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Ultrasound in Patients With Clinically Suspected Submandibular Gland Disease

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Background: The submandibular gland is quite common to be affected by various disease processes in all age groups that may be difficult to differentiate clinically. Its superficial location makes it readily accessible to ultrasound evaluation.

Objective: To evaluate sonographic features of abnormal submandibular gland.

Methods: Ultrasound images and medical records of patients who presented with clinically suspected submandibular gland disease at a single institution were retrospectively reviewed. Demographic data, final diagnoses, further management, and sonographic findings were evaluated.

Results: Eighty-one patients were identified, 56 females and 25 males (mean [SD] age, 53 [16] years; range, 1 - 87 years). The main presenting symptoms were palpable mass (31 [38.3%]) and pain (23 [28.4%]) involving the left (30 [37.0%]), the right (27 [33.3%]), and bilateral submandibular area (24 [29.6%]). Only 6 patients (8.1%) underwent further imaging. The most common final diagnoses were acute sialadenitis (38 [46.9%]), Sjögren syndrome (14 [17.3%]), tumor (6 [7.4%]), and stone (4 [4.9%]). Submandibular glands were normal in 17 of 81 patients (21%); 9 of 17 (52.9%) had abnormal lymph nodes. Among various disease entities, a significant correlation was found between Sjögren syndrome and small gland size, stone and ductal dilatation, and abnormal lymph nodes with enlarged nodal size ($P < .001$).

Conclusions: Two-thirds of the patients had inflammatory/infectious diseases, with tumor and stone in minority. Certain ultrasound findings can suggest diagnosis. Less than 10% underwent further imaging, suggesting that ultrasound can be used to detect and guide further management of submandibular disease.

Keywords: Submandibular gland, Submandibular disease, Salivary, Ultrasound, Sjögren syndrome

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Introduction

Diseases of submandibular gland are quite common in people of all age groups and could indicate variety of conditions. Inflammatory diseases are the most common diseases affecting the submandibular gland.[1, 2] Salivary calculi are most often located in the submandibular gland (60% - 95% of cases),[1,3] whereas salivary gland neoplasms are located in the submandibular glands (10% - 12%).[1]

Patients tend to clinically present with palpable unilateral or bilateral glandular enlargement that may or may not be painful.[4] It is quite difficult to ascertain on physical examination whether such swelling is related to the submandibular gland itself or due to enlargement of an adjacent structure. Clinical examination alone is also not able to differentiate the nature, location, extent and cause of such lesion.

Being highly effective, noninvasive, inexpensive, lack of radiation and easy to perform, salivary gland ultrasound has become widely use among subspecialties to assess salivary gland abnormalities.[5-7] For submandibular gland, ultrasound shows good reliability and high spatial and contrast resolution due to the its superficial location.[5, 8] Furthermore, ultrasound allows both extraglandular and intraglandular lesions to be visualized, localized and differentiated. These lesions may be further characterized as being benign or malignant. Moreover, it can be used to determine the extent of extraglandular component. Ultrasound is the first-line investigation in the assessment of sialolithiasis because of its high specificity and sensitivity.[9, 10] In addition, in the cases of infectious sialadenitis, ultrasound can be used to demonstrate the presence and guide the drainage of abscesses, along with having an important role in the assessment of chronic inflammatory disorders such as Sjögren syndrome.[9]

The purpose of this study is to retrospectively review ultrasound studies in patients with clinically suspected submandibular gland diseases by using histopathology and clinical follow-up as the reference standard. In addition, the authors would like to evaluate whether ultrasonographic findings can suggest or correlate with disease entities.

Methods

Study Population

This cross-sectional retrospective study was approved by the Institutional Review Board prior to data collection. The studied population were patients who had undergone ultrasonography of submandibular gland in consecutive 65-month period (from April 1, 2011, to August 31, 2016) at Ramathibodi Hospital. The inclusion criteria were 1) patients with clinically suspected submandibular gland disease, 2) patients whose medical records were available for review, and 3) patients whose imaging reports and images were available in the picture archiving and communication system (PACS). The exclusion criteria were 1) patients whose clinical and/or imaging data was incomplete or unavailable, 2) patients whose definitive diagnosis was unknown, and 3) patients who had prior surgery/intervention of submandibular gland.

