Acute and Chronic Salivary Infection

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Key Points

1. Sialadenitis can be acute or chronic in nature in the setting of salivary flow obstruction, bacterial/atypical bacterial or viral infections, and autoimmune or granulomatous diseases.
2. Many imaging modalities have been described to aid in diagnosis of sialadenitis including ultrasound (US), computed tomography (CT), sialography, and more recently magnetic resonance (MR) sialography with sialography considered the gold standard.
3. Since the advent of sialendoscopy, the surgical treatment of salivary stones has shifted from gland removal to gland preservation especially for stones <4 mm that are generally amenable to endoscopic removal.
4. Our chapter hopes to provide a management algorithm to help the clinician diagnose and treat a variety of diseases that cause acute or chronic/recurrent sialadenitis.

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Introduction

Sialadenitis, acute, chronic, and recurrent, can occur in the setting of three major categories: obstructive diseases, viral and bacterial diseases, and autoimmune/granulomatous diseases. Acute sialadenitis is the most common condition involving the major salivary glands and is commonly due to a viral or bacterial infectious etiology, while chronic and recurrent sialadenitis typically occurs in the setting of an obstructive process. In this chapter, we will address each category but focus on salivary gland obstruction, mainly due to sialolithiasis and its general management, including with sialendoscopy.

Acute Sialadenitis

Many patients with salivary stones are asymptomatic, but when salivary stones become large enough to block salivary flow, acute onset symptoms can occur. These include facial and/or neck pain and swelling, purulent discharge, possibly systemic symptoms (e.g., fevers, chills, etc.), and tenderness associated with mealtimes, when salivary secretions tend to increase. The diagnosis of acute suppurative sialadenitis has been historically applied to patients meeting certain criteria, including (1) presence of a pathogen on a culture or gram stain of salivary drainage; (2) clinical manifestations of gland infection, such as swelling, tenderness, etc.;

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(3) presence of extra-glandular complications, such as abscess formation, nerve palsy, extreme pain, etc.; and (4) presence of one or more additional risk factors for sialadenitis, such as xerostomia, poor oral hygiene, etc [1]. Physical exam with bimanual palpation may reveal expressible purulence, gland induration, fluctuance at the floor of the mouth, trismus, and, if located in the anterior two third of Wharton's duct, palpable stones [2, 3]. During acute sialadenitis, *Staphylococcus aureus* is most often isolated (50–90%), and *Haemophilus influenzae* and other streptococcal species have been less often isolated [3, 4].

Viral Causes

Mumps can cause salivary gland swelling and inflammation, typically occurs in patients aged 5–15 years (85% of cases occur <15 years of age), and is caused by a virus in the myxo family [4, 5]. Although mumps more frequently involves the parotid gland, it can also affect both submandibular and sublingual glands. Patients present with painful, often bilateral swelling, and systemic symptoms such as fevers, chills, nausea, loss of appetite, or headaches. Lack of purulence upon gland palpation and bilateral gland involvement helps differentiate mumps from acute bacterial infection. Mumps is also diagnosed with positive serology titers in the setting of leukocytosis.

Obstructive Diseases

Salivary calculi frequently present to the otolaryngologist, affecting approximately 1.2% of the population. The majority occur in the submandibular gland (80–90%) and some in the parotid (5–10%) [6]. Salivary stone formation can lead to mechanical obstruction, persistent mealtime swelling, and bacterial infections [2]. Salivary stones occur more commonly in males, generally presenting with glands on both sides equally affected, unusual bilateral involvement, and, more rarely, in the minor salivary glands [2]. All ages may experience salivary stone formation, but there is much higher incidence among patients between the fourth and sixth decade of life, during which presentation of a single salivary stone occurs approximately 70–80% of the time [2]. A higher proportion of salivary stones are found in the submandibular gland relative to the parotid gland, which may be attributed to the former's longer and larger caliber duct, through which saliva flows against gravity at a slower rate, is more alkaline, and has higher relative mucin and calcium content [2].

Salivary stone formation is not completely understood, but it is likely that microscopic stones accumulate during normal salivary activity and produce atrophic foci that serve as proliferation sites for microbes ascending the main salivary duct, leading to inflammation, swelling, and fibrosis [7]. These conditions can cause compression of the large salivary ducts, where calcium-rich material can stagnate and deposit around desquamated epithelial cells, foreign bodies, products of bacterial decomposition, microorganisms, and/or mucus plugs [8].

