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ORIGINAL ARTICLE

Biochemical structure, symptoms, location and treatment of sialoliths

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Abstract *Background/purpose:* Sialolithiasis is the most common disease of the salivary glands, which can cause acute and chronic infections. More than 80% of sialoliths occur in the submandibular gland or its duct, 6% in the parotid gland, and 2% in the sublingual gland or minor salivary glands. Typical symptoms are recurrent swelling and pain in the involved gland, often associated with eating, due to obstructions of the draining duct. The aim of the study was to analyze biochemical structure, symptoms, size, and location of salivary stones as well as concomitance with nephrolithiasis.
Materials and methods: This study was conducted targeting 46 patients with sialolithiasis who visited the Department of Oral Surgery, Medical University of Lodz, Poland in 2009–2015. Medical records containing patients' age, sex, position of the salivary stone, and symptoms were collected and analyzed. Stones were examined ultrastructurally with a scanning electron microscope and X-ray diffractometer.
Results: Multiple stones were found in 1% of patients. We observed that men had sialolithiasis about twice as often as women. The chemical structure of the stones varied but they mainly contained different traces of carbon, calcium, oxygen, phosphorus, and sulfur. Longitudinal sections of the stones revealed elongated, round, and irregular shapes. We noticed that nephrolithiasis was present in 11 (24%) patients. We observed the unilateral location of sialoliths with multilayer structures, mainly composed of inorganic material, such as hydroxyapatite.
Conclusion: We found that the location of the stones influenced the symptoms, and concomitance of sialoliths and nephroliths was common.

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Introduction

The etiology of sialolith formation is still unknown but there are some factors contributing to stone formation: irregularities in the duct system, inflammation or local irritants.[1,2]

Salivary gland stones may form as a result of an infection. However, in certain cases, chemicals may become crystallized and block salivary ducts. It has been speculated that, in the process of calculi formation, degenerative substances are liberated by saliva and calcification subsequently occurs around those substances to finally lead to calculus formation.[3–5] Nevertheless, the exact mechanism of the formation of calculi is still unclear. The causes of formation of sialoliths seem to be as follows: mechanical, chemical, inflammatory, and neurohumoral. Salivary duct stones may occur in all of the salivary glands, but they are mainly found in the submandibular glands (80–90%), especially the submandibular duct (Wharton duct) because of its long, narrow, and winding transection. Sialolithiasis occurs more frequently in men, with a peak incidence between the ages of 30 years and 60 years.[6] Stones should be differentiated from phleboliths, inflammation of maxillary bones, and calcification of lymph nodes. There is some indication that patients with sialolithiasis are more prone to develop nephrolithiasis.[6] Sialolithiasis has been linked with nephrolithiasis in up to 10% of patients.[6] The aim of the present study was to analyze the biochemical structure, symptoms, size, and location of salivary stones, as well as their coexistence with nephrolithiasis. We also tried to assess whether the patient's age or sex, or location of the stones may be characteristic of specific symptoms.

Materials and methods

This study targeted 46 patients with sialolithiasis who visited the Department of Oral Surgery, Medical University of Lodz, Poland in 2009–2015. Medical records, containing patients' age, sex, position of the salivary stone, symptoms, and concomitance with nephroliths, were collected and analyzed. All patients presented to our clinic because of recurrent or persistent salivary gland complaints such as swelling and pain, or recurrent episodes of sialadenitis. Symptoms, measured from the first visit, lasted 20 months on average (range: 2 days–6 years). Due to their location and smaller diameter, parotid stones could, in some cases, only be treated using endoscopic laser lithotripsy. Characteristics of the study population are presented in Table 1. The patients were diagnosed based on history taking, intraoral examination, pantomographic X-ray and occlusal X-ray (Figures 1 and 2).