Imaging Technique

The sonographic imaging was completed by residents in radiology and attending radiologists as part of patient care, using Philips iU22 high resolution ultrasound instrument (Philips Medical Instrument, Bothell, WA, US) with linear transducer (L9-3 MHz, L12-5 MHz). The sonographic examination focused on the symptomatic areas and according to the history and physical examination. Imaging planes varied to the characteristics of the lesions. Both the long and short axes of submandibular glands were studied according to our institutional protocol. Power and/or color Doppler imaging was routinely used to demonstrate whether there was internal blood flow signal within the lesions.

Data Collection

The ultrasound images and reports were reviewed by a final-year radiology resident and an attending radiologist with consensus agreement, using the data available in PACS but blinded to medical record. The demographic data included the age, gender, presenting symptoms, and laterality of the symptoms were collected. The sonographic findings of submandibular gland included the size, echotexture, vascularity, contour of the gland, presence of stone and duct dilatation, and presence of extraglandular lymph nodes were collected. Calcification in the main or intraglandular salivary duct that caused ductal dilatation was regarded as intraductal stone, whereas calcification without ductal dilatation was considered intraglandular calcification. Sonographically calcification is an echogenic structure with a posterior acoustic shadow. The clinical history and clinical reports were blinded.

Follow-Up Results

Patients may undergo further imaging modalities, receive medical/conservative treatment, or surgical treatment. Pathology was available to be reviewed in the group who underwent surgical resection. Those who received medical or conservative treatment were followed for at least 3 months with or without further imaging studies such as computed tomography (CT) or magnetic resonance imaging (MRI).

Statistical Analysis

Continuous variables (age) were present as mean, standard deviation (SD), median, and range. Categorical variables (sex and imaging findings) were summarized as count and percentage using Stata version 14 (StataCorp. Version 14. College Station, TX: StataCorp LP; 2015).

Results

Ninety-two patients, 184 submandibular glands, underwent sonography during this 65-month period. Six patients did not have available clinical information, 6 patients lost to follow-up, and 2 patients had previous surgery of submandibular glands.

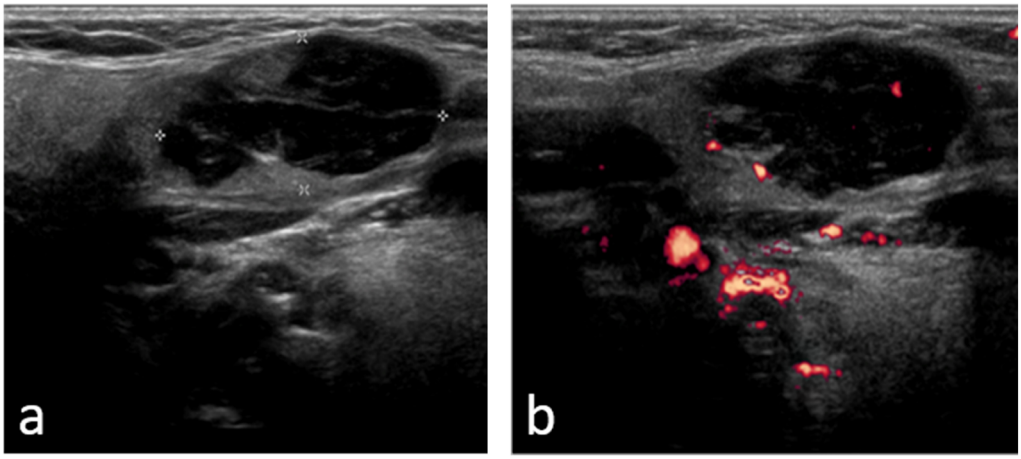
These resulted in 81 patients included in the analysis. The age of the patients ranged from 1 to 87 years (mean [SD], 53 [16] years). Fifty-six patients were female, 25 were male (Supplementary Table S1). The presenting symptoms or indication for ultrasound were palpable mass (31, [38.3%]), pain (23, [28.4%]), suspected Sjögren syndrome (16, [19.7%]), pain and swelling (8 [9.9%]), and swelling alone (3 [3.7%]).

