Chapter 9

Management of Infections of the Salivary Glands

9

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Contents

Core Features

- Infections of the salivary gland most commonly affect the major glands.
- Infections may present as an acute, chronic, or acute and chronic problem.
- The most common pathogens identified are viral and bacterial.
- Children are affected with the same diseases as adults.
- Adults most commonly present with total gland obstruction associated with sialolithiasis, ductal stenosis, or sialectasis.
- Patients with recurrent symptoms should be investigated electively.
- Total gland swelling is more likely ductal disease, as distinct to partial gland swelling which may be neoplastic or inflammatory disease.

Complications to Avoid

- Investigation should be considered in all patients, children and adults, who have recurrent symptoms, swelling ± pain, to exclude reversible disease or a neoplastic process.

Introduction

Infection of the salivary glands is best defined as an acute and/or a chronic condition which presents as swelling, with or without pain, with or without systemic involvement, and which affects the major and minor salivary glands. The most common pathogens identified are viral and bacterial. The most frequent clinical problem is that of an adult who presents with a swelling of the parotid or submandibular gland, with a diagnosis of obstructive sialadenitis associated with sialolithiasis, ductal stenosis, or sialectasis. The probable cause for the obstructive sialadenitis is associated with a bacterial infection. One of the theories proposed for such infectious processes is the retrograde theory of bacterial infection from the oral cavity.

In the general population, mumps is associated with acute swelling of the parotid gland. It is a specific viral disease, contagious and epidemic, which typically affects school-age children. It can also affect adults, mainly the elderly. It is associated with fever, malaise, myalgia, and headache. Most children who present with an isolated acute painful parotid swelling do not have mumps as a diagnosis, but similar symptoms can be caused by other viruses. These viral infections are not epidemic and are non-infectious, but are sporadic and are commonly and erroneously labeled as mumps. Frequently, parents and General Medical Practitioners consider that when an acute parotid gland swelling episode arises it is mumps, but one can only be infected with the mumps virus once because antibodies are precipitated and this prevents a second infection.

Recurrent parotitis of childhood is the most frequent non-viral affection of salivary glands in children, and these distressing symptoms, swelling, pain, and systemic upset, usually resolve around puberty. Its precise origin remains unclear, and as a result no specific treatment exists. Sialendoscopy, when performed, has proven until now to be partly effective.

Swelling of the parotid, acute and chronic, present in two fashions: swelling of the whole gland (such as mumps) or partial swelling of the gland (such as tuberculosis, cat-scratch disease, benign and/or malignant neoplasms).

In the case of submandibular swelling, the whole gland is considered swollen and a swelling of part of the gland is difficult to differentiate clinically. Also, differentiating submandibular gland from adjacent lymph nodes is sometimes difficult and requires the use of radiological imaging. Not infrequently, discrete inflammatory swellings of the parotid or submandibular gland are in fact infections of peri- or intraglandular lymph nodes.

Infectious processes of the minor salivary glands including sublingual, generally present as a painless non-ulcerative swelling similar to that of a neoplasm. The diagnosis frequently requires a tissue diagnosis.

In the past, the classic division of salivary gland diseases and infections relied on a differential diagnosis. A different concept proposed is to classify these diseases according to their clinical presentation, considering the frequency of the episodes and the combinations of the associated symptoms. This understanding necessitates separating glands into submandibular and parotid because of their different etiologies and frequencies of these disorders.

Infectious salivary swellings have to be differentiated into acute and progressive (chronic). Acute is defined as a patient who had a previously normal gland, with a sudden onset of a diffuse ill-defined swelling of the entire gland or a localized swollen area with indiscrete margins associated with pain, and more rarely erythema, and purulent exudate visible at the papilla. Chronic presentation is a gradual awareness of a diffuse swelling of the entire gland or a discrete well defined mass or swelling, most usually not associated with pain, sometimes presenting with skin involvement (which might be a sign of a neoplasm or tuberculosis).

