

CLINICAL REVIEW

Salivary gland swellings

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The investigation and management of salivary swellings have advanced considerably in the past decade, with an emphasis on less invasive techniques and increased preservation of the salivary glands and adjacent structures. Salivary gland swellings usually present on the side of the face, below and in front of the ear (parotid gland), or in the upper part of the neck (tail of the parotid gland and the submandibular gland). A submucosal swelling in the oral cavity should raise suspicion of a sublingual or minor salivary gland neoplasm. Occasionally, intraoral lesions might present with an ulcerated surface.

Because of their anatomical position, parotid and submandibular gland swellings are often mistaken for cervical lymphadenopathy. In addition, salivary neoplasms can be misdiagnosed as chronic sialadenitis, resulting in diagnostic delay. In this article, we aim to provide an overview of the clinical presentation, investigation, differential diagnosis, and contemporary management of salivary swellings.

How common is salivary gland disease and who gets it?

Based on data over a 20 year period (1988–2007) in a stable population in Nottingham, United Kingdom, the annual incidence of benign tumours ranged between 6.2 and 7.2 per 100 000 people.¹ Malignant tumours are rare, with an age standardised incidence ranging between 0.6 and 1.4 per 100 000 people in Europe. In England, about 450 new cases of salivary gland cancer are diagnosed every year, with the incidence increasing by 37% between 1990 and 2006.² Salivary gland calculi account for half of major salivary gland disease, with 5.9 cases per 100 000 people each year in the UK, with a prevalence of 0.45%.³ The condition most frequently affects men aged 30–60 years, with the submandibular gland affected in 80–90% of cases.⁴

What are the causes of salivary gland lumps (box 1)?

Benign neoplasms

The majority of salivary neoplasms are benign (65–70%). Within the parotid gland, nearly 80% of tumours are benign.

Malignant neoplasms

Malignant neoplasms are uncommon. Salivary glands have numerous histological types of malignant neoplasm, but the majority are histological variants of adenocarcinoma (box 2). It is important also to consider metastasis to the paraparotid and intraparotid lymph nodes from locoregional disease, especially from skin cancers (squamous cell carcinoma and malignant melanoma). The proportion of malignant tumours increases as the gland size decreases, with malignancy accounting for 40% of neoplasms in the submandibular gland, 50% of minor neoplasms in the salivary glands, and 90% of neoplasms in the sublingual glands.¹

Salivary duct stones (sialolithiasis) and stenoses

Sialolithiasis and duct stenoses usually present as diffuse glandular swelling, accompanied by a classic history of intermittent swelling and pain of the salivary glands at mealtimes. Intraoral palpation might identify a calculus along the course of the duct, most commonly in the floor of the mouth in the submandibular duct.

Infection

Acute infections of the salivary gland usually present with rapid onset of pain and swelling of the affected gland. These symptoms are commonly caused by mumps, which is typically bilateral. Accompanying systemic features—such as malaise, fever, and lymphadenopathy—help secure the diagnosis. Acute bacterial infections can also occur, most commonly in

Summary points

Investigation and management of salivary gland swellings have advanced considerably in the past decade, with an emphasis on less invasive techniques and increased preservation of the salivary glands and adjacent structures

Owing to their anatomical position, parotid and submandibular gland swellings are often mistaken for cervical lymphadenopathy, or can be misdiagnosed as chronic sialadenitis, resulting in diagnostic delay

The most common causes of salivary lumps are benign neoplasms, malignancy, salivary stones and stenoses, and salivary swelling (adenosis) secondary to systemic diseases such as Sjögren's syndrome or HIV infection

All salivary swellings should undergo assessment and investigation, usually by a head and neck surgeon

The main investigations are ultrasonography and fine needle aspiration; magnetic resonance imaging and contrast sialography have a role in specific circumstances

Salivary neoplasms are usually managed by excision, and salivary stones managed by removal, most commonly using sialography or sialendoscopy

Sources and selection criteria

We undertook a search of Medline, using the terms "salivary", "parotid", "submandibular", "accessory" combined with "neoplasms", "inflammatory", "stones", "sialadenitis", "diagnosis", and "management". We also searched reference lists and used personal reference archives, as well as consulting with other experts.

