Premiere Publications from The Triological Society

Read all three of our prestigious publications, each offering high-quality content to keep you informed with the latest developments in the field.

**Laryngoscope**
Founded in 1896
Editor-in-Chief: Michael G. Stewart, MD, MPH
The leading source for information in head and neck disorders.
[Laryngoscope.com](http://Laryngoscope.com)

**Investigative Otolaryngology**
Editor-in-Chief: D. Bradley Welling, MD, PhD, FACS
Rapid dissemination of the science and practice of otolaryngology-head and neck surgery.
[InvestigativeOto.com](http://InvestigativeOto.com)

**ENTtoday**
Editor-in-Chief: Alexander Chiu, MD
Must-have timely information that Otolaryngologist-head and neck surgeons can use in daily practice.
[Enttoday.org](http://Enttoday.org)

Wiley
Temporoparietal Frey Syndrome: An Uncommon Variant of a Common Syndrome

C. Burton Wood, MD ©; James L. Netterville, MD

Objectives/Hypothesis: To describe a previously unreported variant of Frey syndrome. Gustatory sweating is a common complication of parotidectomy and typically directly overlies the surgical site or parotid bed. In some instances, the sweating may occur beyond the parotid bed or involve tissue that was undisturbed during the procedure.

Study Design: Retrospective case series.

Methods: All cases of temporoparietal Frey syndrome in a single surgeon’s experience were reviewed.

Results: Seven patients were found to have temporoparietal Frey syndrome. Three patients had concomitant first bite syndrome. Three patients had some form of reconstruction at time of surgery. The mean time to onset of symptoms was 11.5 months, with a range of 7 to 21 months. Four patients did not require any treatment for their symptoms, but two patients required intradermal Botox injections for symptomatic relief.

Discussion: This study describes a previously unreported variant of Frey syndrome with symptoms occurring distal to the parotid gland. This likely develops either by regeneration of severed postganglionic fibers into sympathetic targets distally along the course of the auriculotemporal nerve or by regeneration into fibers of the sympathetic plexus traveling along the superficial temporal artery.

Key Words: Parotidectomy, salivary glands, complications, quality of life.

Level of Evidence: 4

INTRODUCTION

Auriculotemporal nerve syndrome, or Frey syndrome, is a well-known complication following parotidectomy, being self-reported in approximately 10% of patients following the surgery.1 This condition has been described since the mid-19th century.2,3 Although Frey syndrome is most commonly associated with parotidectomy in otolaryngology, there have been instances reported of development of Frey syndrome following removal of the submandibular gland4 or even following reduction of mandibular fractures or temporomandibular joint dislocation.5–7 Currently, the only factor shown to be predictive of development of the syndrome during parotidectomy is the size of the tumor being excised.8

Although many patients tolerate Frey syndrome without intervention, it can significantly impact patient quality of life in some instances.9 Treatments for Frey syndrome are anticholinergic in nature,10 taking advantage of the pathophysiological mechanism of the condition. The process involves aberrant regeneration of incised postganglionic parasympathetic nerve fibers into cutaneous secretory and vasomotor sympathetic fibers.11 In most instances, this leads to symptoms including gustatory sweating and flushing over the surgical site, as the parasympathetic fibers within the parotid gland tend to reinnervate sympathetic fibers in close proximity. As such, Frey syndrome classically develops directly over the parotid bed itself.

The objective of this study was to describe a previously unreported presentation of Frey syndrome wherein the symptoms of gustatory sweating occur distal to the surgical site and the parotid bed and, additionally, to propose pathophysiologic mechanisms for the development of this condition.

MATERIALS AND METHODS

This is a retrospective review of cases of Frey syndrome encountered following parotidectomy or infratemporal fossa dissection by a single surgeon at a tertiary care center. Cases of Frey syndrome were identified by a search of electronic medical records. Each case of Frey syndrome was manually reviewed to identify instances in which gustatory sweating was noted to have occurred outside of the parotid bed and/or beyond the surgical site. This unique complication, termed temporoparietal Frey syndrome, was defined as development of gustatory sweating and/or flushing in the distribution of the distal branches of the auriculotemporal nerve beyond the parotid bed. For patients found to have this complication, various demographic and surgical variables were collected. These included age and gender of the patient, date of surgical procedure, time from surgical procedure to onset of symptoms, and whether the patient experienced any additional symptoms other than gustatory sweating. The degree of symptoms and whether or not patients required treatment was determined. Additionally, whether or not patients responded to the
treatment provided was discussed. Finally, operative notes were reviewed in detail. The types of surgical procedures performed as well as pathologic details were recorded. Types of reconstruction for surgical defects were determined.

