

Sialadenitis: A Review of the Literature

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Abstract

Salivary glands are tubulo-acinar exocrine organs responsible for the formation and secretion of the saliva. Salivary gland inflammation is known as sialadenitis which can originate from various non-infectious and infectious causes. Although several other viruses also can involve the salivary glands which include Choriomeningitis, Coxsackie A. ECHO. Cytomegalovirus (in neonatal) and parainfluenza, mumps is the most common viral infection. Most bacterial-infections arise due to ductal obstruction or decreased salivary flow which allows the retrograde spread of bacteria through the salivary ductal system. Viral infections, bacterial infections, allergic reactions, and systemic diseases are the major causes of sialadenitis and it may be acute or chronic. The etiology, diagnosis, and treatment of these conditions are discussed.

Keywords: Salivary glands; Sialadenitis; Etiology, Diagnosis, Treatment.

Introduction

The oral cavity depicts many pathological processes from the ubiquitous collection of tissues. The salivary glands may be classified as major and minor glands. Major glands are paired glands; these are Parotid, Sublingual and Submandibular glands. Inflammation of the salivary glands is known as sialadenitis. Pathogenesis - (1) Retrograde contamination of the duct and parenchymal-tissues by bacteria inhabiting in the oral cavity. (2) Stasis of salivary flow promotes acute suppurative infection. Viral infections, bacterial infections, allergic reactions, and systemic diseases are the major causes of sialadenitis. It may be acute or chronic.

Acute Suppurative Sialadenitis: Acute suppurative sialadenitis most frequently involves the parotid gland followed by the submandibular gland. This may be

explained because of the serous saliva produced by the parotid gland which has less bacteriostatic activity than that of mucinous saliva of the submandibular gland. Although acute suppurative parotitis can occur in individuals of any age, patients most frequently affected are aged from 50 to 70 years. The reduction of the secretory flow and stasis of saliva, typically as a result of dehydration, is an integral pathogenetic factor of acute suppurative sialadenitis. In acute suppurative sialadenitis, bacterial organisms usually enter from the oral cavity in a retrograde fashion. Staphylococcus aureus is the most common causative agent and accounts for 50% to 90% of cases.^{1,2}

Usual clinical presentation is the sudden onset of diffuse swelling of the affected gland associated with induration, erythema, pain, and tenderness. Some patients complain of reduced mandibular movement and difficulty in swallowing. Patients frequently have systemic signs of toxemia, including delirium, high fever, and leukocytosis. Association with systemic sepsis is more common in infections of the parotid gland than the submandibular gland. The respective intraoral duct orifice may become red and swollen with purulent discharge recognized on the massage of the gland. The diagnosis of acute suppurative sialadenitis is based on the clinical features with the culture of the purulent material from the duct. Any abscess formation

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can be determined using computerized tomography or ultrasound scanning. Sialograms are contra indicated in cases of acute suppurative infection of the salivary glands. Initial treatment of acute suppurative sialadenitis should be conservative, with eliminating the causes, improved oral hygiene, adequate hydration to increase the salivary flow, repeated massage of the affected gland, and administration of appropriate oral or intravenous systemic antibiotics, usually for a penicillinase-resistant *Staphylococcus*. Irradiation of the glands is no longer recommended. Incision and drainage by surgical intervention are indicated in cases involving abscess formation.

Obstructive Sialadenitis and Sialolithiasis: This is the most frequent type of chronic sialadenitis, accounting for about 30% of all chronic sialadenitis cases and approximately 1% of all salivary gland diseases^{3,4}. Although sialolithiasis is the most common cause of obstructive sialadenitis by far, two major factors are playing a role in the pathogenesis of the disease⁴. One is a mechanical obstruction by sialoliths, salivary gland cysts and tumors, and lesions of the oral mucosa. The other factor is a disturbance of the electrolyte concentration of saliva, resulting in the development of viscous secretory products. Sialoliths develop as a result of deposition of calcium salts around a nidus such as bacterial colonies, cellular debris, mucous plugs, or foreign bodies.

The peak age of incidence of sialolithiasis is between 30 and 60 years, with a mean of about 45 years³ and slight male predominance. About 80% of cases of sialolithiasis develop in the submandibular gland, followed by the parotid gland³. Then the other salivary glands submandibular gland is more susceptible to sialolithiasis because its saliva has higher mucin content, increased viscosity, a more alkaline pH, higher concentrations of calcium and phosphate, and antigravity flow within the duct. In the submandibular gland, 57% of stones are localized near the hilum, 34% in the distal area of the submandibular duct (Wharton's duct), and 9% in the intraglandular ducts⁵. The formation of sialoliths in the main ducts produces swelling of the distal salivary gland tissue with or without pain. The episodes of the symptoms are frequently recurrent and exacerbated by eating. When sialoliths occur in the submandibular gland duct, induration can be observed on the floor of the mouth, and the duct orifice becomes erythematous and swollen. Sialoliths in the minor salivary glands are mostly asymptomatic presenting as a small, firm nodule. Ductal obstruction blocks secretion and leads to stasis of

the saliva within the duct, which becomes predisposed to retrograde bacterial infection; *Streptococcus viridans* is a commonly involved pathogen.

