ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2021 July 16; 9(20): 5352-5753

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

Contents

Thrice Monthly Volume 9 Number 20 July 16, 2021

EDITORIAL

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Case Control Study

Retrospective Study

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 20 July 16, 2021

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 20 July 16, 2021

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 20 July 16, 2021

Contents

CORRECTION

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 20 July 16, 2021

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Fan-Zheng Meng, MD, PhD, Director, Professor, Department of Pediatrics, The First hospital of Jilin University, Changchun 130021, Jilin Province, China. mengfanzheng1972@163.com

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for *WJCC* as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The *WJCC*'s CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Thrice Monthly

EDITORS-IN-CHIEF
Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2307-8960/editorialboard.htm

PUBLICATION DATE
July 16, 2021

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

E-mail: bpgoffice@wjgnet.com https://www.wjgnet.com

World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2021 July 16; 9(20): 5701-5708

DOI: 10.12998/wjcc.v9.i20.5701

ISSN 2307-8960 (online)

CASE REPORT

Role of ranulas in early diagnosis of Sjögren's syndrome: A case report

Na Chen, Da-Shun Zeng, Yu-Tong Su

ORCID number: Na Chen 0000-0001-7087-2304; Yu-Tong Su 0000-0002-0358-8933.

Author contributions: Chen N and Su YT managed the case, and prepared and revised the manuscript; Zeng DS assisted with the preparation and revision of the manuscript; all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work; all authors take full responsibility for the integrity of the study and the final manuscript.

Supported by the National Natural Science Foundation of China, No. 81801600.

Informed consent statement: Informed consent was obtained from the patient for her inclusion in this report.

Conflict-of-interest statement: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Na Chen, Department of Endocrine and Metabolic Diseases, Shanghai Institute of Endocrine and Metabolic Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Na Chen, Shanghai National Clinical Research Center for metabolic Diseases, Key Laboratory for Endocrine and Metabolic Diseases of the National Health Commission of the PR China, Shanghai National Center for Translational Medicine, Shanghai, China

Da-Shun Zeng, Department of Oral Surgery, The Third Affiliated Hospital of Wenzhou Medical University, Wenzhou 325200, Zhejiang Province, China

Yu-Tong Su, Department of Rheumatology and Immunology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China

Corresponding author: Yu-Tong Su, MD, PhD, Doctor, Department of Rheumatology and Immunology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, No. 197 Ruijin Second Road, Shanghai 200025, China. suyt2015@163.com

Abstract

BACKGROUND

Although the presentations of Sjögren's syndrome (SS) are variable, ranging from mild dryness to wider systemic involvement, ranulas as early clinical signs were scarcely reported. Here, we present an adult patient with SS, who developed a unilateral simple ranula and was diagnosed primary SS 3 years later. We also provide a review of cases of SS and ranulas from 1980 to 2020.

CASE SUMMARY

A 22-year-old girl was found to have a left painless floor-of-mouth lesion 3 years ago, without obvious trauma or inducement. The diagnosis of a unilateral (left) simple ranula was made, and the ranula was surgically treated. Within 3 years after the ranula surgery, she developed acute lymphadenectasis in unilateral parotid twice without inducement, and ultrasonic examination revealed diffuse lesions in bilateral parotids and submandibular glands, which strongly suggested SS. Serologic tests and the unstimulated whole saliva flow rate confirmed the SS diagnosis.

CONCLUSION

Our study underlines that ranulas are early clinical signs of SS. As early diagnosis and early intervention of SS are important to obtain better outcomes, our findings

Manuscript source: Unsolicited manuscript

Specialty type: Rheumatology

Country/Territory of origin: China

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B, B, B, B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: March 9, 2021
Peer-review started: March 9, 2021
First decision: April 4, 2021
Revised: April 13, 2021
Accepted: May 24, 2021
Article in press: May 24, 2021
Published online: July 16, 2021

P-Reviewer: Erkut B, Kai K, Liakina V
S-Editor: Gong ZM
L-Editor: Wang TQ
P-Editor: Xing YX

underline the need for histopathological test after sublingual adenectomy and imaging detection of exocrine glands for the patients with ranulas.