Salivary stones are generally comprised of calcium phosphate with small amounts of magnesium, ammonium, potassium, and carbonate and grow at rate of 1–1.5 mm a year, ranging from 0.1 to 30 mm [9, 10]. The average daily flow of saliva is approximately 1–1.5 L/day. The submandibular gland provides most of the saliva at rest, and the parotid gland contributes as much as 50% of saliva during stimulation [3]. Factors associated with increased inflammation and a decreased rate of salivary flow may also be associated with increased risk of stone formation. These include smoking, low fluid intake, and medication that may decrease salivary output (e.g., anticholinergics) [6, 11]. Other risk factors that may predispose patients to acute sialadenitis include certain medical conditions, including Sjogren's disease, diabetes mellitus, hypothyroidism, and renal failure [4].

Obstructive diseases can be further categorized into sialolithiasis, mucus plugs, ductal strictures or stenosis, foreign bodies, and extra-ductal causes [5]. As noted, patients with salivary stones may be asymptomatic until the flow of saliva is blocked or infection occurs. Once salivary flow is obstructed, particularly postprandial, the gland swells, causing fullness and pain. The degree of

obstruction dictates the rapidity and severity of symptoms [5]. Persistent obstruction of the duct creates a nidus for bacterial infection, transforming sialolithiasis to acute sialadenitis. Similarly, mucus plugs can obstruct salivary flow, but typically to a less severe degree than sialolithiasis, because mucus plugs, unlike salivary stones, are not fully mineralized. Sialadenitis secondary to mucus plugs is therefore more rare [5].

Strictures and stenosis can also obstruct salivary flow. These occur in Wharton's and Stenson's ducts following trauma, scarring, calculi, recurrent infections, previous salivary duct procedures, intraductal tumor, or extra-ductal compression [5]. Treatment depends on whether the ductal stenosis or stricture is located at the papilla.

The presence of foreign bodies in the duct, such as grass, toothpicks, hay, and seeds, may also cause obstruction. These are more commonly found in the Wharton's duct than in the Stenson's duct [5]. Finally, extra-ductal causes, including intraoral tumors and enlarged level cervical/buccal lymph nodes, may be revealed by a thorough otolaryngological history and imaging.

Chronic/Recurrent Sialadenitis

Chronic/recurrent sialadenitis presents repeated or continued episodes of pain and inflammation due to decreased salivary flow, most frequently affecting the parotid gland [12]. Obstruction of the salivary gland duct is followed by recurrent inflammation, causing acinar destruction with lymphocytic infiltration and fibrous replacement with sialectasis [12]. Patients typically present with mild tenderness and recurrent or chronic gland swelling aggravated by eating. Approximately 80% of patients with chronic sialadenitis develop xerostomia over time.

Causes of Chronic Sialadenitis

Tuberculosis can involve the salivary glands and the surrounding lymph nodes and is the most common granulomatous infection of the major salivary glands (most commonly the parotid) [5]. Atypical mycobacteria can also cause peri-glandular lymphadenitis or sialadenitis, typically in young adults and children. Symptoms include acute, non-tender swelling, occasionally with fistula tract formation. Peri-glandular lymphadenitis or sialadenitis must be distinguished from bacterial lymphadenopathy, leukemia, lymphoma, cat-scratch disease, and fungal infections [5].

Sarcoidosis is another granulomatous disease affecting many organs in the body, including the salivary glands. Patients are typically African-American in the age range of 20–40 years [5]. Heerfordt's syndrome affects approximately 8% of sarcoid patients where there is eye, facial nerve, and parotid gland involvement [5]. Heerfordt's syndrome patients present in the second or third decade of life, with fever, illness, uveitis, facial nerve palsy, and parotid gland swelling. It is diagnosed with a biopsy demonstrating non-caseating granulomatous lesions with giant cells [5]. Actinomycosis, specifically *A. israelii*, is part of the normal flora in the oral cavity and can cause retrograde salivary gland infection [5]. Symptoms include mildly tender, non-fluctuant, and indurate salivary glands and can present as acute, subacute, or chronic sialadenitis.