Among these 81 patients, 6 had further imaging; each 2 had plain radiography, sialogram, and MRI (Supplementary Table S2). Final diagnoses were obtained by fine needle aspiration (FNA) alone (n = 1), FNA followed by surgical excision (n = 5), and surgical excision (n = 9). Nonsurgical diagnosis was performed in 66 patients (81.5%) by medical treatment and follow-up.

The final diagnoses were shown in Supplementary Table S3 and Supplementary Table S4. All 81 patients can be characterized into 2 groups; benign (78 [96.3%]) and malignant (3 [3.7%]). There were 56 women (72%) and 22 men (28%) in the benign group, whereas the malignant group had 2 men (66.7%) and 1 woman (33.3%).

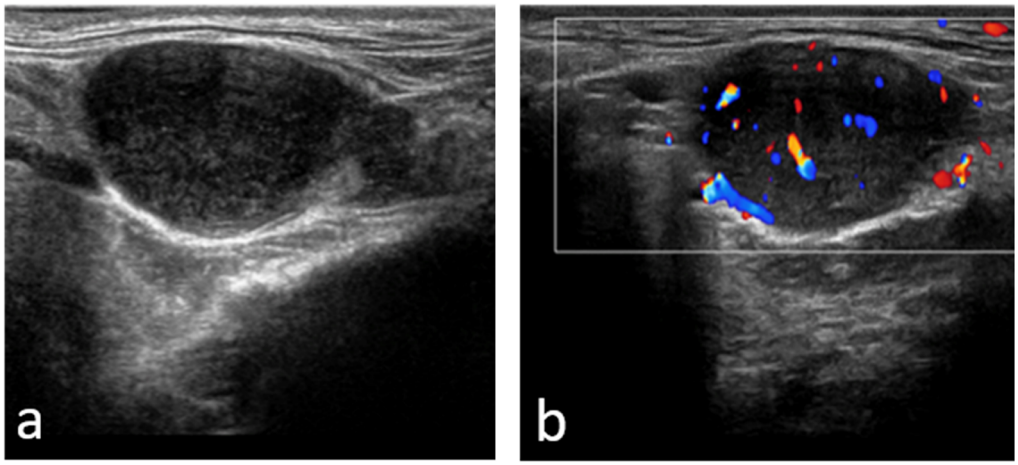
Thirty-one patients presented with palpable mass; 6 of 31 patients were proven to have a mass lesion involving submandibular gland by ultrasound (Figure 1). All 6 patients underwent a biopsy (Supplementary Table S4). In 9 patients, the palpable masses primarily thought to be submandibular diseases, were abnormal lymph nodes with normal submandibular glands (Supplementary Table S3). Pathological diagnoses of lymph nodes were lymphadenitis (n = 6) and reactive lymphoid hyperplasia (n = 2) (Figure 2), and lymphoid proliferation (n = 1). Ultrasound could be used to differentiate between intraglandular and extraglandular lesions in all of our patients.

Figure 1. Mucosa-Associated Lymphoid Tissue Lymphoma



Grey scale (a) and color doppler (b) ultrasound of the right submandibular gland reveals a heterogeneous hypoechoic mass with slight intralesional flow.