Algorithms

The algorithms in Figs. 9.1 and 9.2 show the differential diagnosis of parotid and submandibular swellings.

Investigations of Infectious and Inflammatory Conditions

Most patients who present with an acute swelling irrespective of age are considered to have an inflammatory or infectious course. Such patients are usually treated empirically by antibiotics, even though many such presentations include viral conditions. Therefore, investigation of these patients when the symptoms, most frequently pain, resolve is in the non-acute resolved phase. However, should purulent exudates be evident at the papilla, then it would seem appropriate to take a sample and send it for culture and sensitivity.

In the resolved acute clinical presentation, investigations, if facilities are available, would be in ranked order: ultrasound, followed by sialendoscopy. In the acute unresolved cases (after approximately 2 weeks of treatment), a magnetic resonance (MR) sialogram or plain computed

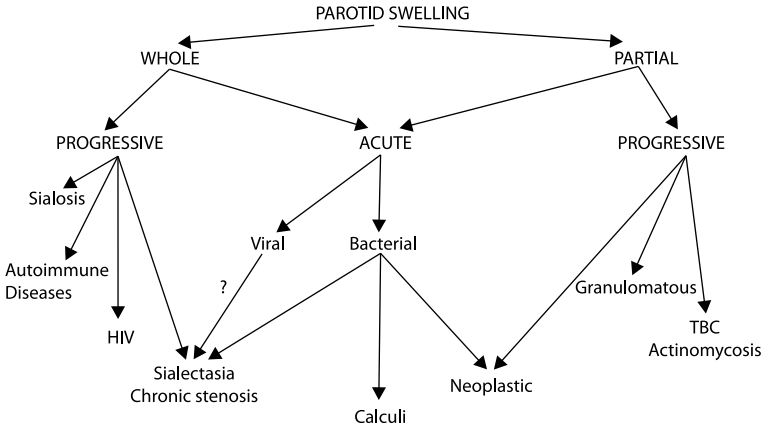

Fig. 9.1: Differential diagnosis of parotid swellings

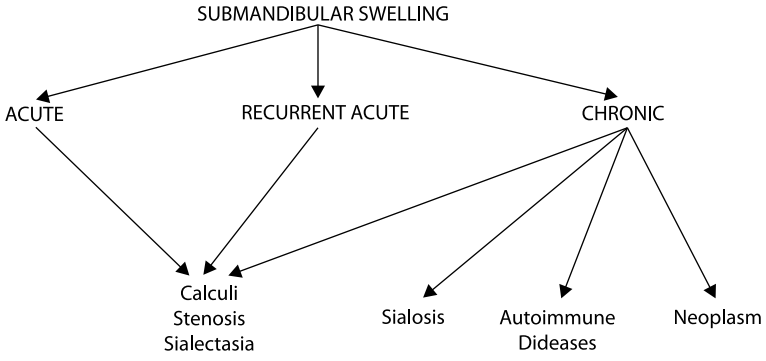

Fig. 9.2: Differential diagnosis of submandibular swellings

tomographic (CT)-MR image would be appropriate. In the chronic situation, a plain CT-MR image, ultrasound (US)-guided fine-needle aspiration cytology (FNAC), or MR sialogram is mandatory.

Treatment of Infectious and Inflammatory Conditions

In the child or infant in an acute situation, the most frequent diagnosis is viral infection. As the child will be toxic and pyrexial and suffers pain, antibiotics, analgesics, and hydration are recommended. In the recurrent acute situation occurring at frequent intervals, anti-inflammatory with analgesia treatment should be given. The parents anticipate a treatment, but its effectiveness in preventing recurrence is much debated and frequently does not shorten or prevent further episodes. In adults, the acute situation is most usually associated with a bacterial infection. They require hydration, antibiotics, anti-inflammatories, and analgesia. In the chronic situation, the patient should be treated according to the result of the previous investigations, described above, including the results of a culture if performed.

