

Management of Frey Syndrome Using Botulinum Neurotoxin: A Case Report

Samson Ng, BSc (Pharm), MSc, DMD, FRCD(C), FDSRCSEd, Dip ABOMP, Dip ABOM;
Cathy Torjek, CDA; **Allan Hovan**, DMD, MSD, FRCD(C), Dip ABOM

Auteur-ressource

Dr Ng
Courriel : dr.s.ng@opusoralhealth.ca



SOMMAIRE

Le syndrome de Frey se caractérise sur le plan clinique par de l'érythème hémifaciale et une sudation provoqués par des stimulus gustatifs. Le syndrome de Frey est habituellement consécutif à une lésion traumatique dans la région parotidienne et il serait attribuable, croit-on, au bourgeonnement anormal de fibres nerveuses autonomes endommagées. Les auteurs de cette étude de cas décrivent les particularités cliniques et psychosociales du syndrome de Frey du point de vue d'un patient, ainsi que la pathophysiologie de cet état, les stratégies actuelles de prise en charge et l'utilisation de la neurotoxine botulique dans le traitement du syndrome de Frey.

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Frey syndrome (also referred to as gustatory sweating or auriculotemporal syndrome) presents clinically as unilateral facial sweating and flushing on salivary stimulation and mastication. It was first described by Duphenix in 1757¹ as a condition following injury to the parotid gland and, subsequently, explained by Dr. Lucja Frey, a neurologist.²

Frey syndrome commonly occurs following parotidectomy. However, it can also occur after other traumatic insults to the preauricular region, including condylar fractures, blunt trauma or incision and drainage of parotid abscesses. The cutaneous flushing phenomenon can develop several weeks to several years after the nerve injury.^{3,4}

In the following case report, we describe the clinical presentation, diagnosis, pathophysiology and nonsurgical management of Frey syndrome, including the use of botulinum neurotoxin (BoNT) as an effective management alternative.

Case Report

A female patient presented with intermittent flushing and sweating in the left preauricular region of her face at mealtimes. In 2001, she had had a left superficial parotidectomy for treatment of pleomorphic adenoma. Two years after her surgery, she began noticing moisture, redness and a warm sensation at the operative site after eating certain foods. Since then, the facial sweating had become more and more prominent. At each meal, she experienced similar transient symptoms. The condition was causing discomfort and embarrassment and interfering with the patient's social life.

To visualize the affected area, the Minor or starch-iodine test was performed. Liquid iodine was painted on the skin in the preauricular area (**Fig. 1a**) and, once dry, the area was dusted with corn starch. The patient was then asked to chew on lemon slices for 5 min-



Figure 1a: Minor test, step 1: application of iodine liquid to the affected area.



Figure 1b: Minor test, step 2: application of starch powder spray to the dried painted area and triggering of gustatory response.



Figure 1c: Minor test, step 3: observe the intensity and extent of the deep-blue colour, which develops as starch dissolves in sweat and reacts with iodine. Outline the involved region with a marker.



Figure 2: Follow-up 2 weeks after botulinum neurotoxin injection. Minor test is negative in the area previously exhibiting gustatory sweating.

utes to trigger gustatory sweating (**Fig. 1b**). The appearance of blue-black spots in the starched area constituted a positive test, as they are generated by the formation of iodine–starch complex on dissolution of starch by sweat. In this case, a distinctive violet patch measuring 5 cm × 5 cm was visible in the left preauricular area, confirming the presence and extent of gustatory facial sweating (**Fig. 1c**).

After obtaining informed consent from the patient, 30 U of BoNT type A (Botox, Allergan Inc., Markham, ON) were injected into the affected skin without local anesthetic. BoNT was supplied as 100 U of freeze-dried powder and was reconstituted with 1 mL of isotonic saline to achieve a concentration of 10 U/0.1 mL. It was delivered using a 0.3-mL 29 gauge needle (BD Ultra-Fine, BD Consumer Healthcare, Oakville, ON) inserted subcutaneously in the region previously delineated by the Minor test. The patient tolerated the procedure well.

The patient reported symptomatic improvement a few days following the injection, a finding confirmed by a negative Minor test administered 2 weeks postinjection (**Fig. 2**). She reported no unwanted side effects. At the 12-month follow-up appointment, the patient reported that she was no longer aware of any facial sweating or facial warmth after eating.

Pathophysiology of Frey Syndrome

Frey syndrome is believed to be the result of misdirected autonomic nerve regeneration following injury to the parotid region. After injury, the sectioned postganglionic secretomotor parasympathetic fibres (auriculotemporal nerves),

which normally innervate the parotid gland, become connected to sympathetic receptors, which innervate sweat glands and result in gustatory sweating.⁵ Thus, stimuli that normally cause salivation (aromatic foods, thinking about certain foods) simultaneously cause pathologic sweating and flushing in the preauricular area on the side of the nerve injury.