Key Words: Sjögren's syndrome; Ranulas; Early diagnosis; Parotitis; Case report

Core Tip: Although the presentations of Sjögren's syndrome (SS) are variable, ranulas as early clinical signs were scarcely reported. Here, we present an adult patient with SS, who developed a unilateral simple ranula and was diagnosed with primary SS 3 years later. We also provide a review of cases of SS and ranulas from 1980 to 2020. By analyzing the symptoms, treatment, and prognosis of these patients, we propose that ranulas could be early clinical signs and manifestations of SS, which may raise the awareness of clinicians and lead to early interventions for SS in order to obtain better outcomes.

Citation: Chen N, Zeng DS, Su YT. Role of ranulas in early diagnosis of Sjögren's syndrome: A case report. *World J Clin Cases* 2021; 9(20): 5701-5708
URL: https://www.wjgnet.com/2307-8960/full/v9/i20/5701.htm
DOI: https://dx.doi.org/10.12998/wjcc.v9.i20.5701

INTRODUCTION

Sjögren's syndrome (SS) is a chronic systemic autoimmune disorder, characterized by lymphocytic infiltration of exocrine glands with a greater predilection in females[1]. The reported prevalence ranges from 0.01% to 0.09% in the general population[2]. The symptoms are various and can involve the whole body, beyond sicca syndromes, and systemic manifestations include inflammatory arthritis, renal involvement, lung lesion, central nervous system involvement, *etc.*[3,4]. Due to insidious onset in early stage, it is difficult to diagnose SS at an early stage in time and accurately.

Ranulas are caused by extravasation of mucus from damage or obstruction of the sublingual gland or its duct[5]. Eating and external blunt trauma could cause damage to the sublingual duct[6], meanwhile, anatomical variations and chronic disease of the sublingual glands could lead to the obstruction[7]. Concomitant ranulas are uncommon in patients with SS. It is reported that ranulas developed as a complication of SS in children[8-10], and limited cases are found in adults[10-13]. However, the association between ranulas and SS remains unknown.

In the present review, we report a 22-year-old girl with a unilateral ranula who was diagnosed as having SS 3 years later. The clinical presentation, laboratory tests, and treatment are described. According to this case and literature review, we aim to draw the attention of early clinical signs "ranulas" for SS, which are easily neglected or inappropriately treated although they are the hints to early diagnosis of SS.

CASE PRESENTATION

Chief complaints

On March 1, 2019, a 22-year-old girl came to our outpatient clinic asking for serologic testing for SS.

History of present illness

The patient denied having dry eyes, dry mouth, parotid enlargement, or other clinical manifestations.

History of past illness

The patient was referred to oral surgery department for evaluation of a left painless floor-of-mouth lesion 3 years ago. The lesion had been present for 1 mo and the patient showed no difficulty eating, drinking, or speaking. Before ranula presentation, there

was no obvious trauma or inducement. A pink, fluctuant, dome-shaped bulge in the floor of the mouth on the left side of the patient's lingual frenulum was found in an oral examination (Figure 1). Palpation revealed that the bulge was confined to the soft tissue. Based on these manifestations, the diagnosis of a unilateral (left) simple ranula was made. Her oral surgeon at the time did not consider anything more than a ranula, and did not perform any further tests. The patient underwent a surgery to remove the entire unilateral sublingual gland with the ranula while the lingual nerve was preserved. The pathology showed a sublingual gland (left) with chronic inflammation, lymphocytic infiltration, and focal mucus extravasation (Figure 2). There was no ranula on her right sublingual gland so far.

In 2017, 10 mo after the ranula surgery, the patient developed acute left submaxillary parotid lymphadenectasis without inducement. Ultrasonic (US) examination revealed patchy hypoechoic areas in the left parotid. Two years after the first parotid lymphadenectasis, she developed acute right parotid gland swelling without inducement as before. US examination revealed scattered, foveolate hypoechoic areas, and lymphadenectasis in bilateral parotids. Treatment with antibiotic and glucocorticoid were given. 1 mo later, US reexamination still revealed diffuse lesion in bilateral parotids and submandibular glands, which strongly suggested SS.