Autoimmune disease such as Sjogren's syndrome, the second most common autoimmune disease after rheumatoid arthritis, can also affect the salivary glands. Its pathogenesis is mediated by lymphocytic destruction of the exocrine glands, leading to xerostomia and keratoconjunctivitis sicca [12]. Approximately 90% of Sjogren's syndrome patients are women. The average age of onset is 50 years old, and it can involve unilateral or bilateral glands [12]. Sjogren's syndrome is further divided into (a) exocrine involvement only and (b) secondary Sjogren's when associated with a definable autoimmune disease, such as rheumatoid arthritis [12].

Juvenile recurrent parotitis is characterized by recurrent episodes of gland inflammation, causing swelling and pain [4]. The exact etiology is unknown, but it presents with either acute or subacute and either unilateral or bilateral gland swelling, typically parotid, with fever and malaise [4]. Such episodes may last for days or weeks and usually occur within a few months [4]. Examples of all acute and chronic diseases discussed so far are summarized in Table 10.1.

Table 10.1 Acute and chronic sialadenitis [9]

	Etiology	Presentation	Physical examination	Diagnosis	Treatment
Acute sialadenitis					
Bacterial	Staph aureus (50–90%), Strep species, H. influenza	Acute onsent of pain, swelling, gland erythema and warmth	Purulence with gland message, tenderness on palpation	Purulence from gland, culture may help in diagnosis	Penicillin with beta-lactamase inhibitors (augmentin), warm compresses, gland messaging, sialagogues, hydration, oral hygiene; Incisional and drainage if abscess present
Viral	Myxo family (mostly parotid; 85% occuring <15 years old), HIV (mostly parotid)	Acute onset of swelling, possible pain w/erythema in children w/ constitutional symptoms (fevers, chills, malaise, etc.)	Tender, pain on palpation, no purulence from duct w/ message	Viral serology titers	Supportive care, anti-retroviral HIV medications
Chronic/recurrent sialadenitis					
Obstructive	Underlying duct anamolies (stenosis, kinks, etc.), salivary stones	Recurrent episodes of pain and swelling associated with meals, possibly recurrent acute infections	Indurated gland, with no saliva expressed on gland message, may be tender	Imaging demonstrating stone or stricture w/possible duct dilation	Hydration, gland message, Sialendoscopy +/− endoscopic intervention (stone removal, duct dilation) or open intervention
Bacterial/fungal	Atypical mycobacteria, cat scratch disease, fungal, actinomyces (most commonly A. Israeli)	Slow onset of gland swelling, mildly painful	Indurated gland, may be tender, no purulence from duct	History of slow growing mass and physical exam with mildly tender gland, unlikely purulence from duct	Long term antibiotics directed at atypical mycobacteria, Bartonella, Actinomyces
Systemic	Sjogren's disease, Rheumatoid arthritis, Lymphoma	Chronic gland swelling, non painful	Indurated gland, non tender, no purulence from duct	biopsy of gland, +/− imaging, inflammatory markers in blood work (RA, ANA, Anti-Ro, Anti-La)	Systemic treatment, hydration
Inflammatory/ granulomatous	Recurrent parotitis of childhood, Sacroidosis, Tuberculosis	Recurrent episodes of pain and swelling not associated with meals in children (Recurrent Parotitis), slow onset of painless gland swelling	Tenderness to palpation with recurrent parotitis in children; indurated, non tender to palpation with no purulence from duct	History and physical exam of tenderness of parotid gland in children; biopsy of gland, PPD, ACE levels	Antibiotics, hydration, gland message, supportive care, possible sialendoscopy for children; System therapy for adults

Imaging

Ultrasound

Standard X-ray films were historically useful in diagnosing ductal stones, but intraglandular and small stones were easily missed, as up to 20% of stones are reported as radiotransparent [13]. It is also difficult to specifically locate stones using this imaging, and it is therefore better used as a screening tool. In studies comparing ultrasound, sialography, and endoscopy, ultrasound has been demonstrated to be 81% sensitive, 94% specific, and 86% accurate [13, 14]. Compared to magnetic resonance (MR) sialography, ultrasound has a demonstrated specificity and sensitivity of 80% [13, 15]. Ultrasound may demonstrate chronic parotid gland inflammation characterized by irregular hypodensities interspersed with hyperechogenetic scar and increased vascular flow as seen in Sjogren's disease, lymphoma, and granulomatous disease (Fig. 10.1).

