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Sialosis: 35 cases of persistent parotid swelling from two countries

Crispian Scully [a,c,*], Jose V. Bagán [b], John W. Eveson [c], Neal Barnard [d], Fiona M. Turner [c,e]

[a] *UCL Eastman Dental Institute, 256 Gray's Inn Road, London, WC1X 8LD, UK*
[b] *Oral Surgery and Oral Medicine, University Hospital, Valencia, Spain*
[c] *Department of Oral and Dental Science, Bristol Dental Hospital and School Lower Maudlin Street Bristol, BS1 2LY, UK*
[d] *Worcestershire Royal Hospital, Charles Hastings Way, Newtown Road, Worcester, WR5 1DD, UK*
[e] *15 Rata Street, New Lynn, PO Box 15 564, Auckland, New Zealand*

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Abstract

Diffuse, non-inflammatory, non-neoplastic enlargement of the major salivary glands (sialosis) is uncommon and has various systemic causes. This paper examines 35 patients whose persistent swelling of the parotid was diagnosed as sialosis, and shows that diabetes mellitus and alcoholism are the most common causes.

Keywords: Oral; Salivary; Sialosis; Diabetes; Alcohol; Bulimia

Introduction

Chronic, bilateral, diffuse, non-inflammatory, non-neoplastic painless swelling of the parotid (sialosis, sialoadenosis, or sialadenosis) was first reviewed nearly 50 years ago in the most comprehensive series published so far, in which 50 patients from the USA were reported.[1] Thirty six (72%) had chronic liver disease, usually cirrhosis, and several of the remainder were obese, or had hyperglycaemia, or both. The first important discussion about sialosis in dental reports was some 35 years ago,[2] the pathophysiology was reviewed extensively 25 years ago,[3] and since then little has been published.[4,5]

Sialosis mainly affects the major salivary glands, particularly the parotid glands, but occasionally affects the submandibular glands and rarely, the minor salivary glands.[6] Several causes have been recorded[7–17] (Table 1), most of which are associated with nutrition, metabolism, or drugs, and have a unifying feature in autonomic neuropathy.[18–20] Changes in salivary aquaporin water channels may also be involved.[16]

There are surprisingly few recent reviews or reports on series of patients with sialosis, so to assess the current position, we have reviewed a series of 35 patients who had sialosis of the parotid.

Patients and methods

All patients with persistent parotid swellings (Fig. 1) who were seen over a period of 5–14 years in three centres (two in UK and one in Spain) were reviewed. A comprehensive history was taken from them all, including special note of current medication, intake of alcohol, liver disease, endocrinopathy, or eating disorders. Investigations included blood analyses for glucose, liver function, thyroid function, and autoim-

* Corresponding author. Tel.: +44 020 7915 1038; fax: +44 020 7915 1039.
E-mail address: c.scully@eastman.ucl.ac.uk (C. Scully).

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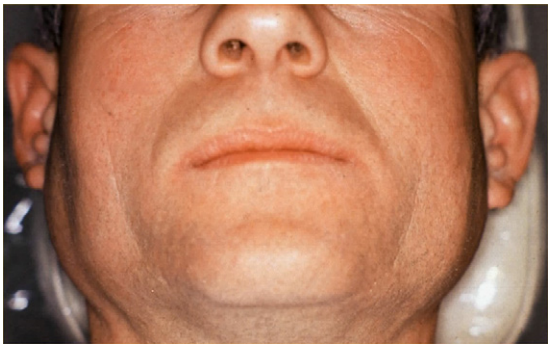

Fig. 1. Typical persistent bilateral swelling of the parotid caused by alcoholism.