Box 1: Differential diagnosis of salivary lumps

- Neoplasms (benign or malignant)
- Sialolithiasis and ductal stenosis
- Infections (for example, viral (mumps) and bacterial sialadenitis)
- Precursors of malignancy (for example, Sjögren's syndrome, HIV infection)
- Sialadenosis (generalised salivary gland swelling)
- Lymphadenopathy
- Non-salivary gland lumps arising from adjacent structures

Box 2: Some common tumours of the salivary gland

Benign

- Pleomorphic adenoma
- Warthin's tumour
- Basal cell adenoma
- Canalicular adenoma

Malignant

- Mucoepidermoid carcinoma
- Adenoid cystic carcinoma
- Acinic cell carcinoma
- Adenocarcinoma not otherwise specified
- Polymorphous, low grade adenocarcinoma
- Carcinoma ex pleomorphic adenoma

dehydrated, elderly people, due to lack of salivary flow or as a consequence of chronic obstruction. Acute bacterial infection is usually unilateral and causes redness of the overlying skin and tenderness of the affected gland. Sequelae include abscess formation and sometimes drainage of pus to the skin surface. Chronic infections might cause painless, tumour-like swellings, and include chronic sclerosing sialadenitis (also called Küttner's tumour) and rarely tuberculosis.

Sialadenosis

Sialadenosis (generalised gland swelling caused by hypertrophy of the acinar component of the gland) can be a presenting symptom of several systemic diseases (box 3). The condition can also be seen in patients with mental health problems, especially in bulimic or alcoholic patients. In patients with bulimia, frequent self induced vomiting stimulates the overproduction of saliva with resultant sialadenosis. In patients

with alcoholism, fatty infiltration of the salivary glands occurs. Sialadenosis usually presents with gradual, bilateral enlargement of the glands. Unlike neoplastic diseases, the swelling is poorly defined on palpation. Typically, the parotid gland is most affected, although submandibular gland enlargement is not uncommon, and several glands might be involved at the same time.

What features suggest malignancy?

Certain "red flag" clinical features (box 4) indicate invasion of neighbouring structures and should raise the index of suspicion of malignancy. In addition, a history of other predisposing conditions (box 4) should raise concern, as should lumps arising from minor salivary glands, which are more likely to be malignant. Nevertheless, since many salivary gland malignancies present without classic red flag symptoms and signs, all lumps

Box 3: Systemic causes of sialadenosis

Endocrine: diabetes mellitus, hypothyroidism, Cushing's syndrome
 Metabolic: alcoholism, anorexia, bulimia, coeliac disease, malnutrition
 Drugs: anticholinergic drugs, heavy metals, psychotropic drugs
 Neurogenic: dysautonomia, Shy-Drager syndrome, depression

in the salivary glands need further investigation to establish the cause.

What systemic problems can present with salivary gland lumps?

HIV associated salivary gland disease has increased in incidence.⁵ Usually the parotid gland is involved, where swellings can be caused by several disease processes: intraparotid and paraparotid lymphadenopathy, lymphoepithelial cyst formation, diffuse infiltrative lymphocytosis syndrome, parotitis, and malignant tumours. These lumps are often accompanied by generalised lymphadenopathy and xerostomia. Regression of the non-neoplastic swellings occurs with antiretroviral treatment.

Systemic inflammatory illnesses can also present with parotid gland swelling, which can be mistaken for salivary gland neoplasia. In sarcoidosis, parotid gland involvement is characterised by painless, diffuse, non-nodular swelling. Primary and secondary Sjögren's syndrome can also present with lumps within the parotid or the submandibular gland. Diagnosis of Sjögren's syndrome is based on the American-European Consensus Criteria.⁶ A linked register study found a 16-fold increased risk of non-Hodgkin's lymphoma in 286 patients with Sjögren's syndrome who fulfilled these criteria. Therefore, persistent diffuse or painful swellings in a patient with Sjögren's syndrome should alert the doctor to the possibility of evolution to lymphoma—most commonly, extranodal marginal zone lymphoma.⁷ These patients should undergo regular follow-up by the physician managing their condition to detect any transformation early.

When should salivary lumps be referred to secondary care?