Table 1 Baseline characteristics.

	n	%
Age (y)		
24–40	16	34.7
41–60	20	43.5
61–70	10	21.7
Sex		
Male	30	65.2
Female	16	34.8
Location		
Within the duct of the submandibular gland: right side	20	43.5
Within the duct of the submandibular gland: left side	10	21.7
Outside the duct of the submandibular gland: right side	9	19.6
Outside the duct of the submandibular gland: left side	7	15.2
Symptoms		
Periodic enlargement of the salivary gland	15	32.6
Enlarged parotid duct	23	50.0
Limiting the secretion of saliva	28	60.8
Redness and swelling of the mucosa	28	60.8
Scanty mucopurulent discharge	28	60.8

Stones were analyzed ultrastructurally by scanning electron microscopy (SEM) and X-ray diffractometry (XRD). During XRD, the samples were pulverized in an agate mortar. XRD was performed on the powder with an X-ray diffractometer (Siemens D 500 Pro; Karlsruhe, Germany) under the following conditions: X-ray beam CaKα, X-ray tube voltage 50 kV, tube current 30 mA, scan speed 2 θ. XRD patterns were obtained for all sialoliths and traces were integrated to present the data in one graph. The XRD pattern of each sample was compared with the standard data for crystalline minerals using powder diffraction files. SEM studies were performed with a Hitachi S300N scanning electron microscope (Tokyo, Japan) with an attached energy-dispersive X-ray (EDX) microanalysis detector system (Nordan MM, Placerville, CA, USA). The sialolith samples kept for SEM were coated with a thin film of evaporated gold. The SEM studies and EDX microanalysis were done at an accelerating voltage of 15 kV and a working distance of 15 mm.

Statistical methods

During the analysis of data the Fischer exact two-tailed test was used to determine the difference between nominal variables. All statistical analyses were performed using StatSoft Statistica for Windows, release 8.0 (StatSoft, Tulsa, AZ, USA). $P < 0.05$ was considered to indicate statistical significance.

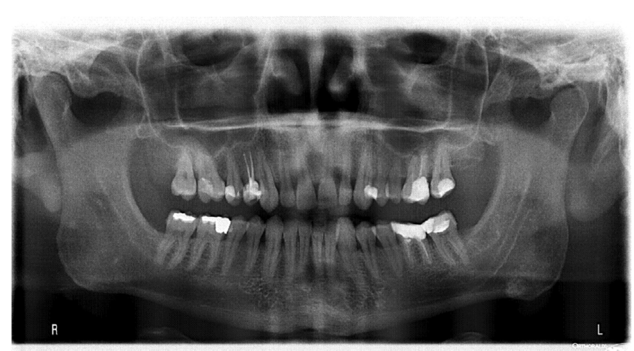


Figure 1 A pantographic X-ray of oral cavity showing a large sialolith in the left submandibular gland.

Figure 2 An occlusal X-ray showing a large stone in the left submandibular duct.

Results

We enrolled 46 patients with sialolithiasis. Multiple stones were found in 1% of patients. The average stone diameter in the submandibular gland was 4.1 mm (range: 1–20 mm). The descriptive analysis of symptoms revealed that, in 16 (34.7%) patients, the periodic enlargement of the salivary gland was reported as the monosymptomatic clinical presentation of the disease. All others patients ($n = 30$, 65.2%) reported co-occurrence of different symptoms. The co-occurrence of symptoms allowed us to classify patients into three different categories (Table 2). Since the S2 category was represented by five patients only, it was combined with the S3 category for comparative analysis. Sialolithiasis located within the duct of the submandibular gland determined Types S2 and/or S3 of the clinical profile, while location outside the duct was usually presented by Type S1 of the clinical profile in our patients.

Table 2 Co-occurrence of symptoms defined as three clinical profiles.

Clinical profile	*n*	%
S1	16	34.7
S2	5	10.8
S3	25	54.3

S1 = periodic enlargement of the salivary gland; S2 = limiting the secretion of saliva + redness and swelling of the mucosa + scanty mucopurulent discharge; S3 = enlarged parotid duct + limiting secretion of saliva + redness and swelling of the mucosa + scanty mucopurulent discharge.

Figure 3 Large sialolith extracted from the salivary gland, with scale.

We observed that men suffered sialolithiasis about twice as often as women. Inflammation was caused by one (Figure 3) or many (Figure 4) stones. The location of the stones influenced the symptoms (Table 3). Hydroxyapatite with the chemical formula $Ca_5(PO_4)_3OH$ was present in all submandibular stones (Figure 5), often together with carbon, calcium, oxygen, phosphorus, and sulfur. The structures of two examples of examined sialoliths are presented in Figures 6 and 7. Longitudinal sections of the stones revealed elongated, round, and irregular shapes. We noticed that nephrolithiasis was present in 11 (24%) patients.