Viral Diseases

Mumps

Mumps is the most common viral infection of the salivary glands [1] and presents with unilateral or bilateral swelling of the parotid glands. In 85% of cases, it affects children under the age of 15 years. Stensen's papilla may be irritated and swollen, but no purulent exudate is visible or expressible. Glandular symptoms are often preceded by 1–3 days of a prodromal period, where the patients complaints might include malaise, discomfort, loss of

appetite, chills, fever, and sore throat. The swelling usually lasts from a couple of days to one week, and there is no purulent exudate at the papilla on examination [2, 3]. Laboratory findings include leukocytopenia, with relative lymphocytosis. Serum amylase can be analyzed: it peaks in the first week and normalizes by the second or third week. Soluble antibodies directed against the nucleoprotein core of the virus appear within the final week of the infection, and disappear within 8 months [4]. Antibodies directed against the outer surface appear several weeks after soluble antibodies, and persist for 5 years [5].

Mumps is due to a paramyxovirus, an RNA virus related to the influenza and parainfluenza viruses. Mumps is spread by aerosol droplets from the saliva and nasopharyngeal secretions of an infected individual and spreads easily in highly populated urban areas. Incubation lasts from 2 to 3 weeks and the patient is infectious from 3 days before the onset of salivary swellings to 7 days after [6]. The peak incidence is at age 4–6 years, but the incidence has dropped in the last decades because of the systematic introduction of mumps vaccine. Studies have shown that more than 95% of adults have antibodies against mumps. Complications include orchitis (25% in young males), pancreatitis, sensorineural hearing loss (1/20,000 in children, being the first cause of acquired sensorineural hearing loss in children), and meningoencephalitis [6]. Mumps might be a cause of abortion during the first trimester of pregnancy because of fetal endocardial fibroelastosis.

Classic treatment includes antibiotics, sialagogues, and rehydration, the treatment depending on the clinical course and on the extent of the disease.

Non-mumps

Other viruses may mimic clinical mumps, such as influenza and parainfluenza viruses (type 1 and 3), Coxsackie viruses (A and B), echovirus, and lymphocytic choriomeningitis virus [4, 7, 8]. Cytomegalovirus and adenoviruses have also been described, mostly in human immunodeficiency virus (HIV) patients. Patients will have the same symptoms as described for classic mumps.

Human Immunodeficiency Virus

Parotid HIV manifestations present as an enlargement of the gland due to multiple lymphoepithelial cysts [9]. These cysts can be assessed by the use of ultrasound and fine-needle aspiration, which reveals serous fluid with the presence of lymphocytes and macrophages. Their presentation has not been associated with the prognosis of the disease [10]. As the parotid gland contains many lymph nodes at different levels, they might be enlarged as HIV virus mainly affects lymphoid tissue. One should not forget the differential diagnosis with solid tumors which also have an increased incidence in the parotid of HIV patients [9]. Infectious causative agents are *Pneumocystis carinii*, adenovirus, histoplasma, and cytomegalovirus (CMV), which can be found in the saliva [11].

Thirty percent of HIV-infected children have proven to have enlargement of their parotid glands [12]

Bacterial Diseases

Clinical Course

The illness is of acute onset, with tender painful swelling of the salivary gland. Parotids are affected more frequently than submandibular glands. One of the possible reasons would be that the bacteriostatic activity of the parotid saliva is inferior to that of submandibular saliva. Palpation of the gland is painful and causes purulent discharge at the papilla. Massaging the gland and expressing purulent exudate and saliva—even though this is painful—relieves the pressure pain of the patient by diminishing the pressure in the ductal system.

Localized infections of minor salivary glands including sublingual glands can be seen, and have the same causative agents. Calculi are also encountered [13].

