Epidemiology of Salivary Gland Infections

Luke Cascarini, BDS, MBBCh, FDSRCS, FRCS[a,*],
Mark McGurk, MD, FDSRCS, FRCS, DLO[b]

KEYWORDS

• Salivary gland infection • Sialadenitis
• Parotitis • Sialolithiasis

Bacterial or viral infections can cause acute or chronic sialadenitis. Sialadenitis of bacterial origin is a relatively uncommon occurrence today and is normally associated with sialoliths. In a study of 877 cases of obstruction, 73.2% were due to salivary calculi and 22.6% were due to salivary stricture formation with no stone present at time of examination.[1]

A hospital study of admissions in the United Kingdom found that the incidence of symptomatic sialadenitis and sialolithiasis was 27.5 and 31.5 per million population respectively.[2] However postmortem studies suggest that the prevalence of salivary calculi might be about 1.2% and they probably form as microcalculi continuously throughout life, being passed spontaneously in most cases without complication.[3]

The most common viral infection of the salivary glands is mumps.

The main factor limiting newer methodologies in, and deeper understanding of, the treatment of salivary disease, appears to be a collective lack of experience. Disorders of the salivary glands are uncommon and, when they occur, experience in managing the process is diluted over a range of disciplines (pediatrics; ear, nose, and throat; general and maxillofacial surgery). The result is that traditional views go unchallenged and are recast unchanged from one textbook to another. This article deviates from this pattern in that sialadenitis is approached on a personal perspective based on 15 years of clinical practice limited mainly to salivary gland diseases.

Ascending acute bacterial parotitis was once a common perimortal event. This is probably because, in advanced disease, the combination of failure to eat and drink leads to dehydration and lack of salivary stimulation, which in combination with immunocompromising comorbidities predispose to infection of the parotid gland by the ascent of oral bacteria. Indeed, President James Garfield died on September 19, 1881, with acute parotitis 2 months after he sustained a gunshot wound followed by several botched procedures that failed to find the projectile.

This scenario is less common today because the advent of antibiotics and improved general hygiene, together with basic modern care, minimize the likelihood of patients becoming very dehydrated.

BACTERIAL INFECTIONS

Acute Bacterial Infections

Acute bacterial sialadenitis is usually caused by bacteria ascending the salivary ducts from the mouth, although bacteremia can occur in the immunocompromised patient. The natural protective barriers to infection are the biologic properties of the saliva, the body's general immune mechanisms, and the physical features of the duct and glandular system. The saliva itself has antibacterial properties and the salivary flow physically washes debris and bacteria out of the duct. It is not widely appreciated that both the submandibular and parotid glands have, in effect, a combination of valves and sphincters to prevent ingress of contaminants.

It follows then that any process that disrupts these natural mechanisms increases the risk of ascending infections. These can be classified as conditions that disrupt the physical flushing effect of saliva through destruction, reduced production

[a] Tonbridge Dental Practice, 155 High Street, Tonbridge, Kent TN9 1BX, UK
[b] Department of Oral & Maxillofacial Surgery, Guy's Hospital, Floor 23, London SE1 9RT, UK
* Corresponding author.
E-mail address: lcascarini@hotmail.com (L. Cascarini).

Oral Maxillofacial Surg Clin N Am 21 (2009) 353–357
doi:10.1016/j.coms.2009.05.004
1042-3699/09/$ – see front matter

of saliva, and impact on the protective action of valves and sphincters. Other causes are generalized immunosuppression.

Acute bacterial sialadenitis is more common in the parotid than in either the submandibular or sublingual glands. An explanation for this may be the higher mucoid content of submandibular and sublingual secretions, which protect against bacterial infection. Certainly mucoid saliva contains lysoszyme, which acts by breaking down the 1–4 link between N-acetyl-muramic acid and N-acetyl-glucosamine, which are two of the main bacterial cell wall mucopeptides.[4] Mucoid saliva also contains significant quantities of secretory IgA and, to a lesser extent, IgM and IgD. Mucins also contain sialic acids, which inhibit bacterial attachment to epithelial cells through agglutinating bacteria and glycoproteins.[5] It may also be relevant that the opening of the parotid duct lies opposite the upper second molar teeth, which may be a ready source of bacteria in the unkempt mouth.

Acute bacterial parotitis

By far the most common cause of acute bacterial parotitis is obstruction by calculi or other foreign body. Looking for the cause should be the first line of investigation when confronted by acute bacterial parotitis. Reduced salivary flow in itself is not a strong risk factor and bacterial sialadenitis infection is not a common feature of Sjögren disease. However, reduced salivary flow has increased significance in the presence of other factors, notably immune suppression. Apart from stones, the other factor often associated with acute sialoadenitis is immunosuppression in all its forms. Systemic disorders, such as hepatic and renal disease, and poorly controlled diabetes may precipitate infection as can immunosuppression medication in its more aggressive form (oncology).