Figure 2. Reactive Lymphoid Hyperplasia

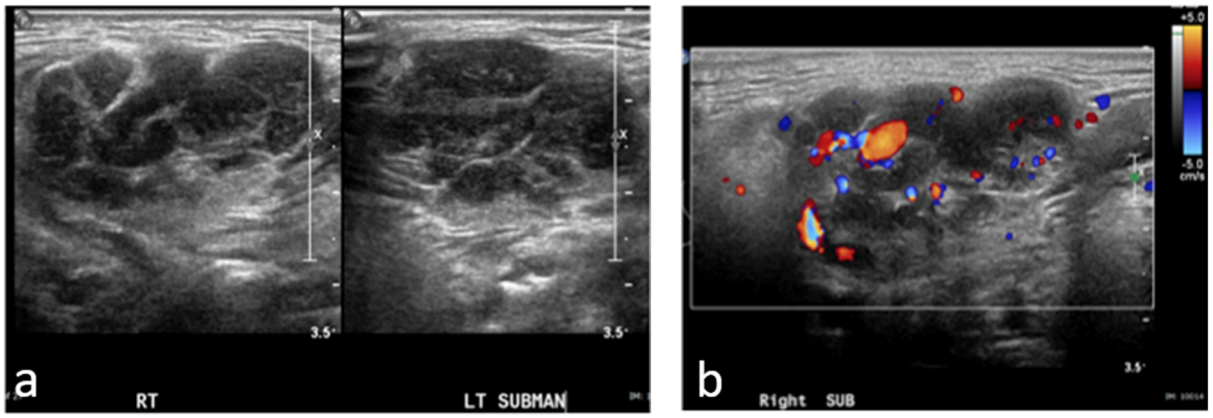


Grey scale (a) and color doppler (b) ultrasound reveals a slightly heterogeneous hypoechoic mass with hypervascularity.

Sixteen of 31 patients who presented with a palpable mass and 50 patients who presented with pain and/or swelling (Supplementary Table S1) were found to have acute sialadenitis (n = 38), calcification detection (n = 4), and normal submandibular gland (n = 8).

In patients with clinically and sonographically suggested acute inflammation, clinical follow-up at least 3 months was used to verify the diagnosis. Among 38 patients with the final diagnosis of acute sialadenitis (Figure 3); 1 of them had an abscess detected by ultrasound, aspiration was performed followed by medication. In 4 patients whom ultrasound revealed calcification; 1 of them was shown on plain radiograph, but the other 3 were not. All 4 patients had main duct (Wharton duct) dilatation; consistent with intraductal stones (Figure 4).

Figure 3. Immunoglobulin G4 -Related Sialadenitis



Grey scale ultrasound (a) reveals enlarged, lobulated, hypoechogenic bilateral submandibular glands. Color doppler scan of the right side (b) shows hypervascularity.

Figure 4. Stone

Grey scale ultrasound reveals a large stone (between cursors) with posterior acoustic shadowing obstructed the Wharton duct, causing ductal dilatation (arrow).

Among 16 patients with clinically suspected Sjögren syndrome, 14 patients had characteristic features of Sjögren syndrome in the submandibular glands on ultrasound (Figure 5). One of these patients underwent a histologic examination which was proved to be Sjögren syndrome. Two patients were diagnosed as chronic sialadenitis by ultrasound, but further clinical and laboratory follow-up did not support Sjögren syndrome.

In 8 patients, submandibular glands were normal. Therefore, a total of 17 patients had a normal submandibular gland by ultrasound.

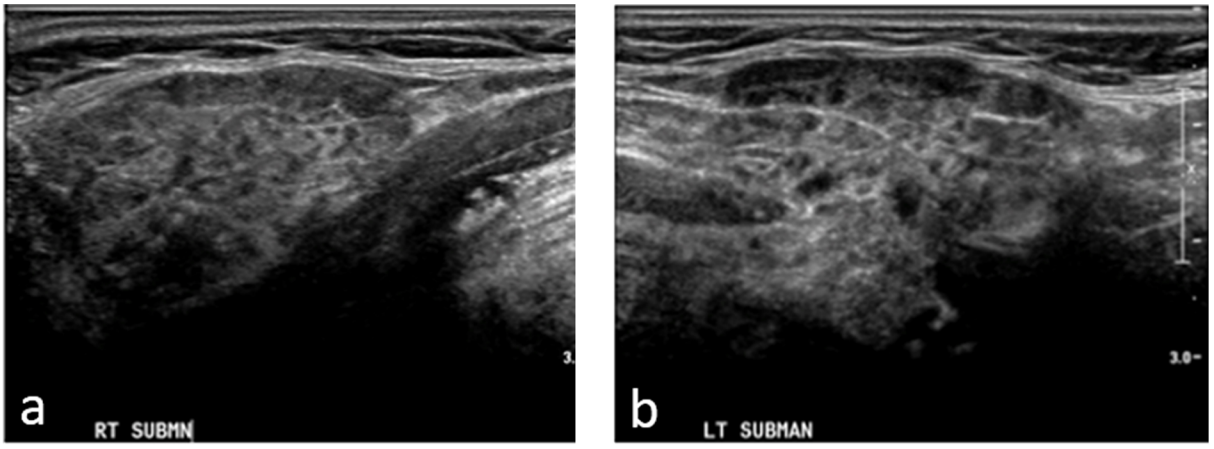
Regarding the laterality of involved submandibular glands, 30 patients had abnormalities on the left side, 27 patients on right side, and 24 patients had the diseases bilaterally.