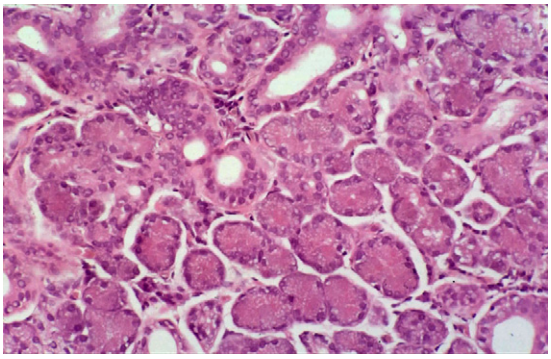

Fig. 2. Microscopy showing acinar hypertrophy with granular cytoplasm and compression of the striated ducts. (Haematoxylin and eosin, original magnification ×150.)

mune profile (SS-A and SS-B antibodies); urinalysis; blood pressure and, where appropriate, salivary imaging (such as sialography, sialometry, scintigraphy, computed tomography (CT), magnetic resonance imaging (MRI), or ultrasonography), or salivary gland biopsy examination. Patients with parotid swelling not caused by sialosis (such as Sjögren syndrome, HIV-salivary gland disease, sarcoidosis, deposits and Warthin tumour) were therefore excluded by history, imaging, and in some instances, biopsy examination, which left 35 with clinical features that were consistent with sialosis. The diagnostic advantages of biopsy examination of the parotid were not thought to outweigh possible complications, so were deemed unjustified in most patients. Five patients, however, had some pain with no obvious cause of sialosis and in two of these it was confirmed by biopsy examination of the parotid gland (Fig. 2).

The presentation, symptoms, other related conditions, reason for presentation, and general details of the patients are given in Table 2.

Results

Twenty-one (60%) of the 35 were men, most of whom were middle-aged or older (median 53 years; range 27–80), and all but two of the 35 (94%) had painless swelling of the salivary glands that were bilateral in 94%. Sialosis was confirmed histologically by biopsy examination of the parotid in two. Results of abnormal investigations are given in Table 2. Twenty-seven patients were from the UK, and eight were from Spain, but there were no notable differences between the groups.

Table 1
Causes of sialosis

Drugs-induced	Endocrine/metabolic	Nutritional
Antihypertensives	Acromegaly	Beriberi
Guanacline	Alcoholism	Bulimia
Iodine	Diabetes insipidus	Gastrointestinal disease
Isoprenaline	Diabetes mellitus	Malnutrition
Lead	Hypothyroidism	Pellagra
Mercury	Cirrhosis of the liver	Amylophagia
Naproxen	Uraemia	Vitamin A deficiency
Oxphenbutazone		
Phenylbutazone		
Sulfisoxazole		
Thiocyanate		
Thiouracil		
Valproic acid		

Twenty-nine patients (83%) had an identifiable aetiology as shown in Table 1. Seventeen (49%) had a history of diabetes – the most commonly identified association in this study. Twenty-five (71%) had sialosis that was clearly attributable to one of the systemic diseases listed in Table 1, and 4 were using drugs that are implicated in sialosis. Nine patients (26%) had a history of alcohol misuse - the other most commonly identified association in this study. Seven patients had abnormal liver function, and two had cirrhosis. Two who misused alcohol were also diabetic. Other defined causes of sialosis included antihypertensive agents,[4] bulimia,[1] and hypothyroidism.[1]

Ten of the 35 patients had a history of oral lesions in addition to sialosis (Table 2), but these were almost certainly unrelated to sialosis. Only one of the patients had xerostomia, but there was no evidence of Sjögren syndrome. MRI in two cases showed enlargement of one parotid and hypoplasia in the other. Both patients were diabetic, which probably indicates congenital hypoplasia in one parotid gland and sialosis-related hypertrophy in the other previously normal gland. One patient had increased activity of angiotensin-converting enzyme in serum, but no other evidence of sarcoidosis.

Discussion

This study confirmed that the major cause of sialosis in the patients studied is diabetes mellitus; another prominent factor is alcohol misuse, particularly with resultant liver disease. Other causes such as drugs and bulimia seem to be uncommon.