Personal and family history

There was no family history of autoimmune disorders.

Physical examination

No abnormality was found on physical examination.

Laboratory examinations

Serologic tests showed an antinuclear antibody (ANA) titer of 1:320, with antibody positivity for the extractable nuclear SS–related antigen A (SSA) as well as an elevated erythrocyte sedimentation rate of 33 mm/h (reference range 0-20 mm/h for females), rheumatoid factor (RF) of 441 IU/mL (reference range 0-20 IU/mL), and IgG of 20.10 g/L (reference range 8.6-17.4 g/L). The unstimulated whole saliva flow rate was 1.7 mL/min (reference range > 2 mL/min). Ophthalmologically, the Schirmer test results were 30 mm on both eyes in 5 min (reference range > 10 mm). The patient's characteristics and laboratory data are shown in Table 1.

FINAL DIAGNOSIS

Along with the characteristic lesions in salivary glands, a diagnosis of primary SS was made.

TREATMENT

Treatment with hydroxychloroquine sulfate tables (400 mg/d) and total glycosides of paeony root capsule (1200 mg/d) was started.

OUTCOME AND FOLLOW-UP

The parotitis did not relapse during the 2-year follow-up.

DISCUSSION

Search strategy

A review of the literature for ranulas with SS was carried out based on the following databases: Web of Science, Scopus Database, and PubMed/MEDLINE up to December 2020. The search was performed with the following MESH terms: "Sjögren's syndrome" and "ranulas" or "floor-of-mouth mucocele". The studies reported on children or adults diagnosed with SS with ranulas in the past 40 years (from 1980 to 2020) were included.

Table 1 Laboratory parameters of the patient with primary Sjögren's syndrome who had a ranula before

Laboratory parameters	Day 1 (March 1 on outpatient service)	After 2 wk of treatment	After 3 mo of treatment	After 6 mo of treatment	After one year and three mo of treatment
WBC (× 10^9/L)	3.42↓	3.97	4.25	4.79	4.25
Neutrophils, %	49.1↓	55.8	55.6	60.2	55.6
Lymphocytes, %	43.3↑	35.7	36.6	31.9	36.6
ESR (mm/h)	33↑	17	10	17	7
ALT (U/L)	23	18	17	13	24
AST (U/L)	31	23	27	24	29
Creatinine (μmol/L)	67	66	86	76	68
EGFR (mL/min)	110.5	112.5	81.7	94.2	107.8
ANA	1:320	-	-	1:320	1:320
Anti-dsDNA antibody	Negative	-	-	Negative	Negative
Anti-RNP/Sm antibody	Negative	-	-	Negative	Negative
Anti-Sm antibody	Negative	-	-	Negative	Negative
Anti-SSA antibody	Positive	-	-	Positive	Positive
Anti-SSB antibody	Positive	-	-	Positive	Positive
IgA (g/L)	1.60	-	-	1.66	1.57
IgG (g/L)	20.10↑	-	-	15.9↑	14.47
IgM (g/L)	1.15	-	-	1.00	1.08
C3 (g/L)	0.69↓	-	-	0.75↓	1.05
C4 (g/L)	0.18	-	-	0.19	0.26
RF (IU/mL)	441↑	-	-	165↑	46.86↑

WBC: White blood cells; ESR: Erythrocyte sedimentation rate; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; EGFR: Estimate glomerular filtration rate; ANA: Anti-nuclear antibody; dsDNA: Double-stranded DNA; RNP: Ribonucleoprotein; SSA: Sjögren's syndrome-related antigen A; SSB: Sjögren's syndrome-related antigen B; Ig: Immunoglobulin; C3: Complement component 3; C4: Complement component 4; RF: Rheumatoid factor.