Although Frey syndrome does not cause significant physiological harm, profuse gustatory flushing and sweating can cause social and psychological distress in some patients.

Evaluating Frey Syndrome

Casler and Conley⁶ reported that 90% of patients develop positivity to the Minor test after parotidectomy. However, most patients with a positive test are asymptomatic; 30% are aware of gustatory sweating but only 10% of patients are bothered by it.

Luna-Ortiz⁷ proposed a clinical criterion for evaluating the severity of Frey syndrome, which consists of assigning a numerical value to 4 clinical features: patient perception, positive Minor test, excessive facial sweating affecting the patient's quality of life and presence of an unpleasant smell. The total score is used to rate the condition from mild to severe; however, the implications of such a classification remain unclear.

Treatment Options

In most cases, Frey syndrome patients do not complain of their symptoms, and are often treated effectively with topical antiperspirant gels applied to the affected area.

However, when symptoms become bothersome, therapeutic options can be offered. Various prophylactic and therapeutic surgical strategies have been proposed to minimize the incidence or severity of Frey syndrome following parotidectomy, including temporal fascia grafting, the application of synthetic materials to the surgical field at the time of surgery and ligation of the auriculotemporal and chorda tympani nerves.³

Patients who are unresponsive to topical therapy may want to consider a trial of BoNT before considering surgical options.

Topical Antiperspirants

A solution of aluminium chloride (hexahydrate) 20% w/v in anhydrous ethyl alcohol (SD alcohol 40) 93% v/v (Drysol, Person & Covey, Glendale, CA) is the most popular topical therapy because it is available as a nonprescription, over-the-counter, self-care product. It is usually applied at bedtime to the dried affected area of the skin and washed off in the morning. Daily application can give symptom relief without side effects and often permits less frequent application over time.⁸ The mechanism of action is postulated to be the induction of eccrine secretory gland atrophy secondary to long-term mechanical obstruction of sweat gland pores by the aluminium salts found in products such as Drysol.⁹

Botulinum Neurotoxin

BoNT is isolated from an anaerobic spore-forming bacterium, *Clostridium botulinum*. This is the same bacterium responsible for botulism food poisoning, which presents clinically as flaccid muscle paralysis. Chemically, BoNT is a 2-chain metalloprotease composed of a heavy and light chain with 8 immunologically distinct serotypes, A to G. Currently, serotype A has been used most widely for a variety of movement and spasticity disorders as well as in cosmetic procedures.¹⁰

BoNT irreversibly blocks the presynaptic release of acetylcholine at the neuromuscular junction, leading to chemodenervation. However, the chemodenervation is temporary, as the neuron regenerates functional synapses at the nerve terminals. In addition to anticholinergic activity at the motor end plate, BoNT also acts on the synapses of the autonomic nervous system, providing anticholinergic effects at the neurosecretory end plates of both the parasympathetic and sympathetic systems.¹¹ This explains its effectiveness in treating axillary and palmar hyperhidrosis.

Local injection of BoNT into the region of gustatory sweating can be an effective treatment in reducing the activity of sweat glands in the preauricular area.¹² The use of BoNT in Frey syndrome management was first proposed in 1995 by Drobik and Laskawi.¹³ Since then, it has been adopted worldwide. Most Frey syndrome patients treated with BoNT remain symptom free for at least

6 months,^{14,15} and there are reports of the effect lasting up to 15 months.¹⁶ Repeated administration seems to decrease symptom severity and the extent of the affected area and increase the time to relapse.¹⁷

However, as mentioned, BoNT may diffuse into the facial muscle motor end plate and result in temporary weakening of the facial muscles, drooping of the eyelids and facial paresis. Localized, short-term reactions at the injection sites, including pain, edema, erythema, ecchymosis and hyperesthesia, as well as allergy reactions were also mentioned.¹⁸

Conclusion

This case report illustrates the clinical presentation, diagnosis, pathophysiology and nonsurgical management of Frey syndrome. BoNT is discussed as an effective and minimally invasive management alternative. ♦

THE AUTHORS



Dr. Ng is a certified specialist in oral medicine and pathology and holds a staff appointment in the oral oncology/dentistry clinic at the British Columbia Cancer Agency. He is clinical assistant professor at the University of British Columbia's faculty of dentistry and director of the Oral Care Program for the Medically Complex Patient at Vancouver General Hospital, department of dentistry. Dr. Ng maintains a consultative oral medicine practice at the lower mainland, Vancouver, British Columbia.



Ms. Torjek is a certified dental assistant in the oral oncology/dentistry program at the British Columbia Cancer Agency, Vancouver, British Columbia.



Dr. Hovan is a certified specialist in oral medicine and provincial practice leader in oral oncology/dentistry at the British Columbia Cancer Agency, Vancouver, British Columbia.

Correspondence to: Dr. Samson Ng, Dentistry, Vancouver General Hospital, 7th floor - 2775 Laurel St., Vancouver, BC V5Z 1M9.

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