Organic diseases that involve the salivary glands, particularly Sjögren syndrome, sarcoidosis, various deposits (e.g. amyloid or iron) and HIV-associated disease of the salivary

Table 2
Characteristics of patients with sialosis

Case No	Age (years)	Sex	History and drugs	Other oral features	Abnormal results
1	42	M	Diabetes, alcoholism	Lichen planus	Reduced vitamin B12, red cell folate
2	29	F	Bulimia, Raynaud's phenomenon	Necrotising sialometaplasia	–
3*	55	F	Systemic sclerosis, hypertension (on nifedipine and pentoxifylline), hypothyroidism	Angular stomatitis, telangiectases	Biopsy-confirmed
4	76	M	Peptic ulceration	Dry mouth	Reduced ferritin
5	58	F	Probable alcoholism	Lichen planus, depapillated tongue	Macrocytosis
6	56	F	Alcoholism, obesity, cirrhosis/diabetes	–	Glycaemia 6.9 mmol/L. Raised alkaline phosphatase and aspartate aminotransferase
7	61	M	Hypertension (on oxyprenolol), pernicious anaemia	Lichen planus	Reduced vitamin B12, reduced ferritin, raised alkaline phosphatase
8	61	M	Alcoholism, choledocholithiasis	History of RAS	–
9	68	M	Gout, osteoporosis	–	Reduced vitamin B12, reduced ferritin
10	36	M	Alcoholism	–	Slightly raised ESR
11*	53	M	Latent diabetes	–	Slightly raised ESR, Biopsy-confirmed
12	56	M	–	–	–
13	29	F	Diabetes, lipodystropy, dermatomyositis, arthritis	–	MRI – large but otherwise normal parotids. Biopsy-confirmed
14	65	F	Poorly controlled diabetes, hypertension, angina, insulin, verapamil, lansoprazole, indapamide	Altered sensation anterior tongue	–
15	69	M	Prostatitis, diverticulitis	–	Raised SACE, MRI - large but otherwise normal parotids. Chest radiograph normal
16	68	M	Diabetes, hypertension, metformin, gliclazide, ramapril	–	–
17	40	F	Poorly-controlled diabetes, hypertension, insulin, metformin, lansoprazole	–	Sialogram normal
18	42	M	Urticaria, antihistamines	–	–
19	42	M	Alcoholism	–	Raised alkaline phosphatase and aspartate aminotransferase
20	52	M	Diabetes, hypertension, metformin, ramipril, atorvastatin	–	–
21	47	M	Alcoholism	–	Patient declined tests
22	27	M	-	Masserteric hypertrophy, dysfunction of the TMJ	MRI - large but otherwise normal parotids
23	66	F	Diabetes, insulin, cimetidine	Xerostomia	Glycaemia
24	43	M	Diabetes, metformin, gliclazide, diclofenac	–	MRI - large but otherwise normal parotids
25	58	M	Diabetes, hypertension, angina, insulin, gliclazide, atenolol, ramapril, atorvastatin	Unilateral parotid swelling	MRI showed enlargement of one parotid and hypoplasia of the other
26	50	F	Diabetes	–	Anaemia
27	80	M	Diabetes	Unilateral parotid swelling	MRI showed enlargement of one parotid and hypoplasia of the other
28*	50	M	Diabetes	–	Glycaemia
29*	56	F	Hypertension (treated with antihypertensive drugs), liver disease	–	–
30	76	F	Hypertension (treated with antihypertensive drugs), Parkinson disease	–	–
31	48	M	Alcoholic liver disease	–	Glycaemia, raised alkaline phosphatase and aspartate aminotransferase
32	39	M	Alcoholic liver disease	–	Raised alkaline phosphatase and aspartate aminotransferase
33	51	F	Diabetes	–	Glycaemia
34	59	F	Diabetes, liver disease	–	Glycaemia, raised alkaline phosphatase and aspartate aminotransferase
35*	58	F	Diabetes, liver disease	–	Glycaemia, raised alkaline phosphatase and aspartate aminotransferase

RAS = recurrent aphthous stomatitis; ESR = erythrocyte sedimentation rate; SACE = serum angiotensin converting enzyme.
* Patients with pain. Case numbers 1–27 were from the UK, 28–35 were from Spain.