Owing to the risk of malignancy, salivary masses need urgent referral and assessment by a head and neck surgeon with experience in salivary surgery. Patients with obstructed glands that do not resolve within a few weeks might need removal of the stones. Patients with sialadenosis might need assessment and management of their underlying systemic condition by a secondary care physician in some cases.

What is the role of imaging studies in salivary gland lumps?

Imaging plays a fundamental role in the diagnosis and management of salivary masses. Radiological investigations can clarify whether a clinical swelling is due to a focal lesion or diffuse process, and whether a mass arises within salivary parenchyma or is non-salivary (that is, extraglandular) in origin. In addition, fine needle aspiration cytology (FNAC) guided by ultrasonography is a valuable diagnostic tool for salivary gland lesions.

High resolution ultrasonography

High resolution ultrasonography is the first line imaging modality. It is quick, safe, and has excellent spatial resolution, facilitating detailed assessment of the margins and internal characteristics of mass lesions. The procedure is able to detect features of malignancy, such as infiltrative margins, skin involvement, and the presence of regional lymphadenopathy. However, there is considerable overlap in the appearance of benign lesions and that of low grade malignant salivary neoplasms, and no specific features exist to differentiate between the most common malignant neoplasms (fig 1). Therefore, diagnostic ultrasound assessment is frequently combined with fine needle cytology to identify malignancy (see below).

Ultrasonography is also valuable in the investigation of non-neoplastic disease of the salivary glands. Diffuse enlargement of the glands is readily appreciated in sialadenosis, allowing differentiation from distinct neoplastic swellings. Parenchymal changes in Sjögren's syndrome and HIV associated salivary gland disease have characteristic appearances but need correlation with the appropriate clinical history. Ultrasonography can also identify and guide drainage of abscess cavities in complicated infections. In patients with suspected obstructive salivary disease, dilated ducts can be traced to assess the level and cause of the obstruction, and is usually correlated with dedicated salivary duct imaging (such as contrast sialography). A study of 24 patients showed both a sensitivity and specificity of 80% for identifying salivary duct stones using ultrasonography, compared with using conventional sialography.⁸

Magnetic resonance imaging

Parotid and submandibular masses that show features of malignancy on clinical or ultrasound examination need cross sectional imaging, as do sublingual and minor salivary gland masses owing to the high probability of malignancy. Magnetic resonance imaging has a better contrast resolution than computed tomography (CT), and this feature enables detailed delineation of tumour margins and accurate local staging. The procedure also provides useful anatomical information about the position of the tumour before surgery, and is particularly helpful in deep parotid lobe involvement (fig 2⇓), usually indicated clinically by an immobile mass on palpation. Perineural tumour spread, which most frequently involves the facial nerve and is particularly associated with adenoid cystic carcinoma,⁹ can also be detected on magnetic resonance imaging, with a sensitivity of 100% and specificity of 85% compared with histopathology, in a retrospective study of 26 patients.¹⁰

CT and positron emission tomography (PET)-CT

The detection of distant metastatic spread is essential in patients with malignant tumours in the salivary gland. The lungs are the most frequent site of distant metastasis from primary parotid malignancy. Contrast enhanced CT is the investigation of choice in this setting because it provides an accurate method of excluding distant metastases and is widely available.

Box 4: Red flag features

Facial nerve weakness (fig 1↓)
 Rapid increase in the size of the lump
 Ulceration or induration (or both) of the mucosa or skin
 Overlying skin fixity
 Paraesthesia or anaesthesia of neighbouring sensory nerves
 Intermittent pain, increasing inexorably
 History of previous skin cancer, Sjögren's syndrome, or previous radiation to the head and neck

¹⁸F-fluorodeoxyglucose PET is taken up by normal salivary parenchyma, with focal uptake seen in both benign and malignant parotid tumours; therefore, PET-CT is unhelpful in the characterisation of parotid masses.¹¹ However, this modality is a sensitive method of detecting recurrence and distant metastases, with a sensitivity and specificity of 74.4% and 100%, respectively, in a retrospective review of 55 patients with salivary gland cancer.¹² Parotid masses are most commonly encountered on PET-CT as an incidental finding during the investigation of cancers not related to the head and neck. In this setting, investigation by other imaging modalities and cytology are needed.