Discussion

The peak incidence of sialolithiasis is between 30 years and 60 years. However, 22% of our patients were >60 years of age. In our study, calculi were located mainly within the ductal system of the parotid gland (65.2%). We observed frequent concomitance of sialoliths and nephroliths. The location of stones influenced the symptoms.

Sialolithiasis is estimated to affect 12 in 1000 of the adult population. Men are more prone to this disease, and it occurs in them twice as often as in women;[7,8] similar results being found in the present study. However, it ought to be stressed that problems with salivary glands may lead to Sjogren's syndrome, which is more common in women — they first develop symptoms during middle age; in our study, none of the patients had Sjogren's syndrome.

Figure 4 Small sialoliths extracted from the salivary gland, with scale.

Table 3 Clinical profiles of symptoms according to age, gender and location of sialolithiasis.

	S1		S3		S2		P (Fisher's exact test)	
	n	%	*n*	%	*n*	%	S1 vs. others	S2/S3 vs. others
Age (y)							0.532	0.532
24–40	3	18.7	10	40.0	3	60.0		
41–60	8	50.0	9	36.0	2	40.0		
61–70	5	31.2	6	24.0	0	0.0		
Sex							0.18	0.18
Male	8	50.0	16	66.7	6	100.0		
Female	8	50.0	8	33.3	0	0.0		
Location								
Within the duct of the submandibular gland: right side							<0.001	<0.001
No	16	100.0	8	32.0	2	40.0		
Yes	0	0.0	17	68.0	3	60.0		
Within the duct of the submandibular gland: left side							0.016	0.016
No	15	100.0	17	68.0	4	66.7		
Yes	0	0.0	8	32.0	2	33.3		
Outside the duct of the submandibular gland: right side							<0.001	<0.001
No	7	43.7	24	100.0	6	100.0		
Yes	9	56.2	0	0.0	0	0.0		
Outside the duct of the submandibular gland: left side							0.001	0.001
No	9	56.2	24	100.0	6	100.0		
Yes	7	43.7	0	0.0	0	0.0		

S1 = periodic enlargement of the salivary gland; S2 = limiting secretion of saliva + redness and swelling of the mucosa + scanty mucopurulent discharge; S3 = enlarged parotid duct + limiting the secretion of saliva + redness and swelling of the mucosa + scanty mucopurulent discharge.

It is also important to emphasize that the location of salivary stones affects the treatment. When stones are located in the submandibular gland, the endoscopic eye is needed. Stones located in the parotid gland are hard to visualize and may cause more surgical risk.[9] In our clinic, we extracted the sialoliths in two ways: the bigger ones needed laser treatment and the smaller ones were extracted using traditional methods. Laser treatment seems to be a promising modality for stone removal, even in acute phases. The most common methods of ultrastructural analysis of salivary calculi are SEM and XRD. X-ray tomography indicates that sialoliths contain a major core with a different level of mineralization compared with the surrounding organic material. SEM observation of the stones shows that the cores most frequently lack layering or do not even have other distinctive features.[3] In our study, all sialoliths had a homogeneous composition; they were predominantly composed of elements comprising hydroxyapatite, carbon, calcium, oxygen, phosphorus, and sulfur. Such a composition of the sialoliths in our population might be due to Polish eating habits and similar microorganisms in the oral mucosa.

The disease process induces gland inflammation, pain, and enlargement. In our study, most salivary stones were located in the submandibular gland. The higher incidence of salivary stones in the ductal system of the submandibular gland might be attributed to its longer duct, salivary flow against gravity, and more-alkaline saliva with a higher calcium and mucine content. The location of sialoliths influenced symptoms in our study. Sialoliths located within the duct of the submandibular gland determined limiting the secretion of saliva, redness and swelling of the mucosa, enlarged parotid duct, and scanty muco-purulent discharge, while location outside the duct usually presented as periodic enlargement of the salivary gland in our patients. All of the patients with parenchymal stones presented with gland enlargement.

