AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

OTO Open
2022, Vol. 6(3) 1–6

DOI: 10.1177/2473974X221116107
http://oto-open.org
SAGE

Minor Salivary Gland Biopsy in Diagnosis of Sjögren's Syndrome

Alex J. Gordon[1], Aneek Patel[1], Fang Zhou, MD[2], Cheng Liu, MD[2], Amit Saxena, MD[3], Paula Rackoff, MD[3], and Babak Givi, MD[1]

Abstract

Objective. Previous studies have questioned the safety and efficacy of minor salivary gland biopsy in the diagnosis of Sjögren's syndrome, citing complications and difficulty of pathologic evaluation. This study aims to determine the rate of biopsy specimen adequacy and the risk of complications after minor salivary gland biopsy.

Study Design. Case series.

Setting. Single tertiary care center.

Methods. We reviewed the records of all patients who underwent minor salivary gland biopsy at our institution from October 1, 2016, to September 1, 2021. Demographics, comorbidities, symptoms, and serologic results were recorded. The primary outcome was adequacy of the tissue sample. Complications of the procedure were recorded. Biopsies with at least one focus of $\geq$50 lymphocytes per 4-mm^2 sample were considered positive.

Results. We identified 110 patients who underwent minor salivary gland biopsy. Ninety-three (85%) were female, and the median age was 49.1 years (range, 18.7-80.5). Seventy-seven procedures (70%) were performed in the office setting, and 33 (30%) were performed in the operating room. Nearly all biopsy samples (n = 108, 98%) were adequate, and 33 (31%) were interpreted as positive. Four patients (4%) experienced temporary lip numbness, which resolved with conservative management. No permanent complications were reported after lip biopsy. Nineteen (58%) patients with positive biopsy results had no Sjögren's-specific antibodies. Most patients with positive biopsy results (n = 20, 61%) subsequently started immunomodulatory therapy.

Conclusion. Minor salivary gland biopsy can be performed safely and effectively in both the office and the operating room. This procedure provides clinically meaningful information and can be reasonably recommended in patients suspected to have Sjögren's syndrome.

Keywords

Sjögren's syndrome, salivary gland, minor salivary biopsy, safety

Received June 30, 2022; accepted July 3, 2022.

Sjögren's syndrome (SS) is an autoimmune disease characterized predominantly by exocrine gland inflammation, leading to xerostomia and/or xerophthalmia, and less commonly systemic manifestations.[1] Each year, an average of 5.8 per 100,000 individuals are diagnosed with SS in the United States, of whom the majority are women.[2] Once this condition is suspected, formal diagnosis relies on a combination of serologic evidence, oral and ocular secretion studies, and pathologic findings.[3]

Minor salivary gland biopsy is an important technique that has been used for >50 years to assess for focal lymphocytic sialadenitis in patients suspected to have SS.[4] Originally, this was performed by excising an elliptical segment of oral mucosa containing labial salivary gland tissue. This procedure has evolved: several techniques have been described, including small linear incisions,[5,6] punch biopsy,[7] and superficial needle-tip biopsy.[8] All of these techniques have been reported to yield adequate tissue samples in most patients with relatively rare procedural complications, such as prolonged bleeding.[5-8]

Previous literature has called into question the benefits of minor salivary gland biopsy, citing concerns with persistent numbness of the biopsy site after incisional biopsy[9] and inconsistent use of formal pathologic criteria.[10-12] Several studies have attempted to identify symptoms, serologic findings, and other patient characteristics that could predict findings of minor salivary gland biopsy, but there is little consensus among their results.[13-15] Improved understanding of these predictive factors may allow providers to determine which patients are most likely to benefit from undergoing

[1]Department of Otolaryngology–Head and Neck Surgery, NYU Langone Health, New York, New York, USA
[2]Department of Pathology, NYU Langone Health, New York, New York, USA
[3]Division of Rheumatology, Department of Medicine, NYU Langone Health, New York, New York, USA

Corresponding Author:
Alex J. Gordon, Department of Otolaryngology–Head and Neck Surgery, NYU Langone Health, 550 First Ave, New York, NY 10016, USA.
Email: Alex.Gordon@nyulangone.org

minor salivary gland biopsy. To further characterize the utility and potential risks of this procedure, we conducted a historical cohort study via chart review. In this study, we describe our center's experience performing minor salivary gland biopsy, both in the operating room and in office settings, with a particular focus on the efficacy and safety of this procedure.

