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Parotidectomy for Unilateral Pain Attributed to Sialosis

Evgeniya Molotkova[1] | Piper Wenzel[1] | Anand Rajan[2] | Henry Hoffman[1]

[1]Department of Otolaryngology, University of Iowa, Iowa City, Iowa, USA | [2]Department of Pathology, University of Iowa, Iowa City, Iowa, USA

Correspondence: Evgeniya Molotkova (emolotkova@uiowa.edu)

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ABSTRACT

This case uniquely provides radiographic and histopathologic correlates offering insight into the poorly understood disorder of symptomatic sialosis (sialadeneosis). Sialosis is often managed conservatively, with surgical intervention reserved for symptomatic cases refractory to conservative management. The rarely employed surgical treatment is highlighted in this patient by relief of presenting symptoms accompanied by later complications.

1 | Introduction

Sialosis (sialadenosis) is a chronic, nonneoplastic, often bilateral enlargement of the major salivary glands associated with endocrine, metabolic, and nutritional abnormalities. Etiology remains uncertain in many cases (idiopathic), although an underlying dysautonomia (autonomic neuropathy) is proposed as a potential unifying mechanism [1]. The parotid enlargement characteristic of sialosis may be disfiguring and often raises concern regarding the etiology of the enlargement. Although sialosis has been classically described as painless, associated facial pain has been reported. This pain has been proposed to result from gland hypertrophy causing pressure necrosis and injury to the salivary acini [2].

First line management of pain and swelling associated with sialosis has been primarily directed to identification and control of underlying disorders. Other management options reported through small studies include pilocarpine, steroid infusion (intraductal or percutaneously into the parenchyma), botulinum toxin injection, and surgery (parotidectomy or tympanic neurectomy) [1]. We report a case of confirmed sialosis in a patient treated surgically, permitting correlation of imaging and histopathology to offer perspective into the surgical management of facial pain associated with sialosis.

2 | Case History/Examination

A 54-year-old male presented to the clinic with four episodes of painful left parotid swelling over the course of a year, beginning in September 2010. Each episode was triggered by eating and lasted about an hour on average, but sometimes longer. Symptoms were relieved with courses of amoxicillin-clavulanate prescribed by an outside provider. Previous computed tomography (CT) scans performed when the patient was symptomatic were reported as normal. Serology revealed normal CBC, ANA, RF, SSA, SSB, and IgG4 immunoglobulin levels. Relevant past medical history identified gastroesophageal reflux disease (GERD), a body mass index (BMI) of 30.5, a remote history of mumps during childhood, and no history of chronic liver disease, diabetes, or heavy alcohol use. Both parotid glands were palpably enlarged and were identified with massage to produce clear saliva through patent Stensen's ducts bilaterally.

3 | Differential Diagnosis

Initial differential diagnosis included sialosis, sialadenitis, and tumor (either benign or malignant). CT imaging initially read as normal was reinterpreted at our institution to reveal mild fatty infiltration of symmetrically enlarged parotid glands associated

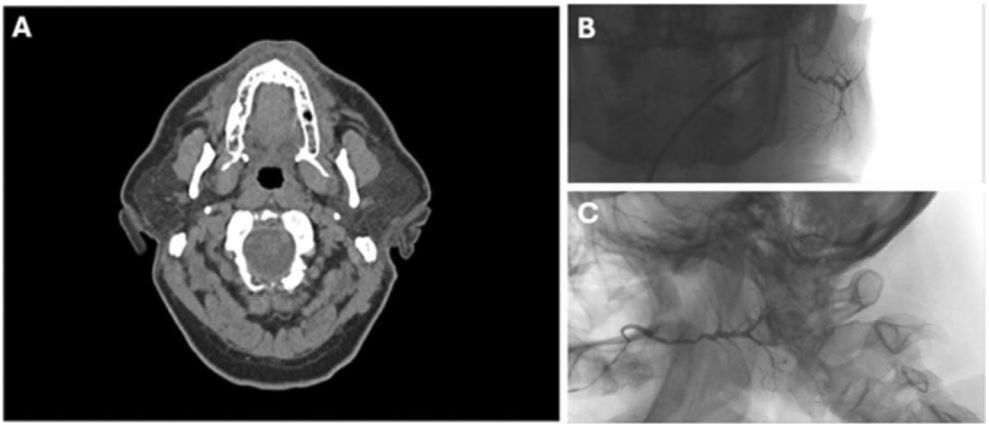

FIGURE 1 | Diagnostic Imaging. (A) CT with IV contrast demonstrates bilateral parotid enlargement with fatty infiltration. (B) AP sialogram view demonstrates splaying of intraglandular ducts consistent with a diagnosis of sialosis. (C) Lateral sialogram view with similar findings as previous.

