Ultrasound Characterization of Salivary Lesions

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ABSTRACT

Evolution in ultrasound technology leads to birth of high frequency, high resolution linear transducers which in turn revolutionized the imaging of superficial structures. The majority of cases presenting to clinician in day-to-day practice as facial lumps or neck lump could be evaluated using ultrasound and help in imaging of salivary gland lesions. The age of the clinical presentation and morphological characteristics of lesions on ultrasound helped us in making confident diagnosis which was correlated on fine needle aspiration cytology/histopathology studies.

Keywords: Salivary glands, Ultrasound, Parotid glands, Submandibular glands, Sialadenitis.

INTRODUCTION

The protocol for imaging of salivary glands in Western countries includes–nonenhanced and contrast-enhanced computed tomography (CT), nonenhanced and contrast-enhanced magnetic resonance (MR) imaging and sialography (also MR sialography).1,2 In general, CT is considered the best single method for assessment of inflammatory diseases and MR imaging is considered the best single method for assessment of salivary gland tumors.1,3 According to Yousem et al2 ultrasonography (US) is not preferred modality in Western countries; but in Europe and Asia, US is widely accepted as the first imaging method for assessment of lymph nodes and soft tissue diseases in the head and neck, including major salivary glands.4-7 In assessment of large tumors and lesions located in deep portions of the glands, 5 to 10 MHz transducers may be useful.12 Entire salivary glands and all lesions have to be evaluated in at least two perpendicular planes during a US examination. The whole neck should also be scanned to assess lymph nodes and search for concomitant or related disease.

NORMAL ULTRASOUND ANATOMY OF SALIVARY GLAND

Parotid Gland

The parotid gland is located in the retromandibular fossa, anterior to the ear and sternocleidomastoid muscle. Parts of the superficial lobe cover the ramus of the mandible and the posterior part of the masseter muscle. The border between the superficial and deep parotid lobes is created by a plane in which the facial nerve and its branches are located (Figs 1A and B). Branches of the facial nerve are not visible at US. Parts of the trunk of this nerve may be demonstrated only with high frequency probes (above 10 MHz).13 Therefore, the retromandibular vein, which usually lies directly above the trunk of the facial nerve,14,15 is used as a US landmark separating the superficial and deep lobes of the parotid gland. The deep parotid lobe can be visualized only partially at US.

The echotexture of the major salivary glands, including the parotid gland, is generally homogeneous and hyperechoic in comparison to adjacent muscles. The echogenicity of the parotid gland is based on the amount of intraglandular fatty tissue (Figs 2A and B).

After leaving the parotid gland, the main excretory duct (Stensen’s duct) lies on the masseter muscle, about 1 cm below the zygomatic arch, then crosses the buccal muscle...
and has its orifice in the parotid papilla at the level of the upper second molar. The length of the Stensen’s duct usually varies between 3 and 5 cm. Along the course of the Stensen’s duct in the soft tissues of the cheek, an accessory parotid gland may be found, unilaterally or bilaterally.

The accessory parotid gland may also be the site of salivary gland tumors, benign or malignant.16-18

In the parenchyma of the parotid gland, lymph nodes may be found.19 They are localized mainly in the area of the upper and lower poles of the gland. Normal intraparotid lymph nodes may be oval or have a longitudinal shape. Almost 60% of parotid nodes have a short axis-to-long axis ratio greater than 0.5. A well preserved hyperechoic hilum is one of the important criteria for the normality of parotid lymph nodes. Their short axis should not exceed 5 to 6 mm in the normal state.6,7

Submandibular Gland

The submandibular gland lies in the posterior part of the submandibular triangle. The sides of the submandibular triangle are created by the anterior and posterior bellies of the digastric muscle and the body of the mandible. The space anterior to the submandibular gland is occupied by connective tissue and lymph nodes. Generally, the shape of the submandibular gland in longitudinal and transverse sections is close to a triangle (Figs 3A and B).

