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Concise report

Salivary gland biopsy: a comprehensive review of techniques and related complications

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Abstract

Objective. This study proposes a revision of the literature on the current techniques employed in salivary gland biopsy.

Methods. A systematic review of the literature between January 1990 and January 2010 was conducted using MEDLINE, Embase and the Cochrane Central Register of Controlled Trials. The search terms were: 'biopsy AND parotid AND Sjögren'; 'biopsy AND sublingual salivary gland AND Sjögren'; 'biopsy AND minor salivary gland AND Sjögren'; 'biopsy AND labial salivary gland AND Sjögren' and 'biopsy AND salivary glands AND connective disorders'.

Results. No study reporting submandibular salivary gland biopsy was found; 3 studies reported sublingual salivary gland biopsy; 1 study reported palate biopsy; 4 studies reported parotid gland biopsy and 21 studies reported minor salivary gland biopsy.

Conclusion. Biopsy of salivary glands must be performed as last investigation and only when the other items are not complete enough to satisfy the diagnosis. The knowledge of complications and sequelae may be useful in order to minimize the risk.

Key words: Sjögren's syndrome, Salivary gland biopsy, Neurological impairment, Lip numbness.

Introduction

Salivary gland biopsy is performed for the diagnosis of sicca syndrome, SS, other connective infiltrative disease, sarcoidosis, amyloidosis and lymphoma succeeding SS [1]. This procedure could be made in any place where salivary glands are present: parotid, submandibular, sublingual, lip and palate. Making a biopsy, the operator has to consider it as a surgical operation with all the possible complications, trying to minimize discomfort for the patients and to obtain an adequate sample. This study revises the current techniques suggested for salivary gland biopsy.

Methods

A systematic review of the literature between January 1990 and January 2010 was conducted using MEDLINE, Embase and the Cochrane Central Register of Controlled Trials. The search terms were: 'biopsy AND parotid AND Sjögren'; 'biopsy AND sublingual salivary gland AND Sjögren'; 'biopsy AND labial salivary gland AND Sjögren'; and 'biopsy AND salivary glands AND connective disorders'.

A total of 202 citations were identified through electronic database and reference lists. Of these, the abstracts were screened and considered to be potentially relevant for further scrutiny. A total of 24 articles indicated the technique employed and were included; complications were reported when described.

Results

Submandibular biopsy

No study reporting submandibular salivary gland biopsy was found.

Sublingual salivary gland biopsy

Techniques

Three studies reported sublingual salivary gland biopsy (Table 1). The oldest study is by Pennec *et al*. [2]; the

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technique employed consisted in a linear incision between the first premolar and the lateral tooth.

Sublingual biopsy is also reported by Adam *et al*. [3]. The technique used provides a mucosal incision, starting 1 cm anterolaterally from the Whartonian duct and prolonged anteroposteriorly for ~1 cm [4]. In the study of Berquin *et al*. [4] the sublingual biopsy was performed according to Adam's technique.

Complications reported. Pennec *et al*. [2] reported no uncomfortable scars. Berquin *et al*. [4] reported three cases of swelling in the floor of the mouth; of these, two disappeared spontaneously and one was re-incised.

Parotid biopsy

Techniques

Four studies reported parotid gland biopsy (Table 1). In the study of Marx *et al*. [5], parotid biopsy was accomplished using the technique of Kraaijenhagen [6]. Parotid tissue excision was limited only by the length of incision (2 cm). In the study of McGuirt *et al*. [7], parotid biopsies were performed as described by Kraaijenhagen [6] in 1975 and more recently by Marx *et al*. [5] in 1988 through a small 1- to 2-cm incision just below the ear-lobe near the posterior angle of the mandible. Baurmash [8] reported a small Y-shaped incision with the anterior arm commencing at the ear-lobe attachment to the skin. Pijpe *et al*. [9] described parotid biopsies taken according to Kraaijenhagen [6]: a 1-cm skin incision performed around the lower ear-lobe.

Complications reported. Absence of complications is reported by Marx *et al*. [5] and McGuirt *et al*. [7]. Pijpe *et al*. [9] reported a subjective temporary change in sensation in the area of the pre-auricular incision in nine patients.

Palate biopsy

Technique

The palate biopsy was performed by Eisenbud *et al*. [10] (Table 1) 1 cm from the midline at the level of the mesial aspect of the second molar. With a 3-mm cylindrical trephine punch a circular incision is made down to the bone.

Complications reported

Eisenbud *et al*. [10] described that two patients experienced persistent post-operative bleeding.

Minor salivary gland biopsy

Techniques

Twenty-one studies reported minor salivary gland biopsy (Table 2). The technique was first described by Chisholm and Mason [11]; they performed an ellipse of oral mucous membrane down to the muscle layer. In 1974, Greenspan *et al*. [12] described a 1.5- to 2-cm linear incision of the mucosa, parallel to the vermillion border and lateral to the midline.