Methods

Patient Selection

The Institutional Review Board of the New York University Grossman School of Medicine approved this case series based on chart review. All patients aged ≥18 years who underwent minor salivary gland biopsy at NYU Langone Health between October 2016 and August 2021 for suspected SS were identified through a query of medical records and cross-referencing in the database of the Department of Pathology for all minor salivary gland biopsy specimens. Patient demographics, comorbid medical conditions, and smoking history were recorded. Presenting symptoms, duration of symptoms prior to biopsy, preoperative oral steroid treatment, and preoperative imaging findings were also recorded. When available, seropositivity was recorded for antinuclear antibodies (ANA), rheumatoid factor, anti-SSA/Ro, anti-SSB/La, or other autoantibodies. The duration of follow-up by an otolaryngologist, rheumatologist, or primary care physician was recorded. All patients underwent incisional minor salivary gland biopsy by 1 of 9 surgeons. Preoperative medical management was not standardized and was directed by the referring rheumatologist or primary care physician. All procedures took place either in an office setting under local anesthesia or in an operating room if a second procedure was concurrently performed (eg, sialoendoscopy) or according to the surgeon's preference.

Surgical Technique

All biopsies were obtained from the lower lip. The mucosal surface of the lip was examined, and a site halfway between the free edge of the lip and gingivolabial sulcus, in the paramedian position, was selected and anesthetized by submucosal injection of lidocaine and epinephrine. A 2- to 3-cm S-shaped mucosal incision was made sharply, and gentle submucosal dissection was performed with tenotomy scissors. Clusters of minor salivary glands were identified in the submucosal space, superficial to the musculature of the lip and the branches of the mental nerve. At least 6 lobules of minor salivary gland tissue were removed by circumferential dissection with scissors. Attention was paid not to injure the branches of the mental nerve. Adequate hemostasis was achieved by manual pressure, and the mucosal incision was closed by simple interrupted absorbable sutures (fast-absorbing catgut). Patients were permitted to resume oral intake immediately.

Statistical Analysis

The primary outcome was adequacy of the tissue specimen for pathologic evaluation. Other measures included evidence of SS on biopsy, defined as the presence of at least 1 focus of ≥50 inflammatory cells per 4-mm^2 section,[3,4,16] and the development of complications such as persistent numbness of the biopsy site. A secondary aim was to compare characteristics of patients with positive and negative biopsy results. Categorical variables were assessed with chi-square or Fisher exact test as appropriate. Continuous variables were assessed via 2-sample *t* test and Mann-Whitney *U* test as appropriate. All analyses were performed with SPSS 28.0 (IBM). Significance testing was 2-sided with a 5% alpha level.

Table 1. Characteristics of Total Study Population (N = 110).

	Median (range) or No. (%)
Age, y	49.1 (18.7-80.5)
Sex (female)	93 (85)
Race/ethnicity	
White	72 (65)
Black	11 (10)
Asian	10 (9)
Hispanic	9 (8)
Other	7 (6)
Unknown	1 (1)
Gastroesophageal reflux disease	30 (27)
Hypertension	20 (18)
Hyperlipidemia	20 (18)
Smoking status	
Never	72 (65)
Former	33 (30)
Current	5 (5)
Preoperative steroids	25 (23)
Symptom duration, mo	11 (1-84)
Xerostomia	90 (82)
Xerophthalmia	85 (77)
Arthralgias	36 (33)
Salivary gland swelling	32 (29)
Salivary gland pain	22 (20)
Dry skin	18 (16)
Visual changes	4 (4)
Anesthesia type	
Local	90 (82)
Sedation	10 (9)
General	10 (9)
Any seropositivity	67 (61)
Antinuclear antibodies	51 (46)
Rheumatoid factor	10 (9)
Anti-SSA/Ro	25 (23)
Anti-SSB/La	12 (11)