The correlation between ultrasound findings and disease entities was revealed (Table 1). Regarding the gland size; only Sjögren syndrome cases were found to have small gland size whereas majority (4 of 6 [66.67%]) of the tumor cases and 24 of 38 (63.16%) of acute sialadenitis cases revealed enlarged gland size ($P < .001$). For the gland echogenicity; all cases of stones and majority (9 of 14 [64.29%]) of Sjögren syndrome revealed heterogenous pattern, whereas majority of other diseases showed homogenous pattern ($P = .001$). Glandular vascularity did not show any significance among diseases ($P = .055$) and was mostly normal. In term of the gland contour; majority (4 of 6 [66.67%]) of the tumor cases exhibited lobulated contour whereas majority of other diseases had smooth contour ($P = .016$). Ductal dilatation was observed in all of the cases of stones, but not in other diseases ($P < .001$). There was 1 case of tumor in which the duct was obstructed by the tumor.

Among the cases with the final diagnosis of abnormal lymph nodes (n = 9), we found that majority (7 of 9 [77.78%]) of such nodes were enlarged, whereas almost all of the lymph nodes that were accompanying other diseases were normal in size ($P < .001$). In addition, the submandibular glands in these 9 cases were all normal.

In summary, about two-thirds (66.7%) of the patients with clinically suspected submandibular gland diseases had inflammatory/infectious diseases of the gland. Stone was found in 4 cases (7.4%), all of which had ductal dilatation. Seventeen patients (21%) had normal submandibular gland by ultrasound; 9 of 17 (52.9%) had abnormal lymph nodes that may account for the clinical palpable masses.

Figure 5. Sjögren Syndrome



Grey scale ultrasound (a, b) of bilateral submandibular glands exhibit typical findings of Sjögren syndrome: many hypoechogenic nodules inside the parenchyma of a rather small-sized submandibular glands.

Table 1. Ultrasound Findings in the Patients With Submandibular Gland Diseases

Ultrasound Finding	No. of Final Diagnose					*P* Value*
	Acute Sialadenitis (n = 38)	Stone (n = 4)	Tumor† (n = 6)	Abnormal LN (n = 9)	Sjögren (n = 14)	
Gland size						
Normal	24	3	2	9	9	< .001
Enlarged	14	1	4	0	0	
Small	0	0	0	0	5	
Gland echogenicity						
Homogeneous	22	0	5	9	5	.001
Heterogeneous	16	4	1	0	9	
Gland vascularity						
Normal	27	2	6	9	13	.055
Increased	11	2	0	0	1	
Gland contour						
Smooth	31	4	2	9	0‡	.016
Lobulated	7	0	4	0	0‡	
Ductal dilatation	0	4	1	0	0	< .001
Extraglandular LNs						
Normal	35	4	5	2	13	< .001
Enlarged	3	0	1	7	1	

Abbreviation: LN, lymph node.

* *P* value from Fisher exact test. *P* value indicates statistical significance ($P < .05$).

† In tumor cases, the parameters of ultrasound findings shown in this table are findings of the submandibular glands, not the tumors.