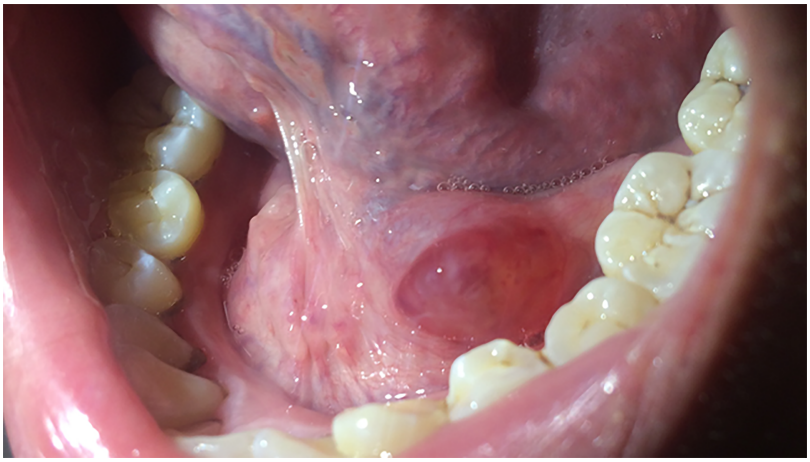

Figure 1 Clinical picture of the unilateral (left) simple ranula.

Literature review

Four series[9-12] and two isolated cases of pSS with ranulas[8,13] have been published, which contain a total of 17 patients including our case (Table 2). Among the 17 patients described, 15 were women and two were men. The turnout is consistent with previous

Table 2 Review of primary Sjögren's syndrome patients associated with ranulas

Ref.	Country	No. of cases	Age/gender	First visit department	Type of ranula	Sicca symptoms	Extra-landular symp-toms	Time interval between pSS diagnosis and detection of ranula	Antibody positivity	Treatment of ranula	Treatment of pSS	Outcome
Katayama *et al*[12], 1993	Japan	2	33, F; 34, F	Patient 1: dermatology department Patient 2: NA	Unilateral	Patient 1: oral dryness, caries, alopecia, and pruritic skin rash Patient 2: oral dryness	NA	Patient 1: after SSPatient 2: 7 yr after SS	ANA, SSA	Surgically treated	NA	NA
Pinheiro *et al*[13], 2017	Brazil	1	37, F	Clinic of the Dental School	Unilateral	Irritation of the eyes, enlargement of the parotid glands, and dry mouth	NA	1 yr after SS	ANA, SSA and SSB	Surgically treated	Prednisone, methotrexate, chloroquine diphosphate, and artificial tears and saliva	Improving all signs and symptoms
Means *et al* [8], 2017	United States	1	10, M	Pediatric Otolaryngology clinic	Bilateral	Bilateral recurrent parotitis, dry eyes, dental caries	NA	4 yr before SS	ANA, SSA and SSB	Transoral excision and marsupial-zation	Routine follow-up	NA
Lieberman *et al*[9], 2018	United States	2	12, F; 8, F	Patient 1: Dental Department; Patient 2: Otolaryngology	Patient 1: Bilateral; Patient 2: Unilateral	Patient 1: Recurrent parotid gland discomfort; Patient 2: No	Patient 1: Severe joint pain; Patient 2: no	Patient 1: 7 yr before SS; Patient 2: Simultaneous	Patient 1: SS-APatient 2: ANA, SSA, SSB and RF	Patient 1: surgically treated; Patient 2: Surgically treated	NA	Patient 1: NAPatient 2: Developed significant dry eyes
Sato *et al* [11], 2019	Japan	3	66, F; 30, F; 26, F	Department of Oral Medicine	NA	NA	NA	Simultaneous	SSA, SSB	Patients 1 and 2: Surgically treated; Patient 3: Naturally resolved	NA	NA
Takagi *et al* [10], 2020	Japan	7	12, M33, F41, F43, F46, F48, F51, F	NA	Patient 1: Bilateral, plunging; Patients 2-7: NA, simple	NA	NA	Patient 1: Simultaneous; Patients 2-7: NA, but before SS	Patient 1: ANA, SSA, SSB and RF; Patients 2-7: NA	Patient 1: Open fenestration; Patients 2-7: NA	Patient 1: Mizoribine and cortices-teroid medication; Patients 2-7: NA	Patient 1: Developed parotitis after 9 mo; Patients 2-7: NA
Present case	China	1	25, F	Oral surgery	Unilateral, simple	Ranula and recurrent parotitis	No	3 yr before SS	ANA, SSA and RF	Surgically treated	Hydroxychloroquine sulfate and total glycosides of paeony root capsule	No symptoms