Results

A total of 110 patients were included in this study. The median age was 49.1 years (range, 18.7-80.5), and 93 patients (84.5%) were female (**Table 1**). Most patients were White (n = 61, 55.5%). Five patients (4.5%) were current smokers, and 32 (29.1%) were former smokers. The most common comorbidities were gastroesophageal reflux (n = 30, 27.3%), hypertension (n = 20, 18.2%), and hyperlipidemia (n = 20, 18.2%).

The most common symptoms were xerostomia (n = 90, 81.8%), xerophthalmia (n = 85, 77.3%), arthralgias (n = 36, 32.7%), salivary gland swelling (n = 32, 29.1%), and salivary gland pain (n = 22, 20.0%; **Table 1**). The average duration of symptoms prior to biopsy was 14.1 months (range, 1-84). Twenty-five patients (22.7%) had been treated with oral steroids in the 12 months prior to biopsy.

Seventy-seven (70.0%) patients underwent biopsy in the office setting under local anesthesia. Thirty-three biopsies (30.0%) were performed in the operating room, of which 13 (11.8%) were performed under local anesthesia, 10 (9.1%) under general anesthesia, and 10 (9.1%) under intravenous sedation. No adverse events or complications were encountered during the procedure. The median duration of follow-up after the procedure was 16 months (range, 0-64). Four patients (3.6%) cited temporary numbness at the biopsy site, which subsequently resolved with conservative management. Two patients (1.8%) indicated prolonged pain after biopsy, which resolved within 1 month. No patients reported permanent complications after minor salivary gland biopsy.

An overall 108 biopsies (98.2%) yielded adequate tissue samples for pathologic analysis; just 2 samples (1.8%) were inadequate. Of the 108 successful biopsies, 33 (30.6%) were suggestive of SS based on focus score. Of these, 20 patients (60.6%) subsequently started immunomodulatory therapy by their rheumatologist. Univariable analysis did not show any associations between biopsy results and patient demographics, smoking status, comorbidities, duration of symptoms, or preoperative steroid use (**Table 2**). Salivary gland pain was the only symptom associated with a positive biopsy result (odds ratio [OR], 3.41; 95% CI, 1.27-9.14; P = .01). Seropositivity for any autoantibody (OR, 3.25; 95% CI, 1.19-8.87; P = .02) and positive ANA (OR, 4.60; 95% CI, 1.73-12.22; P = .001) were associated with a positive biopsy result (**Table 3**). Only patients with immeasurably high titers of Ro (OR, 7.96; 95% CI, 1.86-34.16; P = .004) or La (OR, not applicable, P = .02) were more likely to have a positive biopsy than patients with negative titers. Positive biopsy results were not associated with weakly positive anti-SSA/Ro (OR, 2.35; 95% CI, 0.89-6.22; P = .08), weakly positive anti-SSB/La (OR, 2.83; 95% CI, 0.83-9.64; P = .10), or positive rheumatoid factor (OR, 3.51; 95% CI, 0.86-14.33; P = .07).