The submandibular excretory duct (Wharton duct) runs from the area of the submandibular gland hilum at the level of the border of the mylohyoid muscle, then bends around the free part of the mylohyoid muscle and extends to its orifice at the sublingual caruncle along the medial part of the sublingual gland.

Sublingual Gland

The sublingual gland lies between the muscles of the oral cavity floor: the geniohyoid muscle, intrinsic muscles of the tongue and hyoglossus muscle (medially) and the mylohyoid muscle. Its lateral side is adjacent to the mandible. On transverse sections, the shape of the sublingual gland is close to an oval; on sections parallel to the body of the mandible, the shape is longitudinal and lentiform (Figs 4A and B).
INFLAMMATORY DISEASES

Inflammatory diseases are the most common diseases affecting the major salivary glands.\textsuperscript{1,3}

Acute Inflammation

Acute inflammation presents clinically as painful swellings of the salivary gland and are often bilateral.

Viral salivary gland infections are the most common in children. A particular predilection for the salivary glands is shown by mumps virus and cytomegalovirus.\textsuperscript{20} Acute bacterial infections are usually caused by \textit{Staphylococcus aureus} or oral flora.\textsuperscript{21}

In acute inflammation, salivary glands are enlarged and hypoechoic. They may be inhomogeneous; may contain multiple small, oval, hypoechoic areas; and show increased vascularity (Fig. 5).\textsuperscript{9,22-25} Enlarged lymph nodes with increased central blood flow may be observed in acute inflammation of salivary glands.\textsuperscript{26}

Abscess

During acute sialadenitis, abscess formation may take place. Predisposing factors include dehydration and excretory duct obstruction caused by stones or fibrosis.\textsuperscript{27} At clinical examination, abscesses may be difficult to detect. They usually manifest as painful swelling of the salivary gland with skin reddening.\textsuperscript{28}

At US, abscesses are hypoechoic or anechoic lesions with posterior acoustic enhancement and unclear borders.\textsuperscript{22,28} Central liquefaction maybe distinguished as an avascular area or identified by means of moving debris (Fig. 6).\textsuperscript{9} Organized abscesses may be surrounded by a hyperechoic ‘halo’.\textsuperscript{22} US guidance is helpful for therapeutic drainage.\textsuperscript{28,29}

Chronic Sialadenitis

Chronic sialadenitis is clinically characterized by intermittent swelling of the gland, often painful, that may or may not be associated with food.\textsuperscript{30} In chronic inflammation, salivary glands are normal sized or smaller, hypoechoic, and inhomogeneous and usually do not have increased blood flow at US.\textsuperscript{9,22,24}

At US, chronic and sometimes acute sialadenitis in children as well as acalculous submandibular gland sialadenitis in adults have also been described as showing multiple small, round or oval, hypoechoic lesions distributed throughout glandular parenchyma.\textsuperscript{23,25,31} The differential diagnosis in such cases includes sarcoidosis and other granulomatous diseases, Sjogren’s syndrome, disseminated lymphoma, hematogenous metastases, and benign lymphoepithelial lesions in human immunodeficiency virus (HIV)-positive patients.\textsuperscript{32-35}
Chronic Sclerosing Sialadenitis

A special form of chronic sialadenitis that may mimic a malignant lesion, both clinically and at imaging, is chronic sclerosing sialadenitis (Kuttner’s tumor).36,37 In Kuttner’s tumor, diffuse involvement of the salivary gland (usually the submandibular gland) may occur, with multiple small hypoechoic foci scattered on a heterogeneous background of salivary tissue visible at US.36 In all doubtful cases, verification with FNA/biopsy is recommended.38,39

GRANULOMATOUS SIALADENITIS

Granulomatous sialadenitis occurrence is rare.20 US features of granulomatous sialadenitis are nonspecific: single or multiple hypoechoic areas in an enlarged or normally sized gland or diffuse hypoechoic areas are noted.9,12,19,40-43