Salivary ductal imaging

The architecture of the parotid and submandibular ductal systems can be assessed by contrast sialography. Iodinated contrast media is injected into the ductal system via a fine bore catheter with radiographs obtained to allow detailed assessment of ductal strictures and the presence of calculi (fig 3↓). This imaging modality can be combined with therapeutic salivary interventional procedures (for example, stone retrieval, balloon ductoplasty of strictures) in specialist centres. Fluid weighted sequences of magnetic resonance imaging (magnetic resonance sialography) provide an alternative, non-invasive method of imaging in this patient group. A prospective study of 80 patients showed a sensitivity of 80% and specificity of 98% using magnetic resonance sialography compared with contrast sialography.¹³

How can a tissue diagnosis be achieved in salivary gland lumps?

A recent meta-analysis of 64 studies, including 6169 patients, on the use of FNAC concluded that it was not possible to formulate guidelines on the clinical utility of FNAC because of the variability of study results.¹⁴ FNAC is, however, highly accurate when the diagnostic information is restricted to determining non-neoplastic conditions versus neoplastic conditions (area under the summary receiver operating characteristic (AUSROC) curve 0.99, 95% confidence interval 0.97 to 1.00), or benign disease versus malignant disease (0.96, 0.94 to 0.97).¹⁴ Furthermore, the procedure is acceptable to patients, with minimal morbidity.

The technique is simple to perform and relatively inexpensive. The incorporation of ultrasound guidance and the attendance of a cytologist for immediate diagnosis or determination of specimen adequacy help to optimise the diagnostic information.¹⁵ When a prospective cohort of 292 samples aspirated under ultrasound guidance from a single centre was compared with a retrospective cohort of 600 samples aspirated freehand, the ultrasound group had a 23% improvement in accuracy and 84% reduction in inadequate specimens.¹⁶ However, this procedure depends on the skill of the operator and the reporting cytologist,

and is of limited value in certain settings (for example, lymphoma).

Core needle biopsy has recently emerged as a “minimally invasive” technique for the assessment of salivary gland disease. A recent meta-analysis of five studies, including 277 patients, concluded that core needle biopsy was more accurate than FNAC (AUSROC curve 1.00, 95% confidence interval 0.99 to 1.00).¹⁷ However, the clinical utility of core needle biopsy is limited by the need for local anaesthesia, patient discomfort, and risk of damage to local structures. In the event of an inadequate result on a first FNAC attempt, there was only a marginal improvement in the overall adequacy rates with core needle biopsy, compared with a repeated FNAC attempt, which is more likely to be acceptable to both patients and clinicians alike.¹⁷

How are salivary gland swellings managed?

The management of salivary gland swellings should ideally be conducted in centres that have a multidisciplinary group of clinicians with an interest in salivary disease. This group usually includes a head and neck surgeon (an otorhinolaryngologist or maxillofacial surgeon), radiologist, pathologist, and physician.

Benign and malignant neoplasms

In general, salivary neoplasms need surgical excision with an appropriate margin, taking care not to breach the capsule of the tumour or spill its contents. The surgical specimen provides an opportunity for the pathologists to judiciously sample the tumour and secure a definitive diagnosis, which can be challenging to diagnose.¹⁸ The tumours also usually continue to grow, causing concerns about cosmesis, especially in younger patients. In addition, the most common benign parotid tumour (pleomorphic adenoma) is reported to carry a risk of malignant transformation of about 8%,¹⁹ which is thought to increase the longer the tumour has been left untreated.²⁰ Finally, tumours of the submandibular gland and minor salivary glands have a high probability of malignancy. Therefore, removal of these tumours is indicated, except in patients who are elderly or unfit for surgical resection. If the tumour is considered to be malignant, larger excision margins are needed, and management of occult or clinically evident nodal metastasis, by an elective or therapeutic neck dissection respectively, might be necessary (fig 4↓). Postoperative radiotherapy might also be indicated, with the size and histological grade of the tumour and the surgical resection margins being the main determinants in such a decision.