Discussion

To our knowledge, this is the largest cohort of patients undergoing incisional minor salivary gland biopsy in the United States since 1984.[5] Based on our institution's experience, it is apparent that minor salivary gland biopsy is a low-risk procedure that can be diagnostically informative for most patients. We found that 98.2% of biopsies yielded adequate samples for pathologic evaluation. Moreover, only 3.6% of patients reported temporary numbness, while no patients experienced permanent neurologic complications. This is consistent with previous estimates of the rates of all neurologic complications (2.5%) and permanent neurologic complications (1.5%).[9] This rate of minor self-resolving complications is acceptable, particularly when we consider the high rate of tissue specimen adequacy and the value of the diagnostic information provided by the procedure.

In this study, 30.6% of successful biopsies were positive for evidence of SS. Previous studies reported rates of positive biopsy ranging from 41% to 62%.[12,14] In our study cohort, salivary gland pain was the only symptom associated with a positive biopsy result. In contrast, Bamba et al did not find that any symptoms were independently associated with positive biopsy. However, this group found that sicca symptoms combined with seropositivity to Ro or La successfully predicted biopsy results.[13] In our cohort, just 8 patients (7.3%) presented without xerostomia or xerophthalmia, limiting the utility of a similar analysis.

There is little concordance in the previous literature regarding the predictive value of serologic data on biopsy results. Giovelli et al found that seropositivity for ANA and Ro and/or La was associated with positive biopsy; however, they excluded >25% of their starting patient population due to insufficient data.[15] In contrast, Langerman et al found no association between serology and biopsy results.[14] Interestingly, our results revealed that seropositivity for ANA, but not Ro or La, was independently associated with a higher likelihood of a positive biopsy result. It is possible that the referring rheumatologists are less likely to recommend salivary gland biopsy in patients with positive Ro or La serologies, given the high specificity of these antibodies for SS. Thus, the patients in our cohort with positive Ro or La serologies may have had less severe symptoms, making the diagnosis of SS equivocal by clinical criteria alone. This is consistent with previous suggestions that minor salivary gland biopsy has little utility in patients with clear positive serologic and clinical evidence of SS.[13,17] Accordingly, patients with severe symptoms and seropositivity to Ro or La may be underrepresented in our cohort.

In our study, weak seropositivity for Ro and La was defined as the presence of titers above normal limits but within the measurable range of the laboratory assay performed. However, some patients in our study had antibody titers that exceeded the limits of what these tests could quantify. Of 10 patients, 7 (70%) with immeasurably high Ro titers had a positive biopsy result, as opposed to 21.8% of patients with normal or weakly positive Ro titers (P = .004). Similarly, all 3 patients (100%) with immeasurably high La titers had a positive biopsy result, as compared with 24.5% of patients with normal or weakly positive La titers (P = .02). As the majority of patients with strong Ro or La titers had a positive biopsy result, it is likely that these patients had less to gain from undergoing minor salivary gland biopsy than those with low or absent titers. Here again, the small number of these patients in our study cohort limits the conclusions that can be drawn about this group.

In our series, 31% of patients had a positive lip biopsy confirming the diagnosis of SS, and the majority started immunomodulatory treatment per their physicians. Interestingly, 25% of patients with positive biopsy did not have positive autoantibodies. Obtaining evidence suggesting the diagnosis of SS is an important step in the management of these patients. Severe SS can lead to keratopathy and even significant corneal injury

Table 2. Comparisons Between Patients With Positive and Negative Biopsy Result.[a]