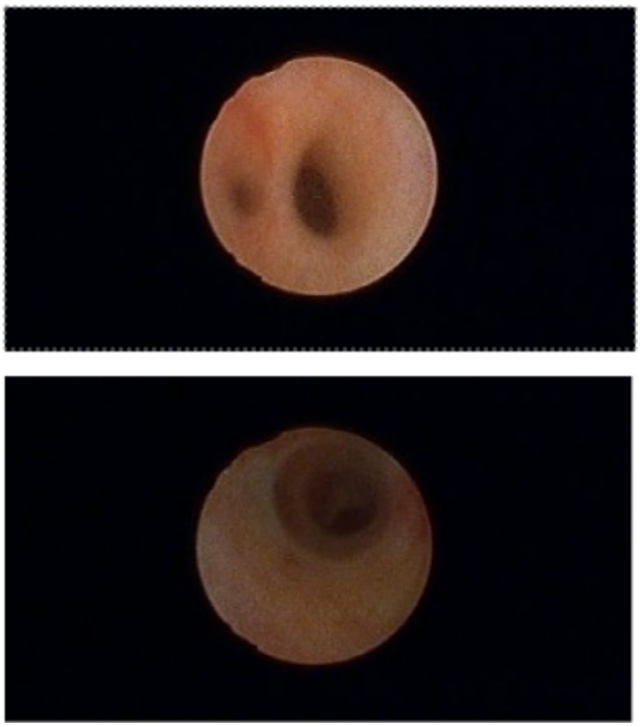

FIGURE 2 | Intraoperative Left Parotid Sialendoscopy. Representative still images captured during intraoperative sialenscosopy demonstrate a normal intraglandular ductal system without evidence of sialolithis or salivary strictures.

with increased enhancement of the symptomatic left parotid (Figure 1A). Left parotid sialography identified splaying and pruning of the distal branches of the intraglandular ductal system, supporting the diagnosis of sialosis (Figure 1B,C).

4 | Conclusion and Results

Initial management to address the facial pain through intraductal triamcinolone (3 mL of 10 mg/mL Kenalog 10) infusion to the left parotid gland offered relief for 3 weeks, at which time the patient had a recurrent episode of sudden-onset pain and swelling. At a clinic follow-up visit 2 weeks later, the patient stated that "he just wants it [the parotid gland] out." A comprehensive discussion of alternatives, including botulinum toxin injections, additional steroid insufflation, sialendoscopy, tympanic neurectomy, and parotidectomy was provided. The patient confirmed that he was well informed, understanding the potential risks and benefits of the options presented to him and requested treatment with parotidectomy.

One month later, a left parotidectomy was performed with concurrent sialendoscopy identifying a normal ductal system (Figure 2). Facial nerve function was preserved, as was the integrity of the posterior branches of the great auricular nerve. He reported relief from the pain with a good cosmetic result (Figure 3). At his four-month follow-up, he reported continued relief of left-sided facial pain.

At his one-year follow-up appointment, he reported discomfort in the left ear canal, especially when laying on the left side at night. Physical exam of the face revealed no lesions or facial asymmetry, and left-sided otomicroscopy demonstrated a normal ear canal and tympanic membrane. This otalgia was initially managed with hydrocortisone/acetic acid 1%–2% drops. When his otalgia failed to respond to conservative treatment, a test injection of 2% lidocaine (2 mL) to the region of the severed anterior branches of the great auricular nerve provided relief of symptoms, confirming a diagnosis of neuroma. At this same follow-up visit, he also reported 6 months of gustatory sweating confirmed as Frey's syndrome through a starch iodine test. He received therapeutic intradermal botulinum toxin injections (40 units) with improvement in gustatory sweating. He subsequently received injections of 40 units of botulinum toxin every 8–26 months to control his symptoms.

Pathologic review of the parotid specimen showed benign salivary gland tissue with abundant parenchymal adipose tissue and mild acinar hypertrophy, confirming the diagnosis of sialosis. Acinar hypertrophy was present, but was not uniform, with enlarged acini observed adjacent to morphologically normal acini. The hypertrophic acini were distended with coarse zymogen granules and measured 60–70 μm in size, nearly 1.5 times larger than adjacent normal acini (Figure 4).