The diagnosis of sialolithiasis is principally based upon clinical and imaging examinations⁵. Sialoliths of the distal area of Wharton's duct and the hilum can be detected by bimanual palpation of the affected area. Plain radiography is a helpful method to diagnose sialolithiasis, but 90% of submandibular stones are radiopaque while most parotid stones are radiolucent. Sialography is very accurate in the diagnosis of sialolithiasis but is usually unnecessary and is contraindicated in the acute setting of sialadenitis. Instead, high-resolution ultrasound and CT are the most useful diagnostic tools. The first steps of management of sialolithiasis in the submandibular and parotid glands include conservative method, such as adequate hydration, sialogogues, and gland massage as well as minimally invasive approaches, such as basket retrieval and interventional sialendoscopy to remove the stones, depending on their location and size⁵. When these measures fail, extracorporeal shock-wave lithotripsy may be the treatment of choice. Extirpation of the affected gland is recommended only in the minority of recalcitrant cases.

Chronic Sclerosing Sialadenitis (Kuttner Tumor): Chronic sclerosing sialadenitis is the salivary gland inflammatory disease, which was first described by Kuttner in 1896⁶. Chronic sclerosing sialadenitis produces a hard swelling of the salivary gland that cannot be easily distinguished clinically from neoplasia. This inflammatory process almost exclusively affects the submandibular gland.

Recently it has become increasingly recognized that chronic sclerosing sialadenitis exists to the group of immunoglobulin G4 (IgG4) related sclerosing (systemic/autoimmune) diseases^{7,8}. This notion is further supported by the fact that chronic sclerosing sialadenitis has been associated with one or more extrasalivary IgG4-related sclerosing diseases, which are characterized by infiltrating of the chronic inflammatory cell containing abundant IgG4-positive plasma cells, accompanied by atrophy of the normal parenchyma and sclerosis. The close association suggests that at least some cases of chronic sclerosing sialadenitis share common pathogenesis with other sclerosing diseases involving disturbance of IgG4 as a systemic disorder. Chronic sclerosing sialadenitis can appear at any age between 12 and 83 years. Clinically, the patients appear

with a firm swelling of the submandibular gland with or without recurrence of pain associated with eating. This appearance of a firm, enlarging growth can lead to the erroneous clinical diagnosis of a neoplastic salivary gland, particularly carcinoma. The glandular involvement is usually unilateral, but it can be bilateral. Cases with swelling of bilateral submandibular glands and lacrimal glands, similar to Mikulicz's disease, have been reported⁹. As mentioned above, chronic sclerosing sialadenitis is sometimes associated with the extrasalivary IgG4- related sclerosing diseases; therefore, a systemic examination is recommended for patients with chronic sclerosing sialadenitis.

Radiation Sialadenitis: Radiotherapy is the most commonly used modality for treatment of the head and neck cancers¹⁰. When the major salivary glands are included within the fields of radiotherapy, many patients develop swelling and tenderness of the irradiated glands as well as elevation of the serum amylase level within hours of receiving even the first treatment in a course of fractionated radiotherapy. These symptoms may be transient, but a significant proportion of the patients will suffer persistent salivary gland dysfunction, resulting in xerostomia accompanied by a variety of complications, such as dysphagia, abnormal taste sensations, oral mucositis, dental caries, and periodontal disease. The saliva secreted from irradiated salivary glands has a lower pH, lower protein and secretory antibody contents, higher salinity, and increased numbers of cariogenic microorganisms. The severity of salivary gland damage and dysfunction depends on the dose and the duration of irradiation. The important pathogenetic factor of radiation sialadenitis is the direct irradiation effect on the salivary gland tissue rather than the result of radiation-induced changes in the vasculature¹¹. Considerably serous acinar tissue of the parotid gland is more radiosensitive than mucous glandular tissue of the submandibular gland¹². The radiosensitivity of the acinar cells depends on the content of secretory granules, containing a large number of heavy-metals limited by the membrane¹³. Released heavy metals as a result of the irradiation may cause membrane lipid peroxidation utilizing a redox system, thus enhancing the process of apoptotic cellular death¹³.