‡ The gland contour in Sjögren syndrome was not recorded in the reports. We did not try to estimate the gland contour in the images, since the nature of this disease may show ill-defined contour that make it difficult to outline.

Discussion

Ultrasonography/sonography can be used by primary physicians and specialists to assess the salivary glands. Submandibular gland is one of the major salivary glands that is easily evaluated by ultrasound due to its superficial location. Only 6 patients (8.1%) in our study required another imaging modality in additional to an ultrasound. Clinicians were comfortable using the ultrasound results to guide their decisions for further intervention and treatment.

In terms of treatment, we found that 49 patients (60.5%) received specific treatment (eg, surgery and specific medical treatment). Other 32 patients (39.5%) received symptomatic treatment and/or reassurance and advice. These may be due to the time interval between the first visit and the ultrasound examination which may be long. The patients may seek specific treatment themselves which was not recorded in the hospital file. At the time of ultrasonographic examination they may be partially or completely treated. The ultrasound findings may be diminished and the clinical setting

was much improved, resulted in no further specific treatment except symptomatic treatment and/or advice. In addition, many patients had normal ultrasound of submandibular glands at first, so no specific treatment was needed.

Inflammatory Diseases

Normally, the echotexture of submandibular gland is homogeneous and slightly higher than adjacent neck muscles.[11] In cases of acute inflammation, submandibular glands are usually enlarged compared with healthy contralateral side, and the echogenicity of the gland becomes more heterogeneous. When abscesses are presented, the echotexture is focally cystic and there may be regional lymphadenopathy. In our study, majority of acute sialadenitis showed significant correlation with enlarged glandular size, homogenous echogenicity, and smooth contour. Increased vascularity showed some correlation with acute sialadenitis but not statistically significant ($P = .055$).

Sjögren syndrome is an autoimmune disease primarily targeting the exocrine glands, and ultrasound is imaging modality of choice for submandibular salivary gland assessment over other imaging modalities.[5, 12, 13] The progression of ultrasound changes reflects the various stages of this inflammation and correlates with histologic involvement.[2] Often, the glands are heterogeneous because of inflammation. In pronounced cases, many hypoechoic lesions or nodules can be shown sonographically and the glands become fibrotic and atrophic. Sjögren syndrome in our study revealed uniquely significant correlation with small gland size whereas other diseases in this study did not show this finding ($P < .001$). Also, there was significant correlation with heterogeneity of the glandular parenchyma. These findings corresponded with previous studies, and suggested that our cases of Sjögren syndrome were chronic cases.

Sialolithiasis

More than 80% of salivary calculi are localized within body of submandibular gland or the Wharton duct.[7] The submandibular gland itself is more likely to produce sialolithiasis due to its anatomical position, its longer and more convoluted canal (ascendant and more sharply angle), and the generation of mucin-rich alkaline saliva. All of these make it more difficult for the saliva to flow against gravity.[14-16] The exact localization of a calcification is important for optimal therapy.[14, 15, 17]

On ultrasound, stones appear as hyperechoic curvilinear foci casting posterior acoustic shadowing. When stone is smaller than 2 mm, this shadow may be missing. Normal intraglandular ducts are only rarely visualized.[7] In symptomatic sialolithiasis, a concomitant ectasia of the ducts and inflammatory changes is often visualized sonographically, along with hypervascularization detected by color doppler scan.[7, 18] Therefore, ultrasound is usually successful in differentiating between intraductal stones that causing ductal dilatation (obstruction) and intraglandular calcifications. Intraductal localized salivary calculi are more prevalent than intraglandular calculi.[3]

About 20% to 40% of salivary calculi are not radiopaque.[7, 19] Our results show that ultrasound is superior to plain film in the detection of submandibular gland calculi due to its ability to detect nonopaque stones. All of our cases with calcification (4 cases) had accompanying ductal dilatation, indicating that such calcifications are all intraductal stones. We did not find intraglandular calcification in this study. We therefore would like to suggest that when the patients present with submandibular gland symptoms and dilated duct, sialolithiasis should be considered.