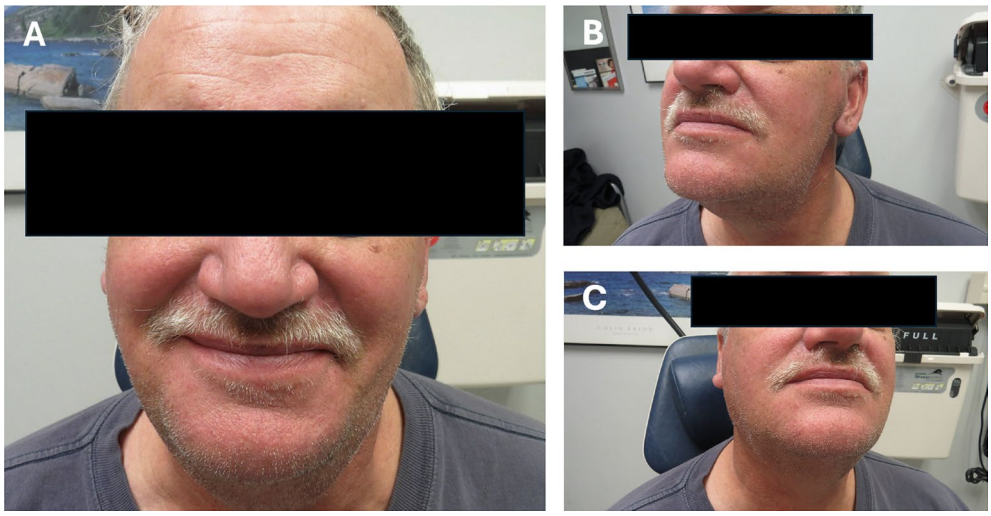

FIGURE 3 | Post-Parotidectomy Cosmetic Outcomes. (A) All photos presented with written patient consent. Frontal view of the patient demonstrates slight right-sided fullness compared to the left side. (B) Left side of the patient's face after parotidectomy appears flat with aesthetically pleasing contours (C) Right side of the patient's face demonstrates slight preauricular fullness.

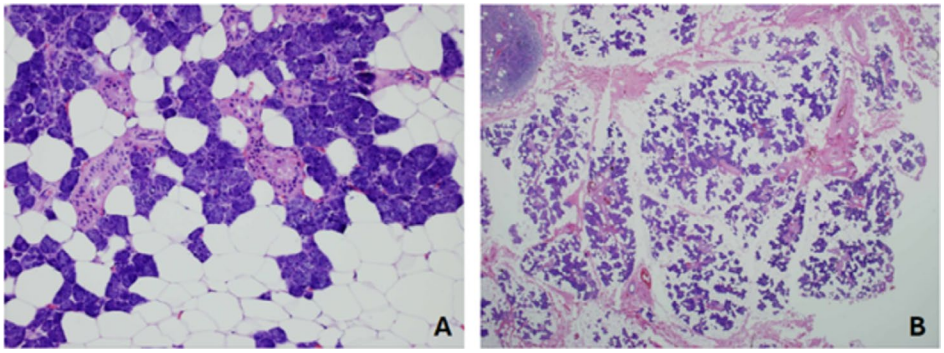

FIGURE 4 | Histopathology of Left Parotid. (A) Highly pigmented, violet color to the acinar cells represents accumulation of coarse granules and acinar hypertrophy. (B) Diffuse fatty infiltration demonstrated by abundance of white (non-staining) fat interspersed throughout hypertrophic acini.

5 | Discussion

Sialosis most frequently affects the parotid glands but can affect any of the major salivary glands. Recognized risk factors for sialosis include metabolic derangement, such as diabetes mellitus and metabolic syndrome, liver disease associated with alcohol use disorder or non-alcoholic fatty liver disease, and nutritional deficiencies, often in combination with primary eating disorders such as bulimia and anorexia nervosa [3, 4]. Half of reported cases do not have an identifiable cause or predisposition. Due to the variety of risk factors, there is currently no widely accepted unifying pathophysiology principle underlying sialosis. Several studies have suggested that development of an underlying autonomic neuropathy may contribute to this disease [4, 5].

Asymptomatic, mild bilateral parotid gland enlargement occurring in patients with recognized risk factors may not require evaluation beyond the history and physical exam to support a working diagnosis of sialosis. Ultrasound is now considered a routine portion of the initial examination for parotid enlargement and, in the case of sialosis often identifies enlarged parotid glands with a greater than normal degree of hyperechoic homogeneity frequently accompanied by deep border loss of definition [6, 7]. Moderate parotid enlargement associated with pain or other concerning characteristics, such as rapid or asymmetric enlargement, may raise concerns for other etiologies and warrant further imaging to support the diagnosis. CT imaging may initially identify unremarkable, symmetric gland enlargement. As the disease progresses, gland enlargement is gradually accompanied by fatty infiltration [4]. Sialographic findings have been reported to demonstrate thinning of the intraglandular ductal system and later pruning of the tertiary ductal system [1].