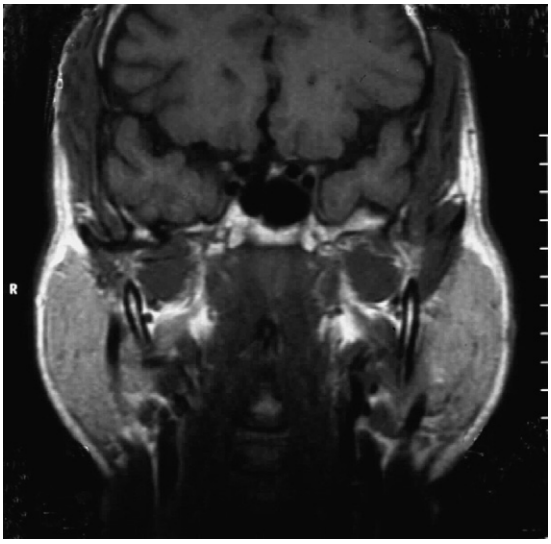

Fig. 3. Magnetic resonance image showing bilateral enlarged parotids.

glands may present with persistent bilateral swelling of the parotid. Sjögren syndrome often presents xerostomia and with discomfort, sometimes with nonoral or systemic manifestations, and usually with classic histopathological changes in the salivary glands. Persistent, bilateral swelling, usually of the parotids without such disorders (Fig. 2), and associated with hypertrophy of acinar cells, is called sialosis or sialadenosis. It is often painless, but not invariably so;[3–5] five of the present series of patients had pain.

The diagnosis of sialosis must exclude inflammatory causes of salivary swelling particularly Sjögren syndrome, HIV infection, sarcoidosis, and lymphoepithelial disease, by the relevant investigations. Physically, the groove between the mastoid process and the ramus of the mandible becomes obliterated, and there is appreciable swelling that gives a trapezoid appearance. Sialography can be useful in diagnosis, but is rarely indicated; "a characteristic leafless winter tree may be seen - the lack of arborisation being caused by the separation of secretory ducts from each other and compression of smaller interlobular canaliculi".[8] CT has been said to help the diagnosis but shows no specific features.[9] MRI is one of the best methods for investigating conditions of the salivary gland[21] and we found it valuable for excluding other diseases (Fig. 3). Fine needle aspiration or open biopsy examination may aid diagnosis, but are rarely needed.[22–24] Salivary sonography is also useful to exclude other diseases,[25] is noninvasive, and often more readily available than other methods of imaging. In contrast, sialochemistry has virtually no benefit in diagnosis,[10] although raised concentrations of potassium and amylase activity have been reported.[11–13] Sialometry is also of little practical value: salivary secretory activity may be increased or decreased depending on aetiology, but it is usually within normal limits, as in virtually all cases here.

Sialosis has various causes (Table 1), and the diversity of associated conditions is intriguing. However, it is now recognised that many of its causes may produce sialosis through the common feature of autonomic nerve dysfunction,[18,20] and it is possible that there are functional changes in salivary aquaporin water channels.[16]

Endocrinopathies, particularly diabetes mellitus, and metabolic causes are known to cause some sialosis, the reported prevalence of sialosis in diabetes ranging from 10% to 80%.[14] Nearly half the patients in the present study (49%) were diabetic; two had diabetes and drank alcohol, and two others had diabetes and damage to the liver. Alcoholism, particularly with cirrhosis of the liver, is a common cause of sialosis. Previous reports have indicated that between 30% and 80% of patients with alcoholic cirrhosis have sialosis[1,7–12] but, if that were universally true, one would expect sialosis to be seen more often than it is. Only nine (26%) patients in the present study had a history of alcohol misuse, and only six had liver damage confirmed by serum biochemistry. One patient had hypothyroidism - a rare association that has been recorded previously.

Among the wide range of drugs that may induce sialosis, antihypertensive agents are prominent; four of our patients were having treatment for hypertension.

Nutritional sialosis has been well-recognised since World War II, but had been described previously as malnutrition.[1–4] Any disorder that affects the digestion of food or its absorption over a prolonged period, can result in sialosis, and malnutrition may contribute to sialosis in alcoholics. Recently bulimia and anorexia nervosa have increasingly become recognised causes.[19] Only one of our patients, a young woman, was known to be bulimic, but she did not have the other oral features of bulimia, such as erosion of teeth.

Table 1 gives several other causes of sialosis that we did not find in our group of patients. Six of them had sialosis of unknown origin.

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