Computed Tomography (CT) Scan

CT is useful to evaluate salivary stones if the stones are large, or if the cuts are fine and performed every millimeter [13]. However, like ultrasound, CT does not reveal duct anomalies or precise stone location in the duct. With conventional contrast-enhanced CT, sialodochitis may present as irregularities in the duct wall and ductal wall thickening and increased enhancement [16]. Dilation of the duct frequently accompanies obstruction, as do hyperdense non-enhancing calcified stones in the same range of Hounsfield units as the bone [16]. With chronic sialadenitis, the acinar atrophy may appear on CT as the so-called "shrunkened" gland, with higher fat content [16]. CT scans of acute sialadenitis demonstrate glandular enlargement and enhancement with surrounding inflammatory changes of the subcutaneous fat and/or an associated abscess or underlying etiology such as a stone (Fig. 10.2).

Sialography

Sialography is the gold standard for evaluating salivary ducts, because it reveals the precise location of salivary stones as well as duct anomalies, after intraductal retrograde injection of water-soluble radiopaque dye [13]. Risks associated with sialography are (1) pain, (2) exposure to irradiation, (3) risk of canal wall perforation, (4) proximal displacement of the stone in the duct, and (4) complications, such as infection or anaphylaxis after dye injection [13].

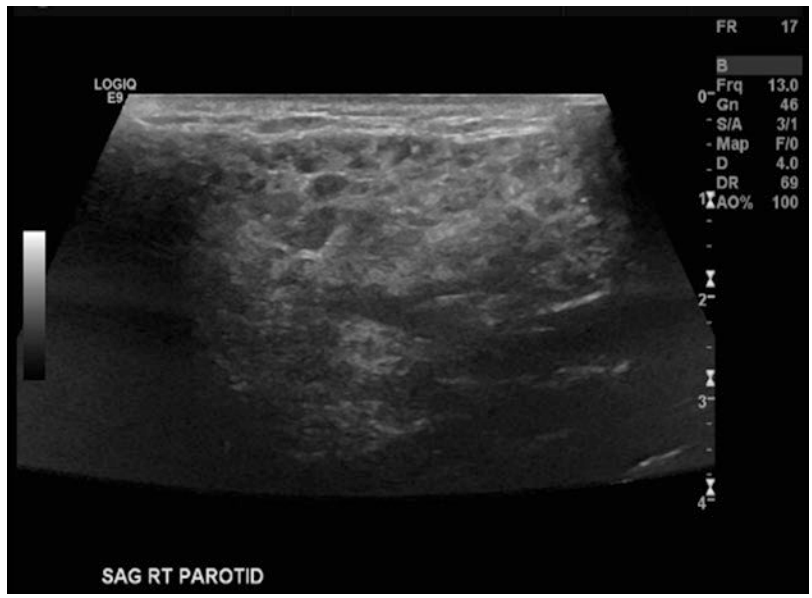

Fig. 10.1 Parotid ultrasound showing characteristic findings of chronic sialadenitis including hypodense fluid collections surrounded by hyperintense scar

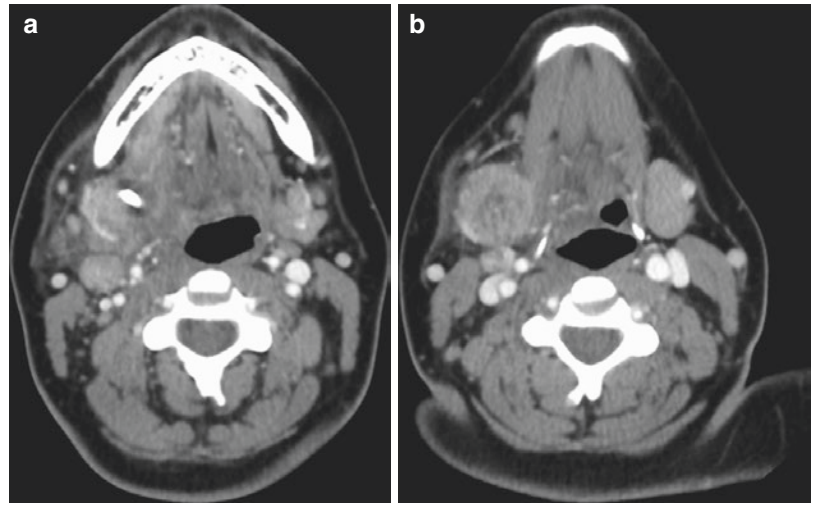

Fig. 10.2 CT scan of right submandibular stone with surrounding hypodensity consistent with early abscess (**a**) extending into an enlarged, edematous gland (**b**)