RESULTS

Seven patients were identified as having the above-described unique presentation of Frey syndrome. A summary of patient characteristics is shown in Table I. Fifty-seven percent (n = 4) of the patients were male and 43% (n = 3) were female. The average age for the cohort at the time of surgery was 45 years (range, 34–64 years). The type of surgical procedure performed will be discussed more fully below for each case. Although all of these patients developed symptoms, these were only problematic enough to warrant treatment for three out of seven patients (43%). Three of seven patients were noted to have concurrent first bite syndrome. Symptoms developed within 11.5 months following surgery on average, with a range of 7 months to 21 months postoperatively. Figure 1 shows a schematic representation of the location of Frey syndrome in each of these patients.

Cases 1 and 2 both underwent superficial parotidectomy for parotid tumors, and both of these patients developed gustatory sweating in the temporal region. In both cases, the patients were recommended either topical antiperspirant or glycopyrrolate cream to be used as needed. In addition to gustatory sweating, the patient in case 2 also developed first bite syndrome, which has previously been shown to occasionally occur in conjunction with Frey syndrome following parotidectomy.12

Case 3 underwent transcervical infratemporal fossa approach for excision of a presumed parapharyngeal space schwannoma. The patient developed gustatory sweating over a small area at the vertex temporal scalp roughly 8 months postoperatively. The patient has tolerated these symptoms and has not required any intervention for them, but he has had symptoms consistent with first bite symptoms that have remained bothersome for up to 5 years following the procedure.

The patient in case 4 underwent superficial parotidectomy for malignant disease. A digastric myocutaneous flap was used for the defect, but the patient developed gustatory sweating anterior and superior to the left auricle. This was tolerable to the patient and did not require intervention.

Case 5 had history of sialolithiasis and underwent total parotidectomy for chronic sialoadenitis. The defect was reconstructed with an abdominal fat. The patient developed neuropathic pain in his left temporal region following the surgery, which was subsequently followed by the development of gustatory sweating in the same region at 7 months postoperatively. This encompassed a large surface area and caused significant distress to the patient. As such, he underwent Botox injections to the area on two separate occasions. He did not experience significant relief from the Botox and ultimately was prescribed a glycopyrrolate cream to apply to the area.

Case 6 had resection of a right-sided carotid body tumor requiring sacrifice of the ipsilateral common carotid artery, vagus nerve, and sympathetic chain. He developed right-sided first bite syndrome as well as gustatory sweating over a large portion of the right scalp and frontal region. The symptoms developed gradually and were not bothersome for several years. As such, the patient was unable to recall the exact timing of onset of symptoms following surgery, and he ultimately did not

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (Years)</th>
<th>Gender</th>
<th>Side</th>
<th>Procedure Performed</th>
<th>Reconstruction</th>
<th>Pathology</th>
<th>Symptoms Present</th>
<th>Time to Onset of Symptoms (Months)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34</td>
<td>F</td>
<td>L</td>
<td>SP</td>
<td>None</td>
<td>Pleomorphic adenoma</td>
<td>GS</td>
<td>14</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>64</td>
<td>F</td>
<td>L</td>
<td>SP</td>
<td>Digastric myocutaneous flap</td>
<td>Pleomorphic adenoma</td>
<td>GS, FB</td>
<td>21</td>
<td>Glycopyrrolate</td>
</tr>
<tr>
<td>3</td>
<td>54</td>
<td>M</td>
<td>R</td>
<td>IT approach</td>
<td>None</td>
<td>Paraganglioma</td>
<td>GS, FB</td>
<td>8</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>43</td>
<td>F</td>
<td>L</td>
<td>Revision SP</td>
<td>Digastric myocutaneous flap</td>
<td>Chronic fibrosis</td>
<td>GS</td>
<td>13</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>62</td>
<td>M</td>
<td>L</td>
<td>TP</td>
<td>Dermal fat graft</td>
<td>Chronic inflammation</td>
<td>GS</td>
<td>7</td>
<td>Botox</td>
</tr>
<tr>
<td>6</td>
<td>15</td>
<td>M</td>
<td>R</td>
<td>CBT</td>
<td>Saphenous vein graft</td>
<td>Paraganglioma</td>
<td>GS, FB</td>
<td>Unknown</td>
<td>Botox</td>
</tr>
<tr>
<td>7</td>
<td>35</td>
<td>M</td>
<td>R</td>
<td>SP with RND</td>
<td>Pectoralis flap</td>
<td>Metastatic NPC</td>
<td>GS</td>
<td>7</td>
<td>None</td>
</tr>
</tbody>
</table>

CBT = carotid body tumor resection; F = female; FB = first bite syndrome; GS = gustatory sweating; IT = infratemporal fossa approach to parapharyngeal lesion; L = left; M = male; NPC = nasopharyngeal carcinoma; R = right; RND = radical neck dissection; SP = superficial parotidectomy; TP = total parotidectomy.
seek treatment for these symptoms until 16 years following the initial procedure. At that time he underwent Botox injection to a large area of the frontotemporal scalp. The distribution of gustatory sweating in this case can be seen in Figure 2.