Fine needle aspiration of a parotid gland tumor, especially a Warthin tumor, has also been shown to rarely introduce infection[6] and 4% of patients treated by lithography have an acute exacerbation of infection due to the release of bacteria from the shattered calculus.[7]

Causes of reduction in salivary flow may be systemic or local. Systemic factors include dehydration and chemical inhibition of salivary stimulation. Traditionally, local factors include radiation, sialectasis, strictures, tumors, and glandular diseases, such as sarcoidosis and Sjögren disease (**Box 1**).

In practice, the risk of acute infection from these local factors is miniscule. The gland most affected by radiation is the parotid, where salivary flow may be all but eliminated. In most cases, debris or mucoid discharge can be milked from the duct, indicating chronic infection, but acute symptoms are uncommon. Similarly, sialectasis due to chronic obstruction does not lead to acute sialadenitis, but sialectasis arising as a result of repeated infection and destruction of the parenchymal tissues of the gland does indeed represent a significant risk for acute infection. Obstruction by stricture or tumors does not lead to acute symptoms, as saliva on its own is a powerful bacteriostatic agent (ranula and mucocoeles do not frequently become infected). Similarly, acute bacterial sialadenitis is an uncommon event with Sjögren disease and sarcoidosis. Occasionally, patients with advanced Sjögren disease report intermittent painful swelling of parotid glands that seem to respond to antibiotics. A careful inspection of the parotid saliva shows it to be clear. In most of these individuals, the acute swelling and inflammation are due to disregulation of lymphocyte function. A parotid tail biopsy reveals many of these patients to have mucosa-associated lymphatic tissue lymphoma, not recurrent

Box 1
Causes of reduced saliva production and flow

- Chemical inhibition (see **Box 2**)
- Dehydration
- Autoimmune disorder
  - Sjögren disease
  - Sarcoidosis
  - Primary biliary cirrhosis
- Cystic fibrosis
- Renal failure
- Infections
  - Hepatitis C virus
  - HIV
- Extremes of age
  - Elderly
  - Neonates
- Menopause
- Autonomic nervous system dysfunction
  - Diabetes mellitus
- Radiation
- Strictures
- Stones
- Tumors
- Iatrogenic damage

infection. A true bacterial infection of the parotid results in a red, inflamed papilla that stands proud of the buccal mucosa.

The parasympathetic secretomotor innervation of the parotid gland starts in the inferior salivary nucleus and travels in a branch of IX (glossopharyngeal) cranial nerve, which synapses in the otic ganglion acting on nicotinic receptors, and the outflow is via the auriculotemporal nerve, which acts on muscarinic receptors of the gland.

Drugs that attenuate this pathway include anticholinergic drugs, which block atropine and tubocurarine receptors, and drugs that inhibit the release of acetylcholine, such as botulinum toxin (**Box 2**).

Other agents that may reduce saliva production and flow are those that affect the hormonal control of salivary glands. For example, aldosterone increases sodium resorption from the striated ducts and antidiuretic hormone increases water resorption by the striated ducts. Other hormonal influences include thyroxin and testosterone, both of which increase saliva secretion.[4]

Other conditions associated with acute bacterial parotitis include psychiatric disease, probably through a combination of the anticholinergic effects of psychiatric medication as well as anorexia and adipsia associated with depression.

Acute bacterial submandibular sialadenitis

The submandibular duct is prone to obstruction by stones. Most cases of submandibular gland infection are related to this foreign body, which physically has the consistency of coral and is a reservoir for bacteria. In a review of 1200 cases of salivary calculi, 83% were in the submandibular system, 10% in the parotid, and 7% in the sublingual system.[7] Again, other reported causes of infection are tumors, strictures, or iatrogenic damage, such as postsurgery to the floor of mouth or secondary to scarring after trauma to the floor of the mouth. These cause symptoms of obstruction but rarely infection.

Acute minor bacterial sialadenitis

Acute bacterial infection of minor salivary glands is a rare entity. It should be differentiated from other conditions, such as cheilitis glandularis or stomatitis glandularis, which are nonspecific inflammatory conditions. Although secondary infection may play a part in the disease process, it seems not to be the initiating factor. Harold Baurmash in 2003 described three cases of suppurative sialadenitis of the upper lip that were treated by excision of the associated minor glands.[8] Suppurative sialadenitis should not be confused with chronic granulomatous disease.