Recurrent Parotitis: Recurrent parotitis is a well-recognized entity in children, represented by recurring episodes of swelling of the parotid gland. Although it is relatively rare, it is still the second most common salivary gland inflammatory disease in children, next to mumps^{14,15}. Recurrent parotitis is generally associated

with nonobstructive sialectasis of the parotid gland. However, the sialectasis may be both the cause and the result of the recurrent exacerbations of the parotitis¹⁶. The age of onset of recurrent parotitis has been reported to be between 3 months and 16 years, but it mostly starts between three and six years with a peak during the first year of school¹⁴ and with a male predilection. Recurrent parotitis presents as an intermittent, painful swelling of either unilateral or bilateral parotid glands during mastication and/or swallowing, generally accompanied by fever and malaise. The disease is often clinically misdiagnosed initially as mumps. The number of attacks varies individually, but most commonly occurs every three to four months^{14,15}. The swelling lasts from several days to 2 weeks, and typically resolves spontaneously, regardless of the treatment. Between the episodes, the patient is free from symptoms. Recurrent parotitis is generally self-limiting, and after puberty, by age between 10 and 15 years. Although it usually is not accompanied by purulent secretion, the majority of affected glands grow bacteria on the culture of saliva. Sialography has been considered the most important and accurate diagnostic tool, though its role has become secondary to ultrasonography now. The main treatments of an acute phase of recurrent parotitis are either conservative observation or antibiotic treatment. Penicillin V is a good choice for acute infections. Other treatments are much more invasive when applied to adults with persistent severe disease, including duct ligation, parotidectomy, and tympanic neurectomy.

Viral Sialadenitis Including Mumps and Cytomegalovirus: Viral infections involving the salivary glands are more common than those of bacterial origin. Viral sialadenitis is a manifestation of a systemic infection, and the salivary glands are affected by a hematogenous spread of virus rather than a direct infection to the organ as in bacterial sialadenitis. A variety of viruses are known as causative agents of sialadenitis, including the paramyxovirus (mumps), cytomegalovirus, HIV, coxsackie A virus, Epstein-Barr virus (EBV), echovirus, herpes virus, lymphocytic choriomeningitis virus, adenovirus, and influenza A and parainfluenza viruses¹⁷. Mumps is by far the most common cause of parotid swelling and is the most common viral agent involving the salivary glands¹⁸. Mumps is caused by a highly contagious paramyxovirus. The frequency has reduced with a vaccine made from attenuated live mumps virus. The peak incidence is between the ages of four and six years, but infection can

be seen in other age-groups. The incubation period is two to three weeks, with a clinical onset characterized by swelling and pain of single or both parotid glands. Systemic symptoms include fever, malaise, myalgia, and headache, and usually, resolve before the parotid swelling. Adults infected with mumps are more possibly to develop severe symptoms and complications, while in children symptoms are usually not severe. Generally based on clinical presentation the diagnosis is made. Demonstrating antibodies to the mumps V and S antigen by enzyme-linked immunoadsorbent assay can confirm the diagnosis. Some laboratories use molecular method that are based on a nested polymerase chain reaction. Many cases are subclinical, and studies have shown that greater than ninety-five percent of adults have neutralizing antibodies. Orchitis occurs in 10% to 20% of infected males, but it is usually unilateral, and sterility only infrequently arises; in about 5% of those infected aseptic meningitis occurs. The disease is generally self-limiting with a good outcome. Swelling and other acute symptoms usually subside within two weeks. There is no specific treatment apart from controlling the symptoms with analgesics.

Cytomegalovirus is a member of *Betaherpesvirinae* in the subfamily of *Herpesviridae*. Most infections are acquired during childhood in developing countries, whereas, up to 50% of young adults are seronegative in developed countries. Cytomegalovirus is not highly contagious, thus the infection requires close contact with an infected person excreting the virus in their urine, saliva, or other bodily fluids. Cytomegalovirus can be transmitted via breast milk and can also be sexually transmitted, transplanted organs, and rarely from blood transfusions. Cytomegalovirus infection without symptoms is common in infants and young children. The symptomatic disease can affect almost every organ of the body in immune-compromised individuals, resulting in fever of unknown origin, encephalitis, pneumonia, colitis, hepatitis, retinitis, neuropathy, uveitis, and myelitis. Cytomegalovirus infections are frequently associated with salivary glands, but significant clinical manifestations of cytomegalovirus-infected patients are usually seen in other organs. Diagnostic procedures include the enzyme-linked immunosorbent assay. Since the majority of infections resolve instinctively no treatment is usually required for cytomegalovirus infection in the healthy individual. Now in infants, antiviral drug therapy is being evaluated.

Conclusion

This article thus deals with various infectious and noninfectious causes of sialadenitis like Acute Suppurative Sialadenitis, Obstructive Sialadenitis, and Sialolithiasis, Chronic Sclerosing Sialadenitis (Kuttner Tumor), Radiation Sialadenitis, Recurrent Parotitis, Viral Sialadenitis Including Mumps and Cytomegalovirus their diagnosis and treatment.

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