Retrograde Theory in Sialolithiasis Formation

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Sialolithiasis is a relatively frequent occurrence; however, cases of sialolithiasis originating around a "foreign body" nidus are rare. We describe a patient with submandibular sialolithiasis organized around a vegetal nidus and discuss the etiology of the case.

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Sialolithiasis is a relatively frequent occurrence, affecting up to 1% of salivary glands, according to autopsy studies.[1] It leads to recurrent painful swelling of the involved gland during meals and is sometimes associated with frank infectious sialadenitis. It is classically described as affecting the submandibular gland in 80% to 90% of cases,[2] although our experience (unpublished data, 1999) favors a more frequent parotid involvement.

Sialolithiasis is composed of organic and inorganic substances, in varying ratios. The organic substances are glycoproteins, mucopolysaccharides, and cellular debris.[3] The inorganic substances are mainly calcium carbonates and calcium phosphates. Calcium, magnesium, and phosphate ions each make up between 20% and 25% of the mass, with other minerals (manganese, iron, and copper) composing the rest. The chemical composition consists mainly of microcrystalline apatite ($Ca^5[PO_4]^3OH$) or whitlockite ($Ca^3[PO_4]^2$).[4] Apatite is the most frequent component present throughout the stone, while whitlockite is mainly found in the core.[4-6] The formation of either component depends on the concentrations of calcium and phosphorus, with low concentrations favoring the formation of apatite and high concentrations favoring the formation of whitlockite.[7,8] Other crystalline forms include brushite and weddellite, which are present in small amounts, mainly at the periphery of sialoliths.[4] These elements might represent the initial form of calcium deposition, followed by subsequent remodeling into apatite.[4]

Often, the organic substances predominate in the center of the stone, while the periphery is essentially inorganic.[3,4] The presence of bacilli in sialoliths has been suggested by scanning electron microscopy,[9] which has identified oval, elongated shapes.

The exact pathogenesis of sialolithiasis remains unknown, and various hypotheses have been proposed.[3] The first theory is based on the existence of intracellular microcalculi, which when excreted in the canal become a nidus for further calcification.[10] The second theory suggests that "mucous plugs" (**Figure 1**), which are present in the ductal system, may represent the nidus. Both hypotheses suppose that there is an initial organic nidus that progressively grows by the deposition of layers of inorganic and organic substance.[3]

Another possible hypothesis for the formation of sialolithiasis is that aliments, substances, or bacteria within the oral cavity might migrate in the salivary ducts and become the nidus for further calcification. We report a case in which a stone formation around a vegetal nidus was proved histologically.

REPORT OF A CASE

A 62-year-old woman, with no particular medical or surgical history, was seen in our

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institution because of an acute episode of a painful swelling of the right submandibular gland. The diagnosis of acute sialadenitis was made, and the patient received antibiotic and anti-inflammatory treatment. Sialography and diagnostic sialendoscopy confirmed the diagnosis of a 8-mm sialolithiasis, partially embedded in the canal-wall. Because of the paucity of symptoms, and because of the embedded stone, no interventional sialendoscopy[11] or submandibular surgery was planned.

After the initial episode, swelling after meals became increasingly frequent, occurring up to 6 times a week. Because of these recurrent infections, the patient finally underwent extirpation of the gland. Histological examination of the submandibular gland showed marked periductal and lobular fibrosis and focal gland atrophy associated with an inflammatory infiltrate showing a mixture of lymphocytes, plasmocytes, and polymorphonuclear leukocytes. Dilated ducts were present, surrounded by a dense inflammatory infiltrate, without myoepithelial islands. A portion of an intraglandular duct exhibited a stone that had developed around a foreign body (**Figure 2**). This foreign material showed bright birefringence on polarized light, consistent with a vegetal nidus (**Figure 3**).