Mycobacterial disease of major salivary glands may manifest as a salivary gland mass, clinically indistinguishable from a neoplasm.44 In the parenchymal type of tuberculosis, Chou et al45 described focal, intraparotid, anechoic areas that might have a cavity or cavities within them. In necrotic caseous cavities, which appear very hypoechoic, no color flow can be detected at US, in contrast to most salivary tumors.45 Salivary gland actinomycosis may mimic a malignant tumor at US; it may manifest as a hypoechoic area with ill-defined margins.46

LYMPH NODES IN SIALADENITIS

In acute or chronic inflammation, lymph nodes may be enlarged; however, their normal echo structure (homogeneous cortex and hyperechoic central hilum) is preserved.

Sialolithiasis

Salivary stones are most often located in the submandibular gland (60-90% of cases) and may be multiple.47-50 Parotid glands are affected in about 10 to 20% of cases.51 On classic radiographs, intraglandular and small stones may be missed, and only about 20% of sialoliths are radiopaque.52 CT allows visualization of large stones but without their precise localization and without the possibility of assessment of the ducts.53

The standard technique for imaging of the submandibular duct and the intraglandular ductal system remains digital sialography.54 A novel, noninvasive, promising method appears to be MR sialography, which also gives very good results in detection of sialoliths.2,54,55

US is a noninvasive method, well-established in cases of clinical suspicion of sialolithiasis, and is used as a primary modality, particularly in Europe.51,54 Although some authors claim that sialoliths smaller than 2 to 3 mm may be overlooked because of the absence of acoustic shadow, these articles are from the 1980s and currently used machines have better resolution and detection possibilities.56,57 Sialolithiasis causes partial or total mechanical obstruction
of the salivary duct, which results in recurrent swelling of a salivary gland during eating and may be complicated by bacterial infection.20,48

Sialoliths in the distal part of the submandibular duct (Wharton duct) may be palpable in the floor of the mouth. However, sialoliths in the proximal portion of the duct or in the parenchyma of salivary glands may be demonstrated only radiologically.

US features of sialolithiasis include hyperechoic foci with distal posterior acoustic shadowing, which represent stone.22 In symptomatic cases with duct occlusion, dilated excretory ducts are visible (Figs 7A and B).22

When sialolithiasis of the submandibular gland is suspected, US may demonstrate whether the stone is located in the glandular parenchyma or in the Wharton duct.58 This distinction is essential for choosing the method of treatment.

In chronic ductal sialolithiasis complicated by chronic or recurrent inflammation, the gland may lose its function. At this stage of disease, stones located in a nondilated duct may be difficult to demonstrate. In about 50% of patients, sialolithiasis coexists with inflammation.23 Hyperechoic bubbles of air mixed with saliva may mimic stones in the Wharton duct and thus be a diagnostic pitfall.19

**SIALOSIS**

Sialosis is a noninflammatory, non-neoplastic, recurrent, painless salivary gland swelling, usually bilateral, which most often concerns the parotid glands. Sialosis has been described in connection with endocrine diseases, malnutrition, hepatic cirrhosis, chronic alcoholism or different deficiency diseases (e.g. avitaminoses).20

US reveals enlarged, hyperechoic salivary glands with a poorly visible deep lobe but without focal lesions.9

**Sjogren’s Syndrome**

Sjogren’s syndrome is a chronic autoimmune disease predominantly affecting women over 40 years of age. It is characterized by intense lymphocytic and plasma cell infiltration and destruction of salivary and lacrimal glands.59 Major clinical symptoms include a dry mouth and eyes. Advanced stages of Sjogren’s syndrome may be recognizable at US examination of the parotid and submandibular glands.60 The disease may affect all salivary glands.

US features of advanced Sjogren’s syndrome include inhomogeneous echotexture of the gland with scattered multiple small, oval, hypoechoic or anechoic areas, usually well-defined, and showing increased parenchymal blood flow on color Doppler studies (Fig. 8).9,32,61

Hypoechoic or anechoic areas are believed to represent infiltration by lymphatic cells, destroyed salivary parenchyma and dilated ducts.