Daniels [13] performed a single 1.5- to 2-cm horizontal incision through the mucosa. Fox [14] employed a medium chalazion clamp and performed a 1.5-cm straight incision through the mucosa. Marx *et al*. [5] described a mucosal incision of 3×0.75 cm according to Greenspan [12]. Delgado and Mosqueda [15] reported a longitudinal incision of 10 mm in the labial mucosa in front of the mandibular cuspid. Pennec *et al*. [2] reported a technique according to Daniels.

Richards *et al*. [16] reported a horizontal mucosal incision, whereas Seoane *et al*. [17] using the chalazion forceps, performed an elliptical incision (1 cm long and 4 mm wide) horizontally and away from the midline. Peloro *et al*. [18] described the x-marks technique: with a surgical pen the yellow papules of the salivary glands were marked, then a superficial stab incision (1.5–2 mm) was made through the area identified and a second stab incision was made perpendicular to the first incision making an 'X' overlying the gland. Guevara-Gutierrez *et al*. [19] proposed the punch biopsy technique performed by using a 4-mm punch just penetrating the epithelium in the lower lip between the midline and the commissure. Friedman *et al*. [20] reported a small (5–7 mm) incision on the inner surface of the lower lip. Mahlstedt *et al*. [21] reported a 1- to 1.5-cm wedge-shaped incision between the midline and commissure. McGuirt *et al*. [7] did not describe the technique used. Gorson and Ropper [22] reported a 1-cm vertical incision behind the wet line through the mucosa and submucosa.

Smith *et al*. [23] reported a vertical incision made on the mucosal surface of the lip immediately lateral to the midline. Berquin *et al*. [4] performed an oblique incision, starting 1.5 cm from the midline and proceeding latero-inferiorly, avoiding the glandular free zone in the centre of the lower lip. Teppo and Revonta [24] described short (2–3 mm) horizontal incisions. The glands were pulled out

Table 1 Studies reporting sublingual salivary gland biopsy, parotid biopsy and palate biopsy

Sublingual salivary gland biopsy			Parotid biopsy			Palate biopsy		
Reference	Cases, *n*	Complications reported	Reference	Cases, *n*	Complications reported	Reference	Cases, *n*	Complications reported
Pennec *et al.* [2]	29	0	Marx *et al*. [5]	75	0	Eisenbud *et al.* [10]	80	2
Adam *et al*. [3]	–	–	McGuirt *et al.* [7]	4	0			
Berquin *et al.* [4]	55	3	Baurmash [8]	–	–			
			Pijpe *et al*. [9]	35	9			

TABLE 2 Studies reporting minor salivary gland biopsy

References	Cases, *n*	Complications reported
Chisholm and Mason [11]	40	0
Greenspan *et al*. [12]	75	1
Daniels [13]	395	3
Fox [14]	–	–
Marx *et al*. [5]	77	3
Delgado and Mosqueda [15]	19	0
Pennec *et al*. [2]	50	0
Richards *et al*. [16]	58	2
Seoane *et al*. [17]	–	–
Peloro *et al*. [18]	–	–
Guevara-Gutierrez *et al*. [19]	50	2
Friedman *et al*. [1]	118	2
Mahlstedt *et al*. [21]	32	–
McGuirt *et al.* [7]	6	0
Gorson and Ropper [22]	54	1
Smith *et al*. [23]	11	0
Berquin *et al*. [4]	24	1
Teppo and Revonta [24]	191	1
Liquidato *et al*. [25]	40	–
Pijpe *et al*. [9]	15	4
Caporali *et al*. [26]	502	64

gently with cup forceps. Liquidato *et al*. [25] performed a horizontal incision parallel to the red part of the lower lip. Pijpe *et al*. [9], according to Greenspan, performed a lower lip mucosal incision of 3 cm. Caporali *et al*. [26] used a small incision (2–3 mm) on the inner surface of the lower lip.

Complications reported

Absence of complications is reported by five studies [2, 7, 11, 15, 23]. No information on complications is reported by five studies [14, 17, 18, 21, 25]. Complications are reported by 11 studies [1, 4, 5, 9, 12, 13, 16, 19, 22, 24, 27]. Greenspan *et al*. [12] reported one case of a 1-cm^2 area of localized anaesthesia of the lower lip for several months. Daniels [13] described that three patients reported a sensory defect in their lip. Marx *et al*. [5] reported three cases of partial loss of lip sensation; one has persisted for >2 years.

Richards *et al*. [16] reported two cases of reduced sensation over an area of the ipsilateral lower lip of ~1–1.5 cm diameter. In one case, completely normal sensation returned within a few weeks. The other patient had reduced sensation after a year but no objective loss on neurological testing. Guevara-Gutierrez [19] reported two cases of transitory numbness in the lip. Gorson *et al*. [22] reported one case of persistent lower lip numbness after the procedure. Berquin *et al*. [4] reported anaesthesia permanent in one patient. Teppo and Revonta [24] reported one case of pyogenic granuloma of the biopsy wound. Pijpe *et al*. [9] reported four cases of subjective temporary change in sensation at the incision site in the lower lip; two of them had persistent subjective hypoaesthesia in the lower lip for >12 months.

