. As a postoperative complication of minor salivary gland biopsy temporary or permanent lip sensitivity can occur [5,8].

Authors' aim with this report is to show a recently introduced and successfully used instrument in the lower lip biopsy of SS patients, that makes easy access to the operative field and makes the procedure as short as possible.

Materials and methods. Minor salivary gland biopsy of the lower lip.

Histologic tissue sample preparation is performed under local anaesthesia, as it follows: after gentle drying the lower lip with a piece of gauze, the appearance of the saliva drops will squarely identify the surgical area around which 1 ml Lidocain-Adrenalin 20 mg/0.01 mg/ml anaesthetic solution was injected (Egis Pharmaceuticals, Budapest, Hungary). The preparation is carried out with the help of the specially designed biopsy forceps (Figure 1 and 2a). The special instrument is an enlarged, angled (about 40° to the horizontal plane) Desmarres-Chalazion forceps widely used in the ophthalmologic practice for sty (hordeolum) removal, its diameter is between 8-12 mms. The active end of the instrument can be round shaped or oval with straight or mildly curved handle to aid grabbing of the tissue. The

handle of the forceps is 9.5 cm long and has a diameter of 2 to 3 cm and has a unilaterally fenestrated oval active end. The other, non-fenestrated side of the forceps compresses the vessels and decreases the bleeding of the surgical area. Due to the 40 °angled handle, isolation can be performed easily, and it provides good access and vision to the operation area. These advantages reduce the duration of the surgical procedure. Employment of this instrument supports proper stabilisation of the lower lip, and the screw in the handle ensures retention and compression. The forceps are made of stainless steel as contact allergy against this type of metal alloy is extremely rare. Similar forceps are mentioned in the literature as S-forceps [9].

During MSGB an approximately 1-1.5 cm long, linear, horizontal mucosal incision is taken on the mucosa of the lower lip with a No15 surgical blade (B-Braun, Aesculap AG, Budapest, Hungary). The middle of the lower lip is rare in minor salivary glands; therefore, it is recommended taking the incision 1-1.5 cm far from the midline [9]. After mucosal incision a further preparation under the mucosa is carried out between the connective- and adipose tissue to explore the minor salivary glands (Figure 2a and 2b). The literature mentions differently designed incision types e. g. circular-, ellipse- or linear incisions (6). The prepared salivary gland samples (5-7 lobuli) are fixed in 10 % of formaldehyde solution in Eppendorf tubes (Eppendorf AG, Hamburg, Germany). Light microscopic assessment of the foci is carried out after haematoxylin-eosin staining of the biopsy sample with 250-x enlargement. (14,22). The wound is closed with 2-3 simple interrupted stitches with HS-15 Supramid 3/0 non-absorbable atraumatic sutures. During the one-week healing period before suture removal chlorhexidine mouth rinse and increased oral hygiene is advised.



Figure 1: Forceps modified by a curved 40° angle to the horizontal plane: screw aids stabilization of the lower lip

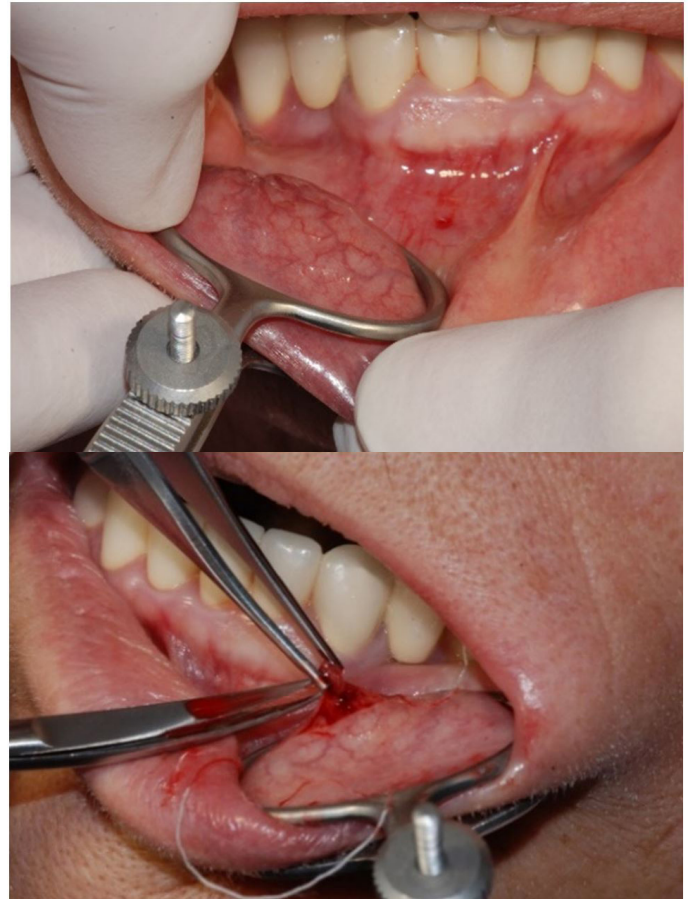


Figure 2(a&b): Histological sample preparation with the modified biopsy forceps in the mouth: Tissue area can be easily fixed, compressed, providing a good accessibility and a proper view

Discussion

Currently, the diagnosis of SS cannot be set up with one laboratory test, clinical symptoms and laboratory markers are further criteria to the decision [3]. As a sum, histopathological section preparation for light microscopic examinations from the lower lip is the easiest way to obtain exocrine glandular tissue for survey and can be carried out appropriately. If serology is negative, the minor salivary gland biopsy (MSGB) is an important contributor. Since MSGB is an invasive, traumatic, dolorous method for the patients, first, instead of histopathological sampling, immune serological test and Rose-Bengal staining is suggested. If one of these examinations are negative and yet the sialometry is positive, the MSGB is necessary for the decision. These delineated novel forceps can be employed successfully to achieve a better access to the operative field and the method described above might highly increase the speed of the lower lip biopsy procedure and reduce the caused trauma of the soft mucosal tissues. It can therefore help providing the patient with an invasive, yet complication free intervention and reduce the risk

of postoperative complications like haemorrhage, haematoma formation, pain or inflammations. Other practitioners developed further novel methods but do not use any forceps for stabilizing the lip. Instead, they use gauze for holding it [10]. Authors think, that for quicker preparation, and for better access it is essential to hold and compress the lip and the operative field firmly.

Conclusion

MSGB is an invasive method, however, it plays a principal role in the diagnosis of SS. Therefore, preparation should be carried out as gentle as possible, with the least trauma in the tissues, causing the least postoperative painful consequences to the patient. The smallest complication can be achieved with proper instruments, like the illustrated forceps which serve as a superior tool in the hand of the operator.

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