Sjogren’s syndrome is frequently associated with both reactive and neoplastic lymphoproliferative disease.62 Further US monitoring for early detection of possible lymphomatous change is required in patients with Sjogren’s syndrome.63,64 Biopsy is recommended for lesions exceeding 2 cm or fast-growing lesions.9

Non-Hodgkin lymphoma manifesting as small multiple nodular disseminations with hypervascularization in the salivary gland has been reported.34,65 In addition, bilateral inflammation (acalculous), granulomatous disease (e.g. sarcoidosis), hematogenous metastases, and benign lymphoepithelial lesions in HIV-positive patients should be taken into consideration in cases of multiple hypoechoic areas scattered in salivary gland parenchyma.23,25,33,35,42,43
Salivary gland neoplasms are relatively rare. Most of them are benign (70-80%) and found in the parotid glands (80-90%). About 10 to 12% of all salivary gland neoplasms are located in the submandibular glands, but almost half of these neoplasms may be malignant.3,66

Benign Neoplasms

The most common benign neoplasms of major salivary glands are pleomorphic adenomas (mixed tumor) and Warthin tumors (adenolymphoma, cyst adenolymphoma, papillary cystadenoma lymphomatosum). Clinically, they manifest as slow growing painless masses.67

Pleomorphic Adenoma

Pleomorphic adenomas occur most often in the parotid gland (60-90%) in people in the fourth and fifth decades of life but may arise at any age.3,66,68 There is a slight predominance in women.66

Pleomorphic adenomas are usually solitary and unilateral.3,66,68 They grow slowly and may be asymptomatic. Nontreated pleomorphic adenomas may undergo malignant transformation after decades.3,68 In exceptional cases, pleomorphic adenomas may be clinically aggressive; they may metastasize and even be fatal.20,69,70

At US, pleomorphic adenomas are hypoechoic, well-defined, lobulated tumors with posterior acoustic enhancement and may contain calcifications.71-73 The feature of lobulated shape is being emphasized in differential diagnosis (Figs 9A and B).73

Vascularization in pleomorphic adenomas is often poor or absent (even when the sensitive power Doppler mode is used) but may be abundant (Figs 9A and B).71,73,74 After inadequate surgery, pleomorphic adenomas often recur, usually multifocally.75

Warthin Tumor

Warthin tumor is the next most common benign salivary neoplasm (5-10% of all benign salivary neoplasms).66,68 It arises most often in men in the fifth and sixth decades of life.66,68,76 The relationship between smoking and development of Warthin tumors has been proved.57

Warthin tumor is usually solitary, unilateral, and slow growing. In about 10 to 60% of cases, tumors may occur bilaterally or multifocally, sometimes metachronously, growing and manifesting clinically at different times.3,68,77,78 Sporadically, the epithelial component of Warthin tumor may undergo malignant transformation.68,79

At US, Warthin tumors are oval, hypoechoic, well-defined tumors and often contain multiple anechoic areas.25,74,78,80 Warthin tumors are often hypervascularized (Fig. 10).

Diagnosis of a Warthin tumor may be supported by results of technetium-99m scintigraphy, which reveals a ‘hot’ tumor because of the increased uptake of the tracer by the tumor.81

Lobulated shape in pleomorphic adenomas and anechoic areas in Warthin tumors, although common, are not pathognomonic and may be found in many other lesions, including malignancies.73,74

Other Benign Tumors

Other benign tumors (e.g. oncocytoma, basal cell adenoma) occur less frequently in the salivary glands. Their differentiation is not possible with US. Among nonepithelial lesions, hemangiomas, lipomas and neurinomas or schwannomas (Fig. 11) may be found in salivary glands.12,87-91

Hemangiomas, the most frequent tumors in infants, may manifest as heterogeneous lesions with sinusoidal spaces and calcifications representing phleboliths (Figs 12A and B).88

Hemangioendothelioma (HAE) of the parotid gland is a benign tumor that presents in infancy as a large, rapidly growing mass that is either small or not noticed at birth, but becomes apparent soon after88 (Fig. 13).