Sialolithiasis and ductal stenosis

Salivary lumps secondary to obstructive causes (such as duct stones or stenosis) are now usually treated by interventions to relieve the obstruction, which have been shown to restore

salivary gland function.²¹ Traditionally, this treatment was performed by incisions (per orally) directly on to the stone within the duct to remove it. More proximal stones, closer to the gland and thus less accessible, had been treated by gland excision. Ductal stenoses were dilated by using small malleable dilators or opening the stenosed area (ductoplasty), or both.

However, the treatment of obstructive salivary disease has undergone considerable advances and transformation in recent times, obviating the need for gland excision in most cases. In an observational multicentre cohort study of 4691 patients with ductal stones managed with minimally invasive techniques, only 3% of patients underwent gland excision.²² Unfortunately, many of these minimally invasive techniques are not widely available.

Extracorporeal lithotripsy, developed in the 1980s, is a non-invasive technique (using probes placed on the skin over the gland) that uses compression shockwaves to fragment salivary stones, thus allowing smaller fragments to be flushed out by saliva. This technique is effective only for stones larger than 2 mm in size, with complete and partial (<2 mm in size) disintegration achieved in 45% and 27% of 322 consecutive patients, respectively.²³

Sialography is also used to identify and remove the stone, using a basket or balloon. The balloon procedure can be used to dilate the duct at areas of stenosis (balloon ductoplasty). This is an effective technique; a prospective cohort study of 34 patients reported immediate success rates of up to 92%.²⁴

A recent development has been the introduction of very fine (0.7-1.2 mm) Hopkins rod endoscopes, which can be inserted into the duct, thus enabling direct visualisation of the debris, stones, or stenoses. Removal or dilatation is then attempted by irrigation, baskets, balloons, or graspers. Studies have reported high success rates; 87% of a cohort of 217 patients examined retrospectively were symptom-free on long term follow-up.²⁵ In addition, laser or intraductal lithotripsy (using compression shockwaves) has been used to disintegrate the stones. However, both these latter techniques have not been adopted widely, owing to the reported high rates of duct perforation.⁴

Minimally invasive techniques carry possible complications. The most common is a transient swelling of the gland, occurring in 80-100% of cases. Other complications are much less common—occurring in less than 5% of cases—and include stenosis, infection, bleeding, and extravasation.^{25 26}

Infection and sialadenitis

The main objective of the management of salivary swellings secondary to medical or mental health disorders is the treatment of the underlying condition by the appropriate clinical team. Salivary enlargement in non-neoplastic disease does not usually need treatment of the affected glands, unless the swelling causes cosmetic concerns. In these cases, resection, usually of the parotid gland by superficial parotidectomy, can be offered to the patient. However, ensure that the patient has received appropriate counselling as part of the consent process (see below).

Viral infections need supportive care with anti-inflammatory medication, adequate hydration, and good oral hygiene. Acute bacterial infections are usually caused by aerobic organisms (34% of cases), such as *Staphylococcus aureus* and *Haemophilus influenzae*, anaerobic organisms (41%), mainly Gram negative bacilli that are usually found in the oral cavity, or a mixture of both (25%), as shown in a prospective cohort of 44 aspirates from acute suppurative infections of the salivary gland.²⁷ Since just over 50% of patients had B-lactamase producing organisms,

appropriate antibiotics should be prescribed according to local guidelines and microbiology advice, in addition to hydration, frequent consumption of sialogogues (such as citrus drinks), and massaging the gland to relieve the pressure. Any signs of an abscess with fluctuation or swinging temperatures should prompt immediate referral to secondary care for intravenous antibiotics and possible drainage.²⁸

What are the possible complications of surgical excision?

The main complication from a submandibular gland excision is damage to the marginal mandibular branch of the facial nerve, reported to be permanent in 10%²⁹ to 25% of cases,³⁰ depending on whether the disease is benign or malignant. This condition results in asymmetrical mouth movement and smiling, and sometimes oral incompetence and drooling. Other complications reported in a retrospective series of 137 operations included neck haematoma (10%), wound infection (9%), temporary tongue numbness or paralysis (7%) secondary to traction on the lingual and hypoglossal nerve, or permanent damage (1%).