In our study, nephrolithiasis was present in 24% of patients with sialolithiasis, which was more frequent than in other studies.[6] Systemic diseases have not been proved to be associated with sialolithiasis except for gout, although its calculi consist mainly of uric acid.

In conclusion, our study showed unilateral location of sialoliths, and the location of stones influenced the symptoms. We observed frequent concomitance of sialoliths and

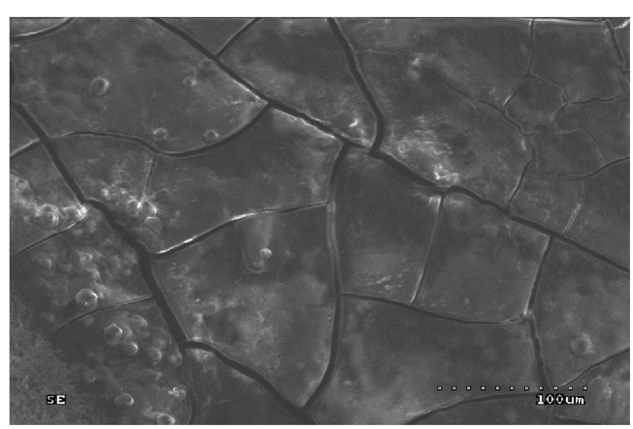
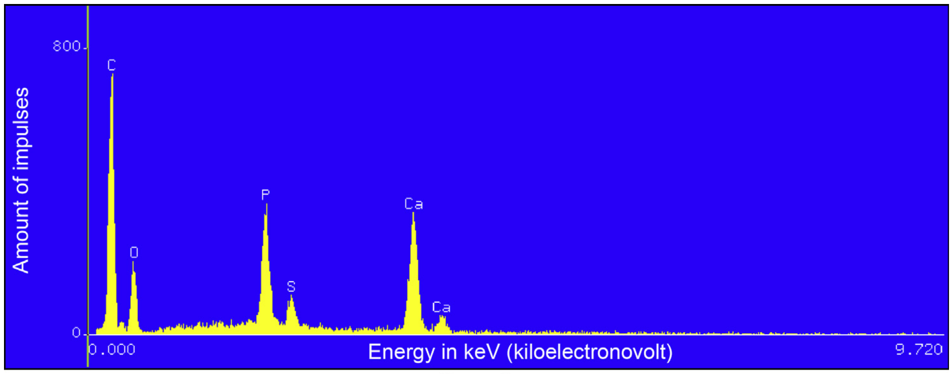
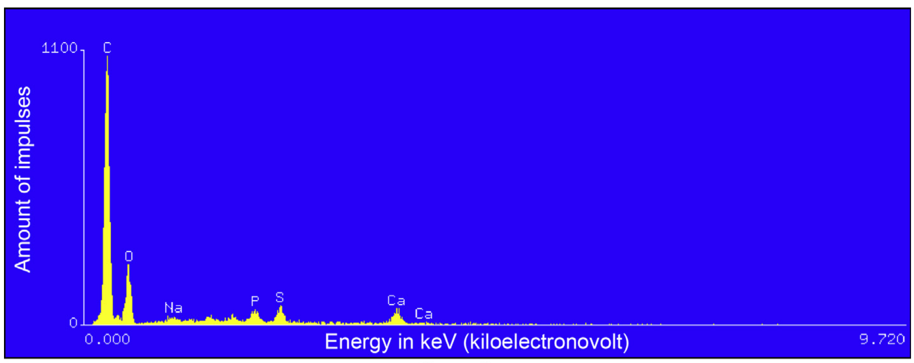


Figure 5 Image of hydroxyapatite, the main content of sialoliths, with scale.



Stone 1

Figure 6 Scanning electron microscopy image of a globular region in a submandibular sialolith with corresponding X-ray maps for Ca = calcium, S = sulfur, C = carbon, P = phosphorus, and O = oxygen.



Stone 2

Figure 7 Scanning electron microscopy image of a globular region in a submandibular sialolith with corresponding X-ray maps for Ca = calcium, S = sulfur, C = carbon, P = phosphorus, and O = oxygen.

nephroliths. Salivary stones were mainly composed of inorganic material, such as hydroxyapatite; sections of the stones showed a multilayer structure.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

Acknowledgments

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