M: Male; F: Female; pSS: Primary Sjögren's syndrome; ANA: Antinuclear antibodies; SSA: Sjögren's syndrome–related antigen A; SSB: Sjögren's syndrome–related antigen B; RF: Rheumatoid factor; NA: Not available.

reports that pSS is a women dominant disease[13]. Ranulas were detected before pSS diagnosis in nine patients, and ranulas were detected simultaneously with pSS diagnosis in six patients[14]. Only three patients were detected with ranulas after pSS was diagnosed[15]. This statistic suggests that ranulas may be the early clinical signs rather than the manifestations in the late period of pSS, according to the studies by Sato *et al*[11] and Takagi *et al*[10]. The time interval from discovery of ranulas to the diagnosis of pSS is 0 to 7 years, which indicates that pSS occurs insidiously. In addition to presenting with unilateral or bilateral ranulas, six (6/17) patients were reported to have sicca symptoms including recurrent parotitis, dry eyes, dry mouth, and dental caries[8,9,12,13], and only one (1/17) patient was reported to have extra-glandular system involvement (joint pain)[9]. Six surgical pathological specimens showed the lymphocytic infiltration. Anti-ANA and anti-SSA were detected in all patients. With regard to the treatment of ranulas, ten (10/17) patients were surgically treated, one (1/17) naturally resolved, and six (6/17) were uncertain. The detailed treatment of pSS was not described in most patients. It may be because that the cases were reported by oral surgeons or otolaryngologists.

SS is a complex and multisystem disorder. The SS patients with both glandular and extra-glandular features suffer from a poor prognosis. The advanced stage symptoms of tooth loss, severe fatigue, and joint and muscle pain impair the quality of life. Moreover, the development of lymphomas increases the mortality[16]. In clinical practice, dryness such as dry eyes and dry mouth often indicates that glandular secretion has been disrupted by chronic soakage of inflammatory cells, which may be too late for treatment and would impair the effect of intervention.

There are several diagnostic criteria for SS in the past two decades, including the 1999 revised Japanese Ministry of Health Criteria for diagnosis of SS (JPN), 2002 American-European Consensus Group Classification Criteria for SS, 2012 ACR Classification Criteria for SS, and 2016 ACR-European League Against Rheumatism Classification Criteria[17]. However, these criteria are mainly to confirm the diagnosis of SS when symptoms have progressed to a certain level, but not to identify the early symptoms. Several valuable biomarkers have been recently identified for early auxiliary diagnosis/stratification of SS[18]. For example, tissue specific autoantibodies, such as parotid secretory protein, salivary protein-1, carbonic anhydrase 6, can be detected before the classic autoantibodies[15,19]. However, in the absence of the typical clinical symptoms of SS (such as dry eyes, dry mouth, or recurrent parotitis), these tests are not routinely performed. Besides, the diversity of symptoms also makes early diagnosis and intervention of SS difficult. Therefore, it is vital to detect early clinical signs in order to treat SS properly in its early stage and to achieve better clinical outcomes.

Ranulas were detected before or at the same time of SS diagnosis in 82.35% (14/17) of patients, which is much higher than the incidence of ranulas after SS diagnosis as a complication (3/17). Ranulas are rare diseases, which have a predominance among teenagers and young adults, and the incidence is 2 per 1000[20]. Recently, Takagi *et al*[10] examined 50 patients with ranulas undergoing magnetic resonance imaging (MRI). Eleven patients were suspected to have SS, and seven of them were then confirmed by the rheumatologist according to the Japanese Ministry of Health criteria (1999)[10]. It is worth noting that the incidence of SS patients was significantly increased among patients with ranulas. The combination of these patients and ours suggests that ranulas may be the early clinical signs of SS.