Lipomas are usually oval and hypoechoic with sharp margins and hyperechoic linear structures regularly distributed within the lesion in a striated or feathered pattern.9,92

MALIGNANT NEOPLASMS

The most common malignant neoplasms occurring in salivary glands are mucoepidermoid carcinoma and adenoid cystic carcinoma.94 Squamous cell carcinoma, acinic cell carcinoma, and adenocarcinoma are less common.
Less than 30% of focal lesions in the parotid gland are malignant, whereas almost 50% of focal lesions in the submandibular gland are malignant.\textsuperscript{3,66} Unlike benign salivary neoplasms, malignant tumors may grow rapidly, may be tender or painful at palpation, and may cause facial nerve paresis or paralysis.\textsuperscript{3,20,94}

Mucoepidermoid carcinoma occurs mostly between 30 and 50 years of age. The macroscopic appearance of the tumor, and similarly its imaging features, depend mostly on the level of malignancy.\textsuperscript{8,20}

Well-differentiated tumors may be similar to benign tumors at US.\textsuperscript{8} Adenoid cystic carcinoma, which is a slowly
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Fig. 11: Sonography of the right parotid gland showed a 14 × 22 mm hypoechoic, well-defined mass within the parotid gland. It showed a homogenous and well-encapsulated appearance. These ultrasound images favor a diagnosis of a benign tumor of the parotid salivary gland. Biopsy of the mass showed it to be parotid gland schwannoma (the tumor having arisen from the facial nerve within the parotid).

Figs 12A and B: (A) Gray scale ultrasound image demonstrates heterogeneous predominantly hypoechoic enlarged right parotid gland (arrows) compared to the left parotid gland, (B) color Doppler image shows hypervascularity of the right parotid gland favors a parotid hemangioma.

Fig. 13: Ultrasound showed a homogeneous mass enlarging and replacing most or all of the visualized parotid gland, with a lobular internal structure, fine echogenic internal septations. Color Doppler imaging showed extremely high vascularity within the mass favors hemangioendothelioma of parotid glands.

growing tumor, shows a particular tendency to nerve infiltration (and thus pain), and late metastases are frequent.20

Classic US features of poorly differentiated or advanced malignant neoplasms of salivary glands are like those in other organs or tissues.

US features of malignant salivary neoplasms include the following: an irregular shape, irregular borders, blurred margins, and a hypoechoic inhomogeneous parenchyma.8,19,25,41,95,96 However, malignant tumors may also be homogeneous and well-defined.18,73,96 The internal structure of a malignant tumor at US may be not only solid but also cystic or cystic with a mural solid nodule.85 Malignant tumors may have a lobulated shape, similar to that of pleomorphic adenomas.96

Vascularization of malignant tumors is not pathognomonic, and assessment with color Doppler power Doppler US does not allow reliable differentiation between benign and malignant salivary gland tumors.72,76
Schick et al\textsuperscript{72} report that high vascularization and high systolic peak flow velocity should raise the suspicion of malignancy (Figs 14A and B). Bradley et al\textsuperscript{97} concluded that tumors demonstrating an increased intratumoral vascular resistance index have an increased risk of malignancy.

The presence of metastatic-appearing lymph nodes accompanying a tumor in the salivary gland strongly suggests a malignancy.

**METASTASES**

Salivary glands are very uncommon sites of metastases. Primary tumors metastasizing to salivary glands may be located in the head and neck region, as well as in more distant parts of the body. Melanoma spinocellular cancer, breast cancer, and lung cancer may produce metastases to intraparotid lymph nodes.\textsuperscript{99-103} Extremely rare are metastases from renal cancer.\textsuperscript{100,104-106}

At US, metastases may be well-defined and oval.\textsuperscript{9} It may be difficult to differentiate multiple metastatic lesions from some patterns of inflammation, Sjogren’s syndrome and granulomatous disease at US.\textsuperscript{23,25,32,33,42,43}

**LYMPHOMA**

Salivary glands may also be affected by lymphoma.\textsuperscript{34} However, primary involvement of salivary glands is rare; they are usually one of the sites of systemic disease.