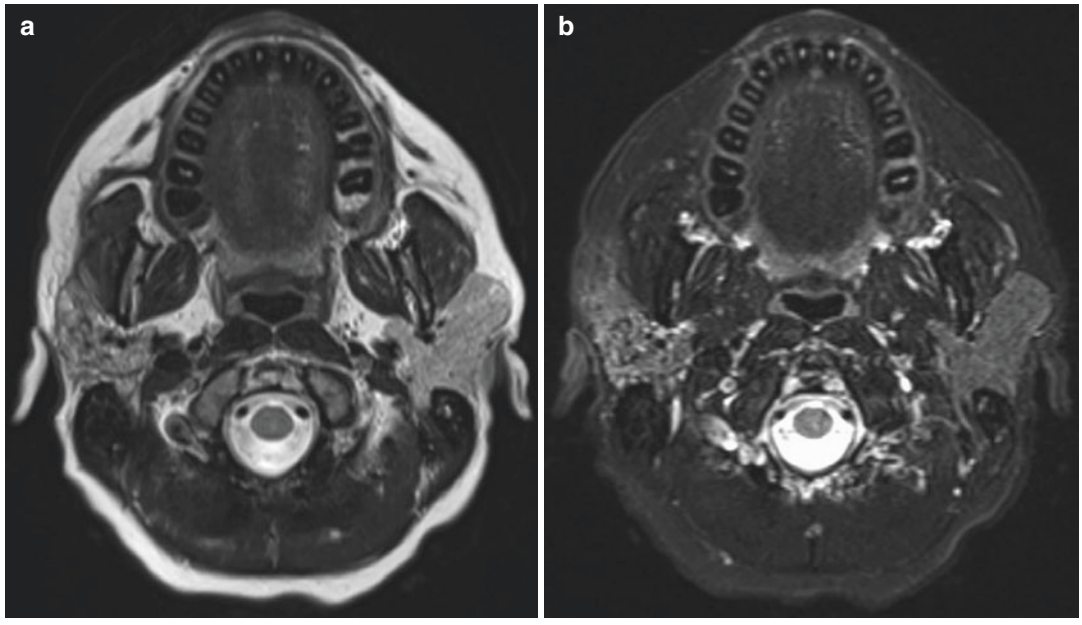

Fig. 10.3 T1- (**a**) and T2- (**b**) weighted axial MRI images with heterogeneous changes in a right parotid gland with chronic sialadenitis

MR and MR Sialography

Even though MR provides superior soft tissue contrast than CT, it is more difficult to distinguish duct obstruction due to calcified stones, air, fibrin, or mucus plugs [16]. Additionally, MR may overestimate the size of a calcified stone by approximately 10–30%, which may deter the selection of sialendoscopic treatment methods [16]. Chronically inflamed parotid glands demonstrate heterogeneous enhancement on MRI (Fig. 10.3). The Marchal and Dulguerov paper in 2003 [13] describes MR sialography using 3 mm T2-weighted sequences in both the sagittal and axial planes. Volumetric reconstruction permitted precise localization of the stones in the duct, with

Table 10.2 Comparison imaging with sialendoscopy in salivary diseases [16]