Previous histologic studies of sialosis have identified patterns that differ according to etiology. Sialosis in patients with diabetes has been characterized by smaller acini and greater fatty infiltration. In contrast, the histopathology of sialosis in those with significant alcohol use identified increased accumulation of secretory granules, acinar hypertrophy, and enlarged excretory ducts [2]. Our case identified a mixture of these two histopathologic patterns.

Ihrler and colleagues proposed that a functional myoepithelial insufficiency (decrease in cytoskeletal elements) allows acinar cells to expand and accumulate an excess of secretory granules. This mechanism was thought to result from an underlying

autonomic neuropathy as has been recognized in association with both alcoholic and diabetic sialosis [5]. Questions persist regarding the underlying pathogenesis of fatty accumulation in sialosis. It is possible that systemic risk factors for sialosis may drive findings at the histopathological level. Alcohol use and metabolic syndrome have been shown to affect insulin resistance and lipid metabolism, increasing lipolysis and release of pro-inflammatory mediators [8]. These mechanisms are associated with the development of hepatic steatosis and therefore may similarly drive the fatty infiltration associated with sialosis. The histopathological findings of both acinar hypertrophy and fatty infiltration in our case may represent multiple factors contributing to the clinical picture of sialosis. This patient did not have identified metabolic or substance use disorders, but he had an elevated BMI which, with a casual drinking history, may have acted synergistically to the development of sialosis.

Sialosis is managed primarily by excluding other causes of salivary enlargement and addressing potential underlying risk factors. Associated pain may be addressed with application of heat and massage, and sialagogues are useful in cases of sialosis with associated xerostomia. Progressive gland enlargement and fatty infiltration may also create concerns regarding cosmesis [4]. Mehler and Wallace identify that this facial disfigurement requires additional treatment considerations in patients with sialosis due to underlying bulimia nervosa. This population has a high rate of mental health comorbidities that may lead to altered perception of body image [4, 9].

Other management options include botulinum toxin injections, intraductal steroid insufflation, and surgery, including tympanic neurectomy and parotidectomy [4]. Treatment with botulinum toxin injections is designed to 'chemodenervate' the gland, as is practiced to diminish salivary production in patients with sialorrhea.

A recent study demonstrated that 80% of patients undergoing regular botulinum toxin injections for sialosis reported at least partial relief of parotid distention-associated discomfort. At follow-up ranging from 3 to 20 months, no patients reported xerostomia associated with this botulinum treatment [10]. A recognized shortcoming to this approach includes the need for repeated injections for continued symptomatic relief and potential to exacerbate baseline xerostomia [4, 10]. Intraductal steroid infusions are effective in treating obstructive and inflammatory sialadenitis [11] in a manner not yet widely reported for the management of sialosis. The proposed mechanism that pain associated with sialosis is due to underlying pressure necrosis within hypertrophic glands offers theoretical support for steroid insufflation to diminish facial pain in the setting of sialosis [2]. This patient's reported short term benefit from steroid insufflation was not sufficient for him to request repeated insufflations.

Support for surgical intervention, including both tympanic neurectomy and parotidectomy, has been reserved for symptomatic patients unresponsive to conservative therapy [1]. Tympanic neurectomy aims to sever the parasympathetic fibers to the parotid gland and mechanically denervate it. Historically, this has been the preferred surgical approach, as it has been reported with favorable results to decrease facial swelling. However, patients may report recurrence of symptoms after several years, which is often attributed to nerve regrowth and regeneration [12]. The parotidectomy in our reported case was successful in relieving the pain but was accompanied by the development of both Frey's syndrome and greater auricular nerve neuroma. These complications were deemed minor by the patient's assessment in comparison to the major improvement derived through relief of the parotid pain ascribed to sialosis.

6 | Conclusion

Short term benefit (relief of pain) from steroid ductal insufflation followed by long term benefit from parotidectomy in this case presentation offers insight into management options for sialosis. Histopathologic review of the resected specimen identified acinar hypertrophy and fatty infiltration as correlates pointing to a potential multifactorial etiology for idiopathic sialosis.

Author Contributions

Evgeniya Molotkova: conceptualization, data curation, formal analysis, visualization, writing – original draft, writing – review and editing. **Piper Wenzel:** conceptualization, data curation, formal analysis, writing – review and editing. **Anand Rajan:** conceptualization, data curation, supervision, visualization, writing – review and editing. **Henry Hoffman:** conceptualization, data curation, formal analysis, supervision, visualization, writing – original draft, writing – review and editing.

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The University of Iowa IRB determined that this case report did not meet the regulatory definition of human subjects research and did not require review.

Consent

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Conflicts of Interest

Dr. Henry Hoffman would like to disclose his roles as an author for UpToDate, a research consultant for MeiraGTx, and a member of the advisory board for RiboX.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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