Management consists of broad-spectrum antibiotics, after having performed a culture looking for the precise etiology of the infection. Associated anti-inflammatory medication may help to reduce the pain and swelling symptoms of the patient. In cases of severe swelling, corticosteroids do diminish the inflammation, and have a rapid effect in relieving the symptoms. The geriatric population is affected by marantic parotitis, caused by dehydration [14].

Small children can also be affected by this disease, in the first 2 weeks of life, in the parotid [15] and more rarely in the submandibular gland [16, 17], and these episodes affect most frequently premature infants who are often dehydrated, showing the importance of dehydration as a probable pathogenic factor.

Type of Bacteria

The contamination mode of the parotid gland in cases of suppurative parotitis is unknown. The retrograde contamination of the gland by bacteria from the oral cavity, and the stasis of salivary flow or a reduced salivary flow might be the main causes. Penicillin-resistant coagulase-positive staphylococcus is commonly encountered, but the flora is usually mixed, containing not only *Streptococcus pneumoniae* and beta-hemolytic streptococcus, but also gram-negative germs, such as coli. Anaerobic bacteria also play a role, and studies have shown the presence of 30–40% of anaerobic bacteria (bacteroides, peptostreptococcus, fusobacteria) [18–21].

Bacteria that affect infants are the same as those that affect adults [7, 22, 23], and *Pseudomonas aeruginosa*, *Neisseria catarrhalis*, and methicillin-resistant *Staphylococcus aureus* (MRSA) have been reported [24]. In South-East Asia, *Pseudomonas pseudomallei* has also been reported [4].

Cat-scratch Disease

This disease involves lymph nodes adjacent to salivary glands and the salivary glands may be involved by continuous spread. Patients usually remember being exposed to cats, and children or young adults are most often involved. *Bartonella henselae*, a gram-negative bacteria, is the pathogen [25]. Laboratory findings include specific polymerase chain reaction (PCR) or serology. Although generally prescribed, antibiotics seem not to be effective in shortening the course of the disease. The affected lymph node disappears spontaneously within a few months.

Actinomycosis

Actinomycosis affects lymph nodes adjacent to salivary glands, masquerading as a salivary gland infection. The pathogen is Actinomyces israelii [26]. Other pathogens include *Actinomyces proprionica*, *A. viscosus*, and *A. odontolyticus*. There are three forms of infections. The first is acute, associated with suppuration. The second is chronic, slowly progressive, with marked induration and may be mistakenly diagnosed as a neoplasm. The third form is subacute and is represented by a slightly tender and tumor-like mass attached to the mandible. The finding of "sulfur grounds" on pathological evaluation are pathognomonic of this condition. Treatment of the acute phase is surgical, with eventual drainage of the exudates. Broad-spectrum antibiotics are administered.

Other Diseases

Recurrent Parotitis in Children

The disease is characterized by recurrent episodes of acute or subacute swellings of the parotid glands, unilateral or bilateral, associated with fever and pain. Mucopurulent saliva can be expressed from the papilla, which is often red. Episodes recur every several months, sometimes more often, but the child is free of symptoms between the episodes. The age of presentation has been described from 8 months to 16 years [5], but more frequently from 5 to 7 years [3], and the symptoms usually decrease or cease at puberty (92% of symptom-free adults at 22 years, independent of treatment) [27]. The histological appearance of the salivary gland reveals massive infiltration with lymphocytes with lymphoid follicle formation, and cystic ductal formations (sialectasis) [27, 28]. No therapy is available for this disease, but antibiotics are usually given. Anti-inflammatory medication also reduces the severity of the attacks. Among etiological factors considered are congenital malformation of the parotid ducts [29, 30], familial background and impaired rates of secretion [31–35], primary or secondary infections, and local manifestations of systemic immunological disease [36]. The sialographic changes remain until adult life [27]. Recently, sialendoscopy has proven to be effective in these cases [37–40]. The sialendoscopic appearance of the duct shows diffuse reduction of the caliber of Stensen's duct [41], associated sometimes with multiple localized stenosis, and sometimes with salivary calculi (personal data). Parotid surgery has been described, as well as ligation of the duct [36, 42] which in our opinion should be absolutely avoided.