Box 2
Drugs that cause a reduction in saliva production

- Antidepressants
  - Tricyclic and selective serotonin reuptake inhibitors
  - Lithium
  - Bupropion
- Alpha-adrenoceptor–blocking drugs
  - Antihypertensive drugs and drugs for treating symptomatic benign prostatic hyperplasia
- Antihistamines
- Antispasmodics
  - Baclofen
  - Tizanidine
- Nicotine replacement therapy
  - Bupropion
- Centrally acting antihypertensives
  - Clonidine
  - Methyldopa
  - Moxonidine (see alpha blockers above)
- Monoamine-oxidase-B inhibitors
- Opioids
- Appetite suppressants
  - Sibutramine
- Diuretics
  - Any if used excessively
- Proton pump inhibitors
  - Atropine
- Amphetamines
- Antipsychotics
- Ephedrine
- Tetracycline
- Botulinum toxin
- Steroids
- Lead (eg, cases of lead poisoning)

Chronic Bacterial Infections

Chronic bacterial parotitis

True chronic bacterial parotitis is a real entity but is uncommon and overdiagnosed. Due to the chronic nature of bacterial parotitis, there is ample ultrasound evidence of fibrosis and microcyst formation in the gland parenychema. The diagnosis is incomplete without these features being present together with a long history of recurrent, often painful swelling of the parotid gland or glands.

The etiology is multifactorial and may involve a sequence of events that make the gland vulnerable to recurrent infections.[9] The initiating event is usually obscure but Maynard showed that about 30% of children with chronic juvenile parotitis carried the disorder into adulthood.[10] The eventual architectural changes with parenchyma damage and stasis are a prelude to recurrent and persistent infections. This leads to a repetitive cycle of infection, gland damage, and reduction of saliva flow. Accumulation of semisolid material in the ducts causes obstruction of the ductal system and perpetuates the swelling.[11] Saliva is a complex thixatrophic fluid, changing consistency in sympathy with its local environment. Nasal secretions are a good analogy. In the presence of an upper respiratory tract infection, they can be thick and mucoid, but in allergy they can be watery thin. Sialoendoscopy shows that, in the presence of an irritant or stagnation, the saliva clots and forms a gel. This form of saliva predominates in chronic infection.

Chronic recurrent juvenile (parotid) sialadenitis

Chronic recurrent juvenile parotitis is probably not a single entity. One form is caused by a congenital abnormality of the salivary gland ducts. These ducts are large and have a poor seal at the sphincter. Also, the parotid lacks functional value when viewed by sialoendoscope. This results in recurrent attacks of ascending infection.[12] The parotid seems to be the only salivary gland affected. In this group, it is possible to blow air up the parotid duct and sometimes symptoms commence when the child takes up a wind instrument. Children who learn how to induce these symptoms can use them as an excuse to get out of school! Chronic recurrent juvenile parotitis is 10 times more common than adult chronic parotitis[12] and mainly affects children between the ages of 3 and 6, with males being more commonly affected. The symptoms peak in the first year of school, and usually begin to subside around mid-teens. It is unusual for symptoms to persist into the third decade of life. When the disease starts after puberty, females are predominantly affected.[13] When this condition first occurs in childhood, it should be treated aggressively with a protracted course of antibiotics supported by steroids. Anecdotally, this approach reduces the number of cases that transfer to a relapsing course of disease.

Chronic submandibular sialadenitis

Chronic recurrent submandibular sialadenitis Chronic recurrent submandibular sialadenitis is due to incomplete resolution of an acute infection that persists as a chronic relapsing condition, usually because of a failure to treat the underlying cause of the acute infection (eg, removal of the stone). A study of 4600 salivary stones treated at five centers demonstrates that there is usually a delay of 4 to 5 years from first obstructive symptoms (mealtime syndrome) to sialadenitis.[13] Traditionally it is claimed that chronic infection persists even after stone removal because of parenchymal damage leading to stasis and chronic sialolith formation. This view is erroneous. Ten-year follow-up studies now available following lithography demonstrate that glands remain symptom-free as long as the stone is cleared. The recurrent stone rate after removal is approximately 4% of cases.[14] Infection in the submandibular gland almost always involves the sublingual gland. The floor of mouth is firm and a discharge can be milked from the submandibular duct.

Chronic sclerosing submandibular sialadenitis (Kuttner tumor) Chronic sclerosing submandibular sialadenitis is the formation of a painful swollen gland, which is more common in the elderly and mainly involves the submandibular gland although similar processes have been reported in the other major salivary glands. Chronic sclerosing submandibular sialadenitis is associated with sialoliths and nonspecific infectious agents. It is an obscure condition and diagnosis is difficult because of a lack of clear objective criteria.