SS is characterized by lymphocytic infiltration of exocrine glands including the sublingual gland. Among patients with SS in early stage, ranulas usually appear without obvious trauma or cause. Sato *et al*[11] hypothesized that ranulas could be caused by the constriction of ducts in the early stage of SS, especially when the obstruction is close to the opening. Considering that acinar atrophy and loss occur in the advanced stage, ranulas are rarely due to the decrease of saliva levels[21]. Indeed, only three patients had a ranula after SS diagnosis in our review.

Recurrent parotitis is a common symptom of SS, which is caused by an ascending ductal infection and the assistant of decreased salivary duct lavage[22], whereas ranulas usually happen when saliva production is unaffected. This suggests that ranulas occur earlier than parotitis. In our case, the first manifestation of parotitis developed 10 mo after the unilateral ranula. Besides, the patient reported by Takagi *et al*[10] developed parotitis 9 mo after SS diagnosis, and the patient reported by Lieberman *et al*[9] had no parotitis or parotid gland swelling throughout. Oral lesions are characteristics of Sjögren syndrome in childhood. No parotid mucocele or submandibular gland mucocele has been reported in SS. We hypothesized that this might be the structure of the glands themselves. The duct of the parotid or submandibular gland is covered with thicker glandular tissue and muscle; however,

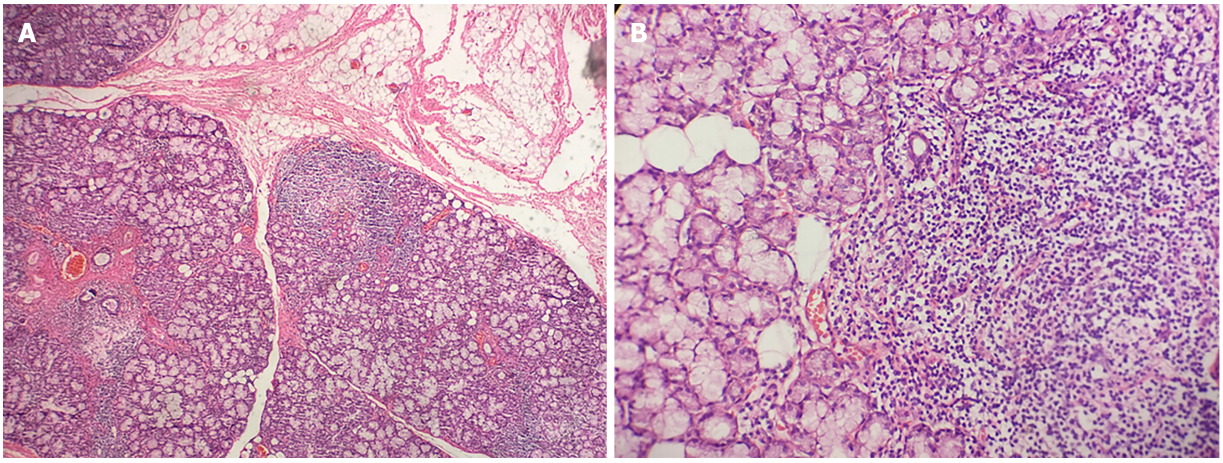

Figure 2 Histopathological findings of the sublingual gland. Chronic multifocal lymphocytic infiltration and ductal epithelial destruction are visible in the sublingual gland. Hematoxylin and eosin staining; magnification: × 40 (A) and × 100 (B).

the sublingual gland is exposed at the base of the mouth.