Case 7 underwent superficial parotidectomy and radical neck dissection for recurrent metastatic nasopharyngeal carcinoma requiring resection of cranial nerves X to XII, sympathetic trunk, phrenic nerve, internal jugular vein, internal carotid artery, and sternocleidomastoid. A pectoralis flap was used for coverage of this graft. No specific reconstruction was performed over the site of parotidectomy, which was only removed in the inferior most aspect of the gland. The patient developed gustatory sweating in his temporal region immediately superior to the right auricle 7 months postoperatively. Although Botox injections were discussed with the patient, his symptoms were never bothersome enough to warrant treatment.

DISCUSSION

The present report details a unique and to our knowledge previously unreported presentation of Frey syndrome, discussed in this series as temporoparietal Frey syndrome. Since 1990, the senior author in this report has performed over 300 parapharyngeal and infratemporal fossa dissections and over 1,000 parotidectomies. This rare variant of Frey syndrome has been seen in only seven patients, suggesting an estimated incidence of less than 0.01% of these surgeries. Based on our experience, it occurs in less than 1% of cases of Frey syndrome. Typically, Frey syndrome presents within 12 months of surgery in the majority of cases, though there are reports of Frey syndrome developing as far out as 14 years following surgery. Our findings in the present study are consistent with the reported literature on more typical cases of Frey syndrome, as four of seven patients (57%) developed gustatory sweating within 13 months and two others in under 2 years. Although one patient could not recall the exact onset of symptoms following surgery (case 6), his symptoms progressed, ultimately leading him to seek treatment approximately 16 years following his initial procedure.

Although the variable timing to symptom onset of Frey syndrome is well described, variations in the location of symptoms have not been reported. This variation may represent an alteration in the mechanism of development of the condition. As noted previously, the severed postganglionic fibers have tendency to regrow into cutaneous sympathetic fibers that are in close proximity. This process may be altered slightly in temporoparietal Frey syndrome by one of two possible mechanisms. In each of these instances, gustatory sweating developed in tissues not involved by the surgery and not overlying the parotid gland. In the first proposed mechanism, rather than regenerating into nearby sympathetic fibers, the aberrantly regenerating parasympathetic fibers undergo Wallerian degeneration followed by regrowth distally along the course of the auriculotemporal nerve. This allows the regenerated fibers to reinnervate the more distal sympathetic targets (e.g., sweat glands) that are well beyond the site of surgery. In the second proposed mechanism, the aberrantly regenerating parasympathetic fibers innervate nearby sympathetic fibers that are traveling along the superficial temporal artery (STA). These sympathetic fibers are part of the external carotid plexus, which is the sympathetic plexus that traverses along branches of the external carotid system until ultimately synapsing in target end organs such as arterial smooth muscle or sweat glands. The location of each of the presented patients’ gustatory sweating is within the distribution of the auriculotemporal nerve as well as the STA, and both of these structures travel through parotid parenchyma. Because of their location, incised parasympathetic fibers either in the parotid or in the infratemporal fossa are near enough to the nerve or the STA to either grow along the auriculotemporal nerve or to regenerate into the sympathetic plexus.

Interestingly, three of seven patients (43%) in this series had concurrent gustatory sweating and first bite

Fig. 2. Sweating distribution for case 6. (A) Side view with sweat droplets evident on forehead. (B) Anterior view with flushing evident. (C) Reclined side few with severe flushing evident after ingestion of food during a pre-Botox clinic visit.
syndrome. First bite syndrome most commonly occurs following surgery involving the infratemporal fossa or parapharyngeal space, including deep parotid lobe surgery.\textsuperscript{16,17} Our results are consistent with the literature in this regard, though one patient did develop first bite syndrome following superficial parotidectomy alone. The most widely accepted mechanism for first bite syndrome involves increased parasympathetic response with chewing (smooth muscle contraction) secondary to disruption of sympathetic input. As indicated above, this has been shown to occasionally coexist with Frey syndrome,\textsuperscript{12} though potential etiologies as to why these two complications coexist are incompletely understood. Given that interruption of the cervical sympathetic chain is strongly associated with risk of development of first bite syndrome,\textsuperscript{16} it is likely that patients who develop these syndromes concurrently are experiencing disruption of both parasympathetic and sympathetic structures during the surgeries that lead to these complications.