	Biopsy, median (range) or No. (%)		
	Positive (n = 33)	Negative (n = 75)	*P* value
Age, y	49.5 (26.4-80.5)	48.4 (18.7-74.1)	.21
Sex: female	30 (91)	61 (81)	.21
Race/ethnicity			
White	25 (76)	46 (61)	.70
Black	3 (9)	8 (11)	
Asian	2 (6)	8 (11)	
Hispanic	1 (3)	7 (9)	
Other	2 (6)	5 (7)	
Unknown	0 (0)	1 (1)	
Gastroesophageal reflux disease	9 (27)	21 (28)	.94
Hypertension	4 (12)	16 (21)	.26
Hyperlipidemia	5 (15)	15 (20)	.55
Smoking status			
Never	20 (61)	51 (68)	.14
Former	13 (39)	19 (25)	
Current	0 (0)	5 (7)	
Preoperative steroids	10 (30)	15 (20)	.24
Symptom duration, mo	7 (1-30)	12 (1-84)	.37
Xerostomia	27 (82)	62 (82)	.83
Xerophthalmia	23 (70)	61 (81)	.28
Salivary gland swelling	13 (39)	18 (24)	.08
Salivary gland pain	**11 (33)**	**10 (13)**	**.01**
Arthralgias	10 (30)	27 (36)	.64
Dry skin	4 (12)	14 (19)	.44
Visual changes	1 (3)	3 (4)	.99
Anesthesia type			
Local	26 (79)	62 (83)	.79
Sedation	4 (12)	6 (8)	
General	3 (9)	7 (9)	
Any seropositivity	**25 (76)**	**41 (55)**	**.02**
Antinuclear antibodies	**22 (67)**	**28 (37)**	**.001**
Rheumatoid factor	5 (15)	4 (5)	.07
Anti-SSA/Ro	10 (30)	13 (17)	.08
Anti-SSB/La	6 (18)	6 (8)	.10
Strong anti-SSA/Ro[b]	**7 (21)**	**3 (4)**	**.004**
Strong anti-SSB/La[b]	**3 (9)**	**0 (0)**	**.02**

[a]Bold indicates statistical significance.
[b]Immeasurably high titers.

resulting in loss of vision. When a biopsy result suggests the diagnosis, these patients can be referred to ophthalmologists for regular examinations, and they can be offered other preventive measures to avoid this serious complication. Additionally, these patients are at increased risk of developing lymphoproliferative diseases, such as non-Hodgkin's lymphoma.[18] Obtaining a biopsy diagnosis suggestive of SS would allow patients and their physicians to implement a proper surveillance routine. Given that immunomodulatory medications used to treat SS are associated with side effects such as retinopathy for hydroxychloroquine[19] or infusion reactions in the case of rituximab,[20] pathologic diagnostic information is quite helpful for the treating physician in deciding whether to start treatment. Therefore, with its low risk and high success rate, lip biopsy could be considered a useful tool in the management of patients with suspicion of SS.

There are several limitations to this case series. As previously stated, the preoperative medical management of these patients was not uniform and was left to the discretion of the referring physicians. Though this was unlikely to affect the adequacy of tissue specimens, this could have affected the results of biopsy evaluation. Despite this, oral systemic

Table 3. Odds of Positive Biopsy Result for Categorical Predictor Variables.[a]

		95% CI		
	Odds ratio	Lower	Upper	*P* value
Sex: female	2.29	0.61	8.62	.21
Race/ethnicity				.70
White	Reference	—	—	
Black	0.69	0.17	2.83	
Asian	0.46	0.09	2.34	
Hispanic	0.26	0.03	2.26	
Other	0.74	0.13	4.07	
Gastroesophageal reflux disease	0.96	0.39	2.41	.94
Hypertension	0.51	0.16	1.66	.26
Hyperlipidemia	0.71	0.24	2.16	.55
Smoking status				.14
Never	Reference	—	—	
Former	1.75	0.73	4.18	
Current	NA	NA	NA	
Preoperative steroids	1.74	0.68	4.42	.24
Xerostomia	1.13	0.37	3.49	.83
Xerophthalmia	0.59	0.22	1.54	.28
Salivary gland swelling	2.17	0.90	5.24	.08
Salivary gland pain	**3.41**	**1.27**	**9.14**	**.01**
Arthralgias	0.82	0.34	2.00	.64
Dry skin	0.63	0.19	2.10	.44
Visual changes	0.72	0.07	7.21	.99
Anesthesia type				.79
Local	Reference	—	—	
Sedation	1.59	0.41	6.11	
General	1.02	0.25	4.26	
Any seropositivity	**3.25**	**1.19**	**8.87**	**.02**
Antinuclear antibodies	**4.60**	**1.73**	**12.22**	**.001**
Rheumatoid factor	3.51	0.86	14.33	.07
Anti-SSA/Ro	2.35	0.89	6.22	.08
Anti-SSB/La	2.83	0.83	9.64	.10
Strong anti-SSA/Ro[b]	**7.96**	**1.85**	**34.16**	**.004**
Strong anti-SSB/La[b]	**NA**	**NA**	**NA**	**.02**