The ranulas are routinely treated by marsupialization or sublingual gland surgical removal[14]. Patients with new-onset ranulas usually visited stomatology or otolaryngology department, and the doctors would not routinely perform serological examinations or detailed glandular tests, unless patients show other symptoms of autoimmune diseases. Therefore, SS was easily neglected even with the discovery of ranulas. In the five patients diagnosed with ranulas and SS simultaneously, the results of MRI examinations in four patients revealed chronic sialadenitis[8,11], and the surgical pathological specimen of one patient showed lymphocytic infiltration, which prompted the imaging detection of exocrine glands and serological examinations of SS in patients who had not yet developed symptoms such as dry mouth, dry eyes, or parotitis. Thus, we recommend ranula patients to undergo postoperative pathological examination and imaging detection, which can be helpful for early detection of SS. Besides, US is a convenient and inexpensive procedure and should be considered a suitable tool for diagnosing juvenile SS[10].

CONCLUSION

In the present review, we summarize all published papers on SS and ranulas. We hope that these cases will raise the awareness of clinicians that ranulas are early clinical signs of SS. As early diagnosis and early intervention of SS are important to obtain better outcomes, we recommend histopathological test after sublingual adenectomy and imaging detection of exocrine gland for the patients with ranulas.

ACKNOWLEDGEMENTS

We thank the Innovative Research Team of High-level Local Universities in Shanghai.

REFERENCES

1 **Thorne I**, Sutcliffe N. Sjögren's syndrome. *Br J Hosp Med (Lond)* 2017; **78**: 438-442 [PMID: 28783408 DOI: 10.12968/hmed.2017.78.8.438]

2 **Qin B**, Wang J, Yang Z, Yang M, Ma N, Huang F, Zhong R. Epidemiology of primary Sjögren's syndrome: a systematic review and meta-analysis. *Ann Rheum Dis* 2015; **74**: 1983-1989 [PMID: 24938285 DOI: 10.1136/annrheumdis-2014-205375]

3 **Ramos-Casals M**, Solans R, Rosas J, Camps MT, Gil A, Del Pino-Montes J, Calvo-Alen J, Jiménez-Alonso J, Micó ML, Beltrán J, Belenguer R, Pallarés L; GEMESS Study Group. Primary Sjögren syndrome in Spain: clinical and immunologic expression in 1010 patients. *Medicine (Baltimore)* 2008; **87**: 210-219 [PMID: 18626304 DOI: 10.1097/MD.0b013e318181e6af]

4 **Mavragani CP**, Moutsopoulos HM. Sjögren syndrome. *CMAJ* 2014; **186**: E579-E586 [PMID: 24566651 DOI: 10.1503/cmaj.122037]

5 **Morton RP**. Surgical Management of Ranula Revisited. *World J Surg* 2018; **42**: 3062-3063 [PMID: 29750326 DOI: 10.1007/s00268-018-4666-y]

6 **Harrison JD**. Modern management and pathophysiology of ranula: literature review. *Head Neck* 2010; **32**: 1310-1320 [PMID: 20054853 DOI: 10.1002/hed.21326]

7 **Carlini V**, Calcaterra V, Pasqua N, Guazzotti M, Fusillo M, Pelizzo G. Plunging Ranula in Children: Case Report and Literature Review. *Pediatr Rep* 2016; **8**: 6576 [PMID: 28191301 DOI: 10.4081/pr.2016.6576]

8 **Means C**, Aldape MA, King E. Pediatric primary Sjögren syndrome presenting with bilateral ranulas: A case report and systematic review of the literature. *Int J Pediatr Otorhinolaryngol* 2017; **101**: 11-19 [PMID: 28964279 DOI: 10.1016/j.ijporl.2017.07.019]

9 **Lieberman SM**, Lu A, McGill MM. Oral lesions as presenting feature of childhood Sjögren syndrome. *Int J Pediatr Otorhinolaryngol* 2018; **113**: 303-304 [PMID: 29764682 DOI: 10.1016/j.ijporl.2018.05.007]