Clinically, salivary lymphomas most often manifest as a painless, progressive swelling.\textsuperscript{107,108} They are usually associated with autoimmune disease, most often with Sjogren’s syndrome, sometimes also with rheumatoid arthritis.\textsuperscript{62-64,109}

At US of cases of lymphoma in the salivary gland, one may observe a solitary, hypoechoic, homogeneous or inhomogeneous lesion, which is oval or lobulated or has irregular margins and sometimes contains echogenic septa or stripes (Fig. 15).\textsuperscript{34,110,111} However, these features are not pathognomonic, and lymphoma may not be reliably differentiated from other neoplastic or non-neoplastic salivary gland tumors with US.

A pattern of multiple hypoechoic lesions with increased blood flow may also be seen.\textsuperscript{34,111} Such a pattern requires differentiation from inflammation, Sjogren’s syndrome, granulomatous disease (e.g. sarcoidosis), and hematogenous metastases.\textsuperscript{23,25,32,33,42,43}

In cases of lymphoma, solitary or multiple salivary gland lesions sometimes associated with microcysts may be observed at CT or MR imaging.\textsuperscript{63,109}

**CYSTS**

Simple cysts are uncommon in salivary glands. They may be congenital or acquired. Some acquired cysts develop due to obstruction of the salivary ducts in the presence of a tumor, stones, or inflammation.\textsuperscript{3} Clinically, they usually manifest as a painless swelling but may be tender when infected.\textsuperscript{41}

US features of a cyst are well-defined margins, anechoic content, posterior acoustic enhancement and avascular at power Doppler or color Doppler imaging (Fig. 16).\textsuperscript{22}

Benign lymphoepithelial lesions in HIV-positive patients may manifest as multiple cysts.\textsuperscript{35}

**EFFECTS OF IRRADIATION**

The major salivary glands are often irradiated during radiation therapy of head and neck neoplasms. A major adverse effect of such treatment is xerostomia caused by functional and structural impairment of salivary parenchyma.\textsuperscript{11,115} Loss of salivary gland function significantly diminishes the patient’s quality of life.\textsuperscript{116}
The most useful method for evaluation of salivary excretory function remains scintigraphy, especially single photon emission CT (SPECT).\textsuperscript{10,11} Carbon 11–methionine positron emission tomography (PET) offers new possibilities for studying the individual response of major salivary glands to irradiation.\textsuperscript{117} After irradiation, salivary glands become hypoechoic and inhomogeneous at US. The salivary glands enlarge in the acute phase and later become smaller because of atrophy.\textsuperscript{19,118,119}

TRAUMA

Traumatic injuries of the salivary glands occur most often in the parotid gland because the other major salivary glands are protected by the mandible. After salivary gland trauma, US may demonstrate a hematoma, other fluid collections (e.g. a sialocele), or a fistula in the parotid gland or surrounding structures.\textsuperscript{13,19,120,121} Suspected damage to the facial nerve or Stensen’s duct warrants application of other imaging modalities (CT, MR, sialography).\textsuperscript{19}

CONCLUSION

US is a valuable and useful method for diagnosis of salivary gland diseases. Not only does it enable confirmation or exclusion of the presence of a mass, but in many cases the nature of underlying disease may also be suggested on the basis of US findings. Use of high resolution high frequency linear ultrasound imaging helps us to evaluate the morphological patterns of salivary gland diseases in day-to-day clinical scenarios. USG-guided FNAC is a great adjunct tool in achieving final tissue diagnosis in evaluation of salivary gland masses.

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