[a]Bold indicates statistical significance. Variables with cells containing zero counts denoted by NA (not applicable).
[b]Immeasurably high titers.

steroid use in the 12 months prior to biopsy was not associated with positive biopsy in our patient population ($P = .24$). The subgroup of patients in our study who underwent biopsies in the office were typically (80.5%) not followed by the surgeons beyond the perioperative period, as is common for office-based procedures; however, patients were aware that they could contact their surgeons if any complications arose. We cannot fully exclude the possibility that some complications were not documented in the medical records. At the same time, patients were followed by their rheumatologists and primary care physicians for a median duration of 16 months (range, 0-64). From the documentation of these follow-up visits, we did not identify any long-term complications arising >2 months postbiopsy. Last, the large number of variables tested for univariable association with positive biopsy does introduce the possibility of type I statistical error; yet, many of the identified factors, such as positive ANA and strong Ro seropositivity, are logical given the pathogenesis of SS. Although our study population includes >100 patients, our cohort lacks adequate statistical power for multivariable analysis, and it is still possible that our study lacked adequate power to identify all the possible differences between positive and negative cases or any rare complications.

Conclusion

Minor salivary gland incisional biopsy is a valuable tool for the diagnosis of SS that reliably yields adequate tissue specimens for pathologic evaluation. This procedure can be

performed safely and efficaciously in the office setting as well as the operating room. Last, few patients experienced complications after biopsy, all of which were resolved with conservative therapy.

Author Contributions

Alex J. Gordon, conception and design of study, acquisition, analysis and interpretation of data, drafting and critically revising work, final approval of manuscript, agreement to be accountable for all aspects of the work; **Aneek Patel**, acquisition, analysis, and interpretation of data, critically revising work, final approval of manuscript, agreement to be accountable for all aspects of the work; **Fang Zhou**, interpretation of data, critically revising work, final approval of manuscript, agreement to be accountable for all aspects of the work; **Cheng Liu**, interpretation of data, critically revising work, final approval of manuscript, agreement to be accountable for all aspects of the work; **Amit Saxena**, interpretation of data, critically revising work, final approval of manuscript, agreement to be accountable for all aspects of the work; **Paula Rackoff**, interpretation of data, critically revising work, final approval of manuscript, agreement to be accountable for all aspects of the work; **Babak Givi**, conception and design of study, analysis and interpretation of data, critically revising work, final approval of manuscript, agreement to be accountable for all aspects of the work.

Disclosures

Competing interests: None.

Sponsorships: None.

Funding source: None.