	Plain X-ray	Ultrasound	CT (contrast enhanced)	Sialography	MR	Sialendoscopy
Radiation exposure	Yes	No	Yes	Conventional sialography-yes; MR sialography-no	No	No
Invasive	No	No	No	Yes	No	Yes
Visualization of duct to surrounding soft tissue structures	No	No	Yes	No	Yes	No
Visualization of duct anamolies	No	No	Limited	Yes	Limited	Yes
Precise location of stone in the duct	No	No	Limited	Yes	Limited	Yes
Availability	Widely available	Widely available	Widely available	Conventional widely available, MR sialography moderately available	Widely available	Moderately available
Cost	Low	Low	Moderate to high	Moderate to high for conventional; high for MR sialography	High	Moderate to high
Risks	Minimal	Minimal	Minimal	Contrast reaction, pain, inadvertant mobilization of stone, duct perforation (conventional); limitation from implants (MR)	Limitation from implants	Duct perforation, failure to remove stone, fistula, pain, facial nerve injury, lingual nerve injury

good visualization of duct anomalies [13]. The advantages of MR sialography over conventional sialography are that it is noninvasive and has no dye, pain, or radiation exposure, and it allows for rapid reconstruction of images after scan [13]. Limitations of MR sialography include cost, unavailability due to the presence of cochlear or other similar implants, and lengthy scan acquisition time of 45 min. All modes of imaging discussed so far and compared with sialendoscopy are summarized in Table 10.2.

Medical Management of Salivary Disease

The provider must first determine whether a patient is presenting with acute or chronic/recurrent sialadenitis. The cause of sialadenitis is most frequently obstruction by salivary stone(s) (60–70% frequency), followed by stenosis (15–25% frequency), inflammation of the duct (around 5–10% frequency), and, least frequently, other obstructions, duct anomalies, or foreign bodies (around 1–3% frequency) [17].

Treatment for acute suppurative sialadenitis is typically antibiotic therapy targeted for gram-positive and anaerobic organisms, which are generally both penicillin sensitive [4]. As such, Augmentin® is usually the antibiotic of choice and is accompanied by gland massaging, sialagogues, warm compresses, and improved oral hygiene. When available, culture-directed antibiotics are a superior treatment. Treatment of underlying medical problems, such as diabetes, is also indicated, as is possible surgical or needle drainage in the event of abscess formation. With respect to chronic and recurrent

sialadenitis, the underlying cause of duct obstruction can be investigated with imaging, sialendoscopy, gland biopsy, gland excision, or open surgery.

Viral sialadenitis is treated with supportive care. Suspected granulomatous diseases may be diagnosed by performing a biopsy and drawing rheumatoid serologies [4].

Surgical Management of Salivary Disease

Under direct visualization, sialendoscopy provides the most accurate information concerning stone location and ductal pathology. Typically, sialendoscopy is appropriate for patients with chronic or recurrent sialadenitis or gland swelling of uncertain origin [13]. The Marchal and Dulguerov study looked at 450 diagnostic sialendoscopy cases and described successful stone localization in 98% of such cases [13]. The Zenk et al. study described failed stone localization in 7% of submandibular gland cases and in 21% of parotid cases out of 1154 sialendoscopy cases [18]. Risks associated with sialendoscopy are overall minor, such as failure to retrieve the stone or stone fragments, damage or perforation to the duct, possible swelling at the floor of mouth, or need to remove gland [19]. Patients with stones measuring <3 mm in the parotid duct, or <4 mm in the submandibular duct, are generally amenable to interventional sialendoscopy with wire basket extraction alone [13, 19]. Larger palpable or intraglandular stones likely require a transoral open excisional approach, with or without the guidance of sialendoscopy. Stone removal by transoral ductal incision may be the first-line treatment for impacted stones or stones >5 mm [17]. Another treatment option is by intracorporeal laser through the working channel of the sialendoscope, in order to divide a large stone and create smaller, more mobile fragments [19]. Stones ranging from 5 to 7 mm usually require a concomitant sialolithotomy and/or may be amenable to laser fragmentation [19].

Stones that are not accessible with sialendoscopy may be amenable to treatment with extracorporeal shock-wave lithotripsy (ESWL), which uses ultrasound technology to break up a stone into fragments that can then be removed with wire basket [19]. This technique is less successful where the stone(s) is larger than 10 mm in size [19].

Stone removal may be complicated when encountering kinks in the ducts, or severe serpentine bends that do not permit endoscopic entry and typically obstruct salivary flow and can lead to chronic sialadenitis [18]. Stenosis of the duct may be treated with papillotomy or balloon dilation, depending on the location, severity, and segmental length [18]. An algorithm of how to initially treat acute and chronic sialadenitis is presented in Fig. 10.4.