HIV

HIV-associated salivary gland disease is not an infection of the salivary glands per se but a reaction of the glands to the HIV agent. The resultant enlargement of the glands is termed HIV-associated salivary gland disease. This condition results in reduction of salivary gland function and may lead to secondary ascending infection. The ultrasound appearance is almost diagnostic with the appropriate clinical history. The gland is packed with microcysts, an appearance that is also seen in mucosa-associated lymphatic tissue.

MUMPS

Mumps, a common childhood infection worldwide, is a nonsuppurative infection caused by the mumps virus. It is spread by saliva and urine and typically produces painful swelling of the parotid gland. Complications of mumps include meningitis, encephalitis, thyroiditis, hepatitis, and myocarditis, as well as orchitis and oophoritis, which can affect adults. Other less common complications include deafness and pancreatitis.[15] Apparently in 25% of cases, the salivary

swelling may be unilateral, which may serve to obscure the diagnosis unless attention is paid to systemic symptoms.

The condition usually starts with 1 to 2 days of malaise, anorexia and low-grade pyrexia with headache followed by parotid gland enlargement without purulence. The parotid enlargement affects 95% of symptomatic individuals. The swelling progresses over a couple of days and lasts about a week. The orifice of the Stensen duct may be swollen and edematous. In 90% of cases, the contralateral gland is also affected but there may be a time delay between the two sides. In about 10% of cases the submandibular and sublingual glands are affected, which is usually bilateral concomitant with the parotid swelling.[15]

Cerebrospinal fluid pleocytosis occurs in over 50% of cases of mumps, usually without other signs or symptoms of meningitis.[16] Mumps meningitis occurs in 1% to 10% of cases and encephalitis in 0.1%.[16] Epididymo-orchitis affects 15% to 30% of adult males. Five percent of adult females develop oophoritis and mastitis has also been reported. Although mumps meningitis is very benign, mumps encephalitis has approximately 1.5% mortality.[16]

REFERENCES

1. Ngu RK, Brown JE, Whaites EJ, et al. Salivary duct strictures: nature and incidence in benign salivary obstruction. Dentomaxillofac Radiol 2007;36:63–7.
2. Escudier MP, McGurk M. Symptomatic sialadenitis and sialolithiasis in the English population, an estimate of the cost of treatment. Br Dent J 1999;186(9):463–6.
3. Brown JE. Interventional sialography and minimally invasive techniques in benign salivary gland obstruction. Semin Ultrasound CT MR 2006;27(6): 465–75.
4. Lavelle CLB. Applied oral physiology. 2nd edition. Chapter 14. Bristol (UK): Wright; 1998. p. 139.
5. Tabak LA, Levine MJ, Mandel ID, et al. Role of salivary mucins in the protection of oral cavity. J Oral Pathol 1982;11:1–17.
6. Bahar G, Dudkiewicz M, Feinmesser R, et al. Acute parotitis as a complication of fine-needle aspiration in Warthin's tumour. A unique finding of a 3-year experience with parotid tumor aspiration. Otolarngol Head Neck Surg 2006;134(4):646–9.
7. Rausch S, Gorlin RJ. Diseases of the salivary glands. In: Gorlin RJ, Goldman HM, editors. Oral pathology. St. Louis (MO): Moseby; 1970. p. 962.
8. Baurmash HD. Suppurative sialadenitis of the upper lip: a report of 3 cases of an infrequent lesion. J Oral Maxillofac Surg 2003;61:1361–5.
9. Motamed M, Laugharne D, Bradley PJ. Management of chronic parotitis: a review. J Laryngol Otol 2003;117(7):521–6.
10. Maynard JD. Recurrent parotid enlargement. Br J Surg 1965;52(10):784–9.
11. Baurmash HD. Chronic recurrent parotitis: a closer look at its origin, diagnosis, and management. J Oral Maxillofac Surg 2004;62:1010–8.
12. Chitre VV, Premchandra DJ. Recurrent parotitis. Arch Dis Child 1997;77(4):359–63.
13. Iro H, Zenk J, Escudier MP, et al. Outcome of minimally invasive management of salivary calculi in 4691 patients. Laryngoscope 2009;9(2):263–8.
14. Zenk J, Bozzato A, Winter M, et al. Extra corporeal shock wave lithotripsy of submandibular stones; evaluation after ten years. Ann Otol Rhinol Laryngol 2004;113(5):378–83.
15. Hviid A, Rubin S, Muhlemann K. Mumps. Lancet 2008;371(9616):932–44.
16. Bang HO, Bang J. Involvement of the central nervous system in mumps. Acta Med Scand 1943;113: 487–505.