ORCID iD

Alex J. Gordon https://orcid.org/0000-0001-9312-8166

References

1. Ramos-Casals M, Tzioufas AG, Font J. Primary Sjögren's syndrome: new clinical and therapeutic concepts. *Ann Rheum Dis*. 2005;64(3):347-354.
2. Maciel G, Crowson CS, Matteson EL, Cornec D. Incidence and mortality of physician-diagnosed primary Sjögren syndrome: time trends over a 40-year period in a population-based US cohort. *Mayo Clin Proc*. 2017;92(5):734-743.
3. Shiboski CH, Shiboski SC, Seror R, et al. 2016 American College of Rheumatology/European League against rheumatism classification criteria for primary Sjögren's syndrome: a consensus and data-driven methodology involving three international patient cohorts. *Arthritis Rheumatol*. 2017;69(1):35-45.
4. Chisholm DM, Mason DK. Labial salivary gland biopsy in Sjögren's disease. *J Clin Pathol*. 1968;21(5):656-660.
5. Daniels TE. Labial salivary gland biopsy in Sjögren's syndrome: assessment as a diagnostic criterion in 362 suspected cases. *Arthritis Rheum*. 1984;27(2):147-156.
6. Fox PC. Simplified biopsy technique for labial minor salivary glands. *Plast Reconstr Surg*. 1985;75(4):592-593.
7. Guevara-Gutiérrez E, Tlacuilo-Parra A, Minjares-Padilla LM. Minor salivary gland punch biopsy for evaluation of Sjögren's syndrome. *J Clin Rheumatol*. 2001;7(6):401-402.
8. Comini LV, Lazio MS, Taverna C, et al. A new, easy, and swift technique for minor salivary gland biopsy in Sjogren's syndrome. *Laryngoscope*. 2020;130(4):873-875.
9. Varela Centelles P, Sánchez-Sánchez M, Costa-Bouzas J, Seoane-Romero JM, Seoane J, Takkouche B. Neurological adverse events related to lip biopsy in patients suspicious for Sjögren's syndrome: a systematic review and prevalence meta-analysis. *Rheumatology (Oxford)*. 2014;53(7):1208-1214.
10. Wicheta S, Van der Groen T, Faquin WC, August M. Discrepancies in interpretation of the minor salivary gland biopsy in the diagnosis of Sjögren syndrome. *J Oral Maxillofac Surg*. 2019;77(8):1628-1635.
11. Vivas Á J, Bautista-Vargas M, Portacio S, et al. Reproducibility of minor salivary gland biopsy reports in Sjögren's syndrome and its correlation with disease biomarkers. *Clin Rheumatol*. 2021;40(6):2285-2292.
12. Teppo H, Revonta M. A follow-up study of minimally invasive lip biopsy in the diagnosis of Sjögren's syndrome. *Clin Rheumatol*. 2007;26(7):1099-1103.
13. Bamba R, Sweiss NJ, Langerman AJ, Taxy JB, Blair EA. The minor salivary gland biopsy as a diagnostic tool for Sjogren syndrome. *Laryngoscope*. 2009;119(10):1922-1926.
14. Langerman AJ, Blair EA, Sweiss NJ, Taxy JB. Utility of lip biopsy in the diagnosis and treatment of Sjogren's syndrome. *Laryngoscope*. 2007;117(6):1004-1008.
15. Giovelli RA, Santos MCS, Serrano ÉV, Valim V. Clinical characteristics and biopsy accuracy in suspected cases of Sjögren's syndrome referred to labial salivary gland biopsy. *BMC Musculoskelet Disord*. 2015;16:30-30.
16. Cleary KR, Batsakis JG. Biopsy of the lip and Sjögren's syndrome. *Ann Otol Rhinol Laryngol*. 1990;99(4, pt 1):323-325.
17. Lee M, Rutka JA, Slomovic AR, McComb J, Bailey DJ, Bookman AA. Establishing guidelines for the role of minor salivary gland biopsy in clinical practice for Sjögren's syndrome. *J Rheumatol*. 1998;25(2):247-253.
18. Pavlidis NA, Drosos AA, Papadimitriou C, Talal N, Moutsopoulos HM. Lymphoma in Sjogren's syndrome. *Med Pediatr Oncol*. 1992;20(4):279-283.
19. Jorge A, Ung C, Young LH, Melles RB, Choi HK. Hydroxychloroquine retinopathy—implications of research advances for rheumatology care. *Nat Rev Rheumatol*. 2018;14(12):693-703.
20. Paul F, Cartron G. Infusion-related reactions to rituximab: frequency, mechanisms and predictors. *Expert Rev Clin Immunol*. 2019;15(4):383-389.