Sialendoscopy has progressed over the past 10–15 years, but 5% of patients still ultimately require gland removal. Gland removal is generally necessary for patients with: (a) intraparenchymal stones not transorally accessible, (b) multiple intraparenchymal stones, (c) three failed ESWL attempts, or (d) megasialoliths >1 cm that cannot be transorally removed [19].

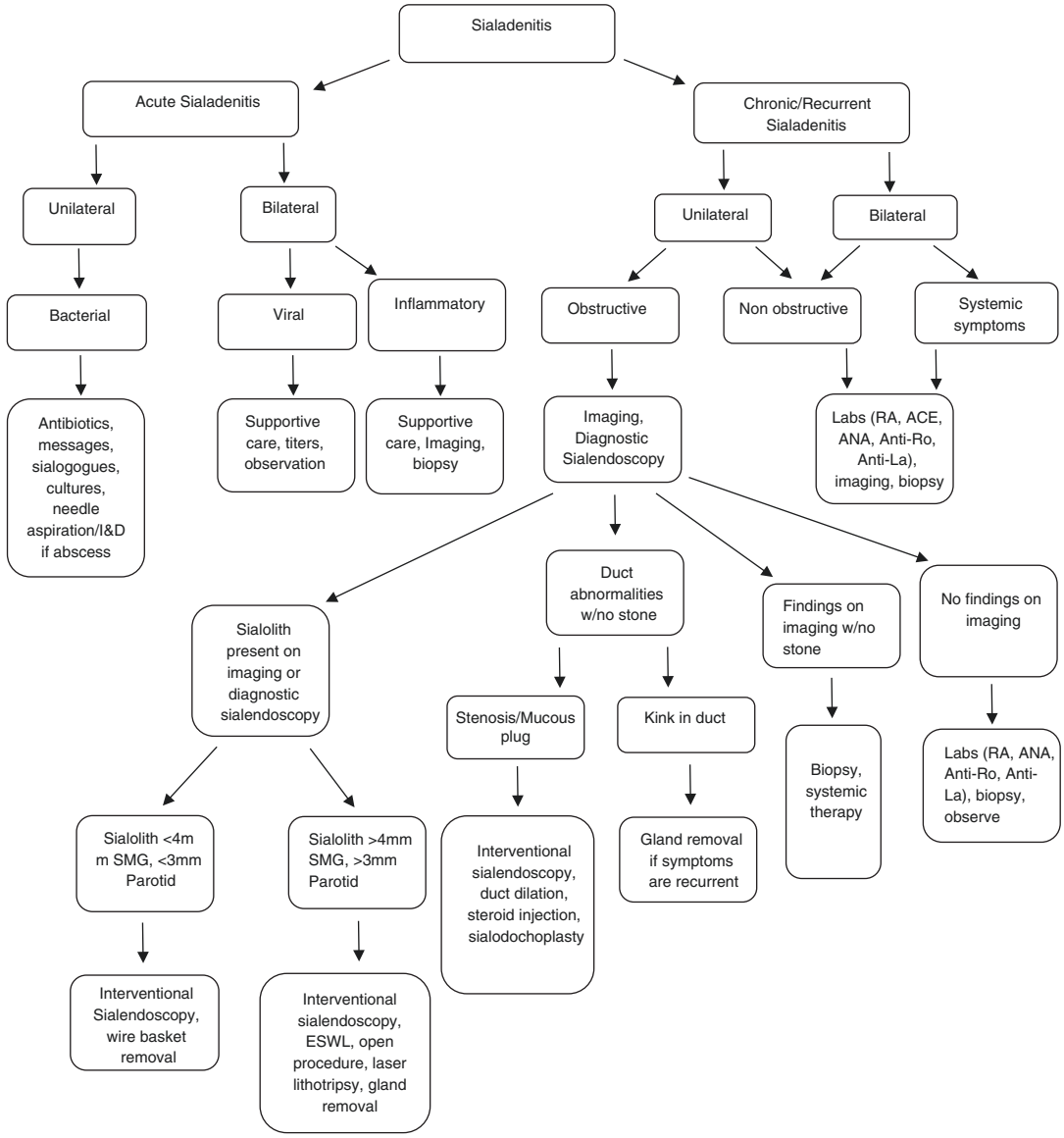

Fig. 10.4 Treatment algorithm for the management of acute and chronic sialadenitis

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