Space-Occupying Lesions

Salivary gland tumors are more frequent in parotid gland, with only 14% of salivary gland tumors occurring in submandibular gland. However, there is a greater

incidence of malignancy of submandibular gland tumors; approximately half of submandibular gland tumors are malignant compared with 10% of all parotid gland tumors.[9] Pleomorphic adenoma is the most common salivary gland neoplasm (24% - 71%) and being the most common submandibular gland neoplasm as well.[2, 15, 20, 21]

On ultrasound, these tumors are well-defined with rather-homogenous hypoechogenicity and lobulated margin.[9, 15] All tumors in our study were well-defined heterogeneously-hypoechoic with increased vascularity. Two cases of pleomorphic adenomas in this study showed ultrasound appearance similar to other tumors, and therefore cannot be diagnosed sonographically.

Primary lymphoma rarely occurs in the submandibular gland and the gland is usually involved secondarily via hematogenous spread.[9] Another cause of lymphoma in salivary gland is the increased incidence in Sjögren syndrome.[7] The ultrasound findings of lymphoma are rarely described. Our study found 2 cases of primary lymphoma and ultrasound findings of heterogeneous hypoechoic masses with hypervascularization, not differ from other tumors found in this study.

Metastases to submandibular gland are rare, occurring mainly via hematogenous spread. They are mainly from head and neck tumors or melanoma. The ultrasound findings of submandibular gland metastasis are not well-described.[9] Our study found only 1 case of submandibular gland metastasis from nearby tonsillar carcinoma. The ultrasound findings demonstrated a large heterogeneous hypoechoic lesion occupying almost entire submandibular gland, not differ from other tumors found in this study. The adjacent pathologic lymph nodes were also detected.

Not all space-occupying lesions are tumors. One mass-like lesion in our study was reactive lymphoid hyperplasia seen as a well-defined heterogeneous hypoechoic lesion with hyperemia; the findings that were similar to other tumors in this study.

In summary, our study cannot differentiate between benign and malignant masses as well as the pseudotumor. Hence, ultrasound could be used to guide further intervention or further imaging.

No Sonographic Abnormality of Submandibular Gland

In this series; no abnormality was detected in submandibular glands of 17 patients totally, but there were abnormalities in the adjacent lymph nodes in 9 cases. The pathologic lymph nodes appear enlarged in 7 of 9, in which they appeared round and loss of normal fatty hilum.

Limitations

Certain limitations deserve to be acknowledged. First, this is a routine-to-research study which is retrospective in nature. Some data may not be completed. Second, the reviewers used static images along with the reports available in PACS, the reviewers did not perform all studies themselves. Third, the small number of patients (n = 81) hence limited the statistical analysis. Further study with larger number of patients will provide more impact information.

Conclusions

In patients with clinically suspected submandibular gland diseases in this study; about two-thirds were due to inflammatory/infectious diseases of the gland. Stone was found in 4 cases and all showed ductal dilatation. About one-fifth of patients had normal submandibular gland by ultrasound; half of them had abnormal lymph nodes. Only 6 patients (8.1%) in our study required another imaging modality in additional to an ultrasound. Clinicians were comfortable using the ultrasound results to guide their decisions for further intervention and treatment. Ultrasound should be performed on both sides of the submandibular glands because many diseases occur bilaterally. When comparing among diseases, certain

ultrasound appearances of submandibular glands showed significant correlation with some disease entities. Almost all cases of ductal dilatation correlated with stone, and small glandular size correlated with Sjögren syndrome in this study.

Article Information

Ethics Approval

This research project was approved by the institutional review board of the Faculty of Medicine Ramathibodi Hospital, Mahidol University. The protocol number is ID 08-59-55 (MURA2016/541, approved on September 29, 2016).

Financial Support

No financial support was provided for the study.

Conflict of Interest

The authors declare no competing interests.

Supplementary Information

Supplementary Table S1-S4 download from https://he02.tci-thaijo.org/index.php/ramajournal/article/view/270410/184989

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