Treatment of Frey syndrome involves topical or targeted anticholinergic therapy to interrupt the pathophysiologic process that is occurring.\textsuperscript{18} In this particular cohort, treatment was approached in the typical fashion. Topical glycopyrrolate and scopolamine have been used historically,\textsuperscript{19} and glycopyrrolate was used in three of seven cases in this series. In addition to topical treatments, intradermal Botox injections is an alternative therapy for Frey syndrome and represents a widely accepted and implemented treatment.\textsuperscript{20,21} Botox injections offer substantial symptomatic relief for most patients, but there can be varying responses, often requiring escalation of Botox dosing at subsequent treatments. Additionally, Botox is only a temporary solution lasting typically 3 to 6 months, and as such patients are exposed to repeated injections if they choose to continue with this means of therapy.\textsuperscript{22} In this current series, two of seven patients pursued Botox injections, and only one of these patients had significant symptomatic relief.

Given the discomfort associated with Botox injections and the varied response to therapy, prevention of Frey syndrome is ideal. It has been known for decades that a thicker skin flap over the parotidectomy site lowers the instance of aberrant nerve regeneration.\textsuperscript{23} This is routinely performed at our institution and involves raising a skin flap that includes subcutaneous adipose tissue, thereby leaving a more substantial barrier between cut parasympathetic fibers and cutaneous sympathetic fibers. Other methods for prevention of Frey syndrome include recreating barriers between the nerve fibers by using nearby muscle tissue. These include interposition grafts with a superficial musculoaponeurotic system\textsuperscript{24,25} or sternocleidomastoid muscle.\textsuperscript{26,27} Another common method of barrier reconstruction is use of acellular human dermal matrix.\textsuperscript{28} Although each of these techniques can reduce the likelihood of developing Frey syndrome, none of them do so in all cases. The literature indicates that Frey syndrome still occurs in nearly 10% of patients no matter the type of reconstructive method used.\textsuperscript{29} One method for reconstruction commonly employed in our institution involves the posterior belly of the digastricus as an added barrier between parotid tissue and skin. In this technique, the posterior belly is freed of all surrounding attachments, and the common tendon is divided. The muscle is then rotated posteriorly to overlie the neurovascular bundle, and the tendon is closed to the parotid capsule. This technique was employed in two of the seven patients in this series, and a dermal fat graft was used in another patient. Obviously, all of these patients developed Frey syndrome whether any reconstruction was attempted or not. Based on the proposed mechanisms for temporoparietal Frey syndrome, it is unlikely that increasing the barriers between the parasympathetic fibers and cutaneous tissue would prevent this complication, as the fibers do not reinnervate cutaneous sympathetic fibers in the surgical site.

This case series and included discussion does have limitations. First, given its retrospective nature, it is possible that the actual incidence is higher than reported, as some patients with the syndrome may have not complained about these symptoms in follow-up. Additionally, we did not perform starch testing over the parotidectomy site in the patients who underwent parotidectomy, and as such it is possible that these patients may have had subclinical Frey syndrome symptoms overlying the surgical site. However, based on the robust sweating and flushing in the areas described above, it is unlikely that symptoms at the surgical site would have gone unnoticed. Finally, the proposed mechanism has not been confirmed experimentally. We do not feel that this would be helpful though, as the above mechanisms are physiologically plausible, and experimental methods that could include auriculotemporal nerve sectioning or superficial temporal artery ligation may pose unnecessary risk.

**CONCLUSION**

We describe in this series an uncommon and previously unreported variation in the presentation of Frey syndrome, wherein gustatory sweating occurs distal to the surgical site and parotid bed. As with typical Frey syndrome, treatment is often not necessary but when warranted involves topical glycopyrrolate or intradermal Botox injection. Based on our proposed pathophysiologic mechanism, local muscular flaps or acellular human dermal matrix would be unlikely to prevent development of this uncommon variant of Frey syndrome.

**ACKNOWLEDGMENTS**

The authors acknowledge Luke Flener of Prolific Digital for assistance with the production of the figures.

**BIBLIOGRAPHY**

6. Kanath RAD, Bharani S, Prabhakar S. Frey’s syndrome consequent to an unusual pattern of temporomandibular joint dislocation: case report with