10 **Takagi Y**, Hashimoto K, Katayama I, Eida S, Sumi M. Juvenile primary Sjögren's syndrome with ranula: is ranula a clinical sign that leads to early detection of Sjögren's syndrome? *Oral Radiol* 2021; **37**: 328-335 [PMID: 32803681 DOI: 10.1007/s11282-020-00473-8]

11 **Sato K**, Yoshida Y, Sakai K, Shibui T, Hashimoto K, Baba A, Nomura T. Sjögren's syndrome and ranula development. *Oral Dis* 2019; **25**: 1664-1667 [PMID: 31141241 DOI: 10.1111/odi.13130]

12 **Katayama I**, Yamazaki S, Nishioka K. Giant mucocele of oral cavity as a mucocutaneous manifestation of Sjögren syndrome. *J Dermatol* 1993; **20**: 238-241 [PMID: 8315114 DOI: 10.1111/j.1346-8138.1993.tb03868.x]

13 **Pinheiro JB**, Tirapelli C, Silva CHLD, Komesu MC, Petean FC, Louzada Junior P, León JE, Motta ACF. Oral Nodular Lesions in Patients with Sjögren's Syndrome: Unusual Oral Implications of a Systemic Disorder. *Braz Dent J* 2017; **28**: 405-412 [PMID: 29297564 DOI: 10.1590/0103-6440201601013]

14 **Delli K**, Spijkervet FK, Vissink A. Salivary gland diseases: infections, sialolithiasis and mucoceles. *Monogr Oral Sci* 2014; **24**: 135-148 [PMID: 24862601 DOI: 10.1159/000358794]

15 **Beckman KA**, Luchs J, Milner MS, Ambrus JL Jr. The Potential Role for Early Biomarker Testing as Part of a Modern, Multidisciplinary Approach to Sjögren's Syndrome Diagnosis. *Adv Ther* 2017; **34**: 799-812 [PMID: 28283891 DOI: 10.1007/s12325-017-0501-3]

16 **Brito-Zerón P**, Baldini C, Bootsma H, Bowman SJ, Jonsson R, Mariette X, Sivils K, Theander E, Tzioufas A, Ramos-Casals M. Sjögren syndrome. *Nat Rev Dis Primers* 2016; **2**: 16047 [PMID: 27383445 DOI: 10.1038/nrdp.2016.47]

17 **Tsuboi H**, Hagiwara S, Asashima H, Takahashi H, Hirota T, Noma H, Umehara H, Kawakami A, Nakamura H, Sano H, Tsubota K, Ogawa Y, Takamura E, Saito I, Inoue H, Nakamura S, Moriyama M, Takeuchi T, Tanaka Y, Hirata S, Mimori T, Matsumoto I, Sumida T. Comparison of performance of the 2016 ACR-EULAR classification criteria for primary Sjögren's syndrome with other sets of criteria in Japanese patients. *Ann Rheum Dis* 2017; **76**: 1980-1985 [PMID: 28330998 DOI: 10.1136/annrheumdis-2016-210758]

18 **Baldini C**, Ferro F, Elefante E, Bombardieri S. Biomarkers for Sjögren's syndrome. *Biomark Med* 2018; **12**: 275-286 [PMID: 29460647 DOI: 10.2217/bmm-2017-0297]

19 **Shen L**, Suresh L, Lindemann M, Xuan J, Kowal P, Malyavantham K, Ambrus JL Jr. Novel autoantibodies in Sjogren's syndrome. *Clin Immunol* 2012; **145**: 251-255 [PMID: 23123440 DOI: 10.1016/j.clim.2012.09.013]

20 **Huzaifa M**, Soni A. Mucocele And Ranula. 2021 Feb 13. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 [PMID: 32809690]

21 **Bayetto K**, Logan RM. Sjögren's syndrome: a review of aetiology, pathogenesis, diagnosis and management. *Aust Dent J* 2010; **55** Suppl 1: 39-47 [PMID: 20553243 DOI: 10.1111/j.1834-7819.2010.01197.x]

22 **Myers EN**, Ferris RL. Salivary gland disorders. Springer Science & Business Media, 2007

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com