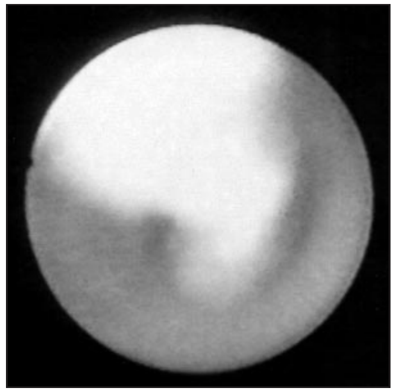

Figure 1. *Sialendoscopic view of floating mucous plugs in the Wharton duct.*

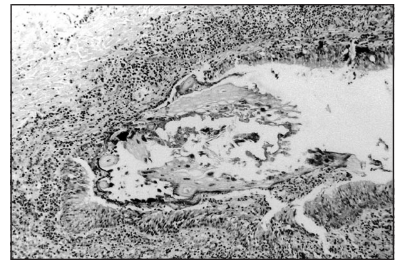

Figure 2. *Portion of an interlobular excretory duct with a dense inflammatory infiltrate. The lumen contains a foreign body, surrounded by calcifications (hematoxylin-eosin, original magnification ×100).*

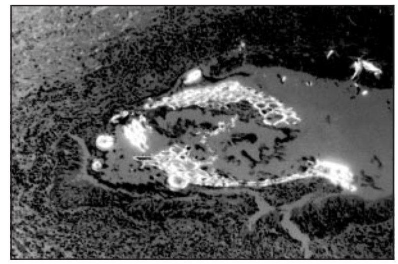

Figure 3. *Same duct as Figure 1. The intraductal foreign body, strongly birefringent on polarization microscopy, is consistent with vegetal material (hematoxylin-eosin, original magnification ×100).*

COMMENT

Despite the relative frequency of sialolithiasis, the etiology has received little attention and remains unclear. Traditional theories suggest that the formation of sialolithiasis proceeds in 2 phases: a central core and a layered periphery.[1] The central core is formed by the precipitation of salts, which are bound by certain organic substances. The second phase consists of the layered deposition of organic and nonorganic material. Other factors, such as changes in pH, reduced salivary flow, or increases in calcium concentrations, are seen as contributing to the precipitation of calcium, rather than as actual etiologic factors.[3]

Westhofen et al[12] were first to recognize the presence of microcalcifications in the secretory granules and the acinar lumen, by inducing salivary stimulation and hypercalcemia in rats. Later, Epivantianos et al[10] and Epivantianos and Harrison[13] demonstrated microcalcifications in normal salivary glands of cats and humans, respectively. These microcalculi are lamellated structures made of crystals and amorphous organic material that are thought to represent autophagosomes of redundant secretory vesicles.[14] The high-ionized calcium concentration within secretory granules is thought to precipitate the phospholipids of degenerating membranes, resulting in microliths, which measure 2- to 8-μm intracellularly and 15- to 30-μm in the acinar lumen.[10] The calcification of microliths is variable and seems more important in the acini than in the ducts.[15] Glandular inactivity, induced by parasympathectomy in cats, increases the incidence of microliths, mainly in the submandibular gland.[14] However, despite extensive investigation of microliths in the pathogenesis of sialolithiasis by Harrison et al,[16] several clinical and experimental considerations, such as the paucity of microliths within the parotid gland, cast doubts that microliths play a central role in the formation of sialolithiasis. These microliths might be just one of the components of the mucous part and/or mucous plugs (Figure 1) of the saliva.

A few cases have been reported in which a foreign body is supposed to have acted as a nidus for the observed sialolithiasis.[17-19] Takeshita et al[17] provide an extensive review of several reports in Japanese. In the majority of cases, the foreign body is bony and has penetrated the Wharton duct through a wound in the floor of the mouth. In our case, the patient had no memory of such an injury. While these cases are rare, no thorough investigation of frequency of foreign body material within sialoliths has been published. The case reported herein supports the possibility that some sialoliths might result from a retrograde migration within the salivary ducts of aliments, substances, or bacteria from the oral cavity.

Based on multiple diagnostic sialendoscopy procedures performed on 120 submandibular glands,[20] we have observed the presence of a sphincter system in the first 3 cm of the Wharton duct in most cases (90%). In our case, however, diagnostic endoscopy did not confirm the presence of such a sphincter. Although the exact anatomical and physiological basis of a possible sphincter in the Wharton duct requires further studies, it is possible that variation of such a sphincterlike mechanism within the salivary ducts could be responsible for an easier retrograde migration of oral materials.

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