The most serious complication of a parotidectomy is facial paralysis, which might be partial or complete. The symptom can be temporary (recovering within weeks or months)—reported in 29% of a prospective series of 259 parotidectomies performed by the same surgeon.³¹ It can also be permanent—reported in 5.6% of the same series of operations.³¹ The permanent effect is more likely to occur in patients with malignant tumours needing neck dissection, and the marginal mandibular branch of the facial nerve is most commonly affected.³¹

Other complications involve hypertrophic scars, haematoma, infection, sialocele (collection of saliva in the wound), and salivary fistula. These complications are usually managed by repeated aspiration. Patients often have numbness of part of the ear, cheek, or face, owing to sacrifice or neuropraxia of the greater auricular nerve. Frey's syndrome can be detected on investigation with a modified starch test in up to 80% of patients,³² but causes appreciable symptoms in only 5-18% of patients. The syndrome is caused by re-innervation of the skin from underlying autonomic nerve endings of the parotid. The symptoms include sweating, redness, and warmth of the skin overlying the parotid bed during eating. This syndrome can be treated by botulinum toxin injection. Despite the above risks of surgery, the majority of patients achieve satisfactory postoperative cosmesis, with no functional deficits.

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Additional education resources*Resources for general practitioners*

Capaccio P, Torretta S, Ottaviani F, Sambataro G, Pignataro L. Modern management of obstructive salivary diseases. *Acta Otorhinolaryngologica Italica* 2007;27:161-72—excellent article on the current management of salivary stone disease and advances in the field

British Association of Otorhinolaryngologists-Head and Neck Surgeons of the UK (ENTUK). 2011 head and neck cancer multidisciplinary management guidelines (https://entuk.org/docs/prof/publications/head_and_neck_cancer)—good summary of the recommended management for salivary cancer, endorsed by four other relevant specialty associations

National Cancer Institute. Head and neck cancer (www.cancer.gov/cancertopics/types/head-and-neck)—good summary of recommendations for the management of salivary cancer by the National Cancer Institute in the United States

Resources for patients

UK National Cancer Action Team. Cancer patient information pathways (www.cancerinfo.nhs.uk/cancer-patient-information-pathways)—rigorously generated resource providing comprehensive, up to date, peer reviewed information

ENTUK. Detailed information about the surgical procedures performed for salivary glands (https://entuk.org/ent_patients/head_neck_conditions/) and downloadable patient information leaflets (https://entuk.org/ent_patients/information_leaflets)

British Association of Maxillofacial Surgeons (www.baoms.org.uk/page.aspx?id=78)—detailed information for patients

National Cancer Institute (www.cancer.gov/cancertopics/pdq/treatment/salivarygland/Patient/page1)—comprehensive resource for readers new to the topic

Patient.co.uk (www.patient.co.uk/health/Salivary-Gland-Stones.htm)—easy to read website for information about salivary gland stones and their management

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Figures

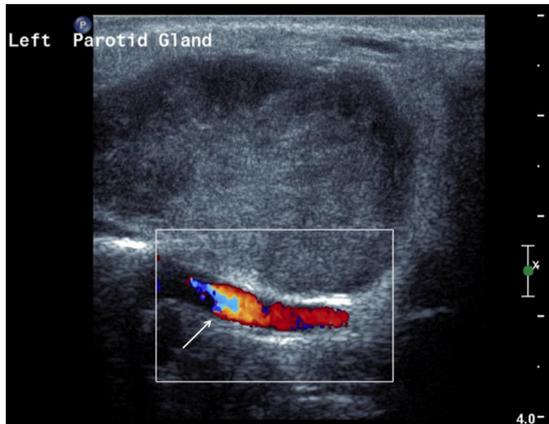


Fig 1 Longitudinal colour Doppler ultrasound image of large pleomorphic adenoma in superficial lobe of the left parotid gland. The deep tumour margin closely follows the retromandibular vein (white arrow)



Fig 2 Magnetic resonance imaging of large deep lobe component to a pleomorphic adenoma of the parotid gland (white arrow)



Fig 3 Contrast sialogram of catheter in the distal duct and normal ductal appearances



Fig 4 Axial contrast enhanced CT of male patient with a right parotid mass and facial nerve palsy. Image shows the right parotid mass infiltrating the subcutaneous fat (solid arrow), and regional spread to a right upper jugular chain (level 2) lymph node (dotted arrow). The tumour was confirmed as a high grade parotid malignancy on ultrasonography guided FNAC