Caporali *et al*. [27] reported 64 cases (12.7%) of transient adverse events: paraesthesia (57), external haematoma (8), local swelling (27) and other [granulomas, bleeding and internal scarring (5)]. Friedman *et al*. [1] reported as immediate complications: incision extended (3), minor bleeding (2), vagal reaction (5), adrenaline-induced tachycardia (1) and local pain (1); as short-term complications (within 3 weeks post-procedure): local swelling (5), local infection (2), suture failure (4), local pain (3) and cheloid formation (1); and as long-term complications (within 3 weeks post-procedure): local numbness.

Discussion

Salivary gland biopsy is performed under three usual circumstances: presence of sicca syndrome, suspicion of SS and suspicion of another systemic disease. In case of sarcoidosis, granulomatous lesions could be identified. In case of amyloidosis, amyloid deposits could be identified in the salivary glands, supporting the use of biopsy as a method for the diagnosis of secondary amyloidosis [4]. Finally, parotid biopsy is employed in the diagnosis of lymphoma arising on SS.

The accuracy of salivary gland biopsy is well established and focal sialoadenitis in minor salivary gland biopsy is one of the main criteria of the revised classification criteria proposed by the American–European Consensus Group. Although the submandibular gland shows the most diagnostic alterations regarding salivary flow rates in SS, there are no studies reporting submandibular biopsy, probably due to invasiveness of the procedure and to the need for general anaesthesia.

Sublingual salivary gland biopsy is reported by three authors [2–4]. Adam *et al*. [3] proposed biopsy of the sublingual gland, underlining the quantity of tissue obtained [4]. Complications reported with sublingual salivary gland biopsy are scanty, only swelling of the floor of the mouth.

Parotid biopsy is reported in four studies [5, 7–9]; complications of this procedure include a temporary change in sensation in the pre-auricular area, recovering within 6 months. In experienced hands, sialocele and facial nerve damage are seldom reported.

Though it would be of value to obtain a major salivary gland biopsy in patients with Sjögren's disease, Chisholm and Mason [11] suggest that this cannot be justified because of the inconvenience to patients and the possible complication of salivary fistula. Despite the abundance of salivary glands, palate biopsy is reported in only one study [10] and complications are represented by swelling and bleeding. Biopsy of labial minor salivary glands is reported in 21 studies [2, 4, 5, 7, 9–21, 23–26]. Many differences have been noticed in comparing techniques reported in the selected articles.

As regards the shape of the incision, some authors [11, 17] suggested an elliptical incision, whereas others [12–16, 25] reported horizontal incision; two authors reported vertical incision [22, 23] and two others [4, 21] reported wedge-shaped incision. The position and the shape of the labial branches of the mental nerve are accurately described by Alsaad *et al*. [28] and Alantar *et al.* [29] who, therefore, did not agree on the direction of the

incision. As regards the size of the incision, it starts from 1.5 to 2 mm [18, 24, 26] in the technique named x-marks and in the minimally invasive technique; then others [15, 20, 22] reported an incision of 7–10 mm; lastly the incision reached 2 or 3 cm [5, 9, 12, 13, 17, 21]. Another characteristic is the localization of the incision; in almost all articles, the area chosen is lateral to the midline, between the midline and the commissure.

Complications of labial salivary gland biopsy include persistent hypoaesthesia of the lower lip, arterial bleeding due to an inadequate (or too deep) incision, vasovagal collapse and burning of the mouth while drinking hot beverages due to a temporary loss of sensation because of anaesthesia. The advantages of biopsy within the lower lip include the large number of salivary glands, accessibility, ease of anaesthesia, lack of major structures susceptible to damage, avoidance of skin incisions and the relative absence of post-operative pain [28].

In the literature, the parotid gland has proved to have unique value for assessing disease activity and progression of SS but lacking surplus diagnostic value compared with minor salivary glands, or opposed to this, to be superior to minor salivary gland when it comes to diagnosing several conditions, including sarcoidosis, lymphomas and SS [30]. Furthermore, the labial salivary gland biopsy suffers from relevant false positivity as well as false negativity [30]. Another substantial difference between a parotid specimen, obtained from an incisional biopsy and a minor salivary gland specimen is the large difference in size; during a labial salivary gland biopsy, only a few small glands are harvested, whereas a parotid biopsy yields a much larger tissue sample for microscopic examination. Consequently, sample size errors are far more likely to occur after minor salivary gland biopsy as compared with major salivary gland biopsy.

Conclusion

Salivary gland biopsy could be considered as a surgical operation and, even though rarely, could suffer from several complications, first of all lip numbness. The knowledge of complications and sequelae may be useful to minimize the risk, and to obtain informed consent. Finally, as a unique invasive procedure of the revised classification criteria proposed by the American–European Consensus Group in diagnosis of SS, it must be performed as a last investigation and only when the other items are not satisfying enough for the diagnosis.

Rheumatology key messages

- Salivary gland biopsy had to be considered as a surgical operation with both advantages and disadvantages.
- This study revises the techniques for salivary gland biopsy to define the easiest method.

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