Granulomatous Sialadenitis

They are of different types of granulomatous diseases affecting salivary glands (Table 9.1). Ductal obstruction secondary to calculi or more rarely to tumor is the commonly identified cause [29]. The parotid gland is involved in most of cases. Symptoms include painless firm nodules in the parotid area. Histological confirmation of the disease include typical non caseous granulomas.

Mycobacteria

Mycobacterium tuberculosis and atypical mycobacterium both affect lymph nodes adjacent to salivary glands or intraglandular lymph nodes [43–47]. Usually, they are contaminated by the local infection affecting the mouth, the pharynx, or the lungs [43, 44, 48, 49]. The clinical presentation can be an acute inflammatory lesion or a chronic tumor-like lesion.

Diagnosis of *Mycobacterium tuberculosis* is best made by a purified protein derivative (PPD) skin test followed by a fine-needle aspiration to avoid unnecessary surgery. Treatment relies on medical management using a combination of antibiotics including isoniazid, rifampicin, and pyrazinamide.

In cases of atypical mycobacteria, adults and infants can be infected, but it is commonly seen in children between 2 and 5 years, and adults suffering from immunodeficiency disorders [50]. *Mycobacterium avium-intracellulare* and *M. scrofulaceum* are the organisms responsible [51], and the diagnosis is made either by culture performed after therapeutic excisional biopsy of the lymph node or by a specific PPD test. Its diagnosis is often delayed, as the classic PPD test remains negative. Treatment is surgical and excision but sometimes curettage may eradicate the localized infection depending on its location, but chemotherapy may play a role in suboptimal surgery.

Sarcoidosis

Sarcoidosis is a systemic disease involving multiple organs. Its etiology remains unclear, but several hypotheses have been made, including autoantigens and infectious organisms [52]. Salivary glands are usually affected, and specifically the parotid glands. Symptoms include swellings and dry mouth. Laboratory findings include amylase and kallikrein diminishing during the acute phase of the disease, and the finding of angiotensin-converting enzyme (ACE test). Diagnosis is confirmed if there is radiological and histological evidence of non-caseous epithelial granulomas. Biopsies can be obtained either from minor salivary glands with a less good sensitivity than parotid biopsies [53, 54]. Corticosteroids are the best therapeutic option.

Heerfordt's disease, also called uveoparotid fever, associates parotid enlargement with uveitis and facial palsy. It is a rare form of sarcoidosis occurring in young patients in their 20s.

Hydatic Disease

This diagnosis is suspected in endemic areas and is extremely rare. Salivary glands suffer from a cystic condition and the diagnosis is usually made postoperatively [55].

Take Home Messages

- Mumps is the most common viral cause of parotid swelling in children, but is a "once in a lifetime" infection.
- Recurrent parotitis in children should be treated symptomatically.
- Antibiotics should only be given when a specific bacterial infectious diagnosis is suspected or proven.
- Partial salivary gland swellings, after investigation, may require excision to prove the likely pathogens if infection is the cause, or to exclude the possibility of a malignant neoplastic process.

Table 9.1. Types of granulomatous sialadenitis

Tuberculosis
Crohn's disease
Melkersson-Rosenthal syndrome
• Cheilitis granulomatosa Miescher
Granulomatous giant cell sialadenitis
• Submandibular or sublingual
Xanthogranulomatous sialadenitis
Wegener's granulomatosis
Churg-Strauss granulomatosis
Sialadenitis after sialography
Inflammatory pseudotumors
• Eosinophilic granuloma
• Kimura's disease
• Angiolymphoid hyperplasia with eosinophilia
• Lymphomatous granulomatosis
• Rosai-Dorfman disease

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