Frey’s syndrome. The postponed danger.

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Frey’s syndrome is a complication of parotidectomy that occurs as a result of aberrant regeneration of the postganglionic parasympathetic nerve fibers, which supply the parotid to the ones of the facial sweat glands. It is characterized by sweating and flushing in the parotid area after gustatory stimulation and is often combined with generalized pain or discomfort in the area innervated by n. auriculotemporalis (1). Frey’s syndrome can be socially debilitating. According to the literature its latency period can reach 50 years (2).

Our aim was to review the contemporary literature and share our experience with Frey’s syndrome. We present a 61 years old woman, referred to our clinic for assessment of gustatory sweating in the left parotid area of our series of more than 250 patients with onset 5 years after parotidectomy. The gustatory stimulation test caused profuse, thick whitish sweating, warmth sensation and discomfort, but no flushing.

Results and discussion
Frey syndrome is characterized by unilateral sweating and flushing of the face in the parotid region during meals. It was first described in 1923 by the French neurologist Lucia Frey. This condition can be caused by parotid surgery, radical neck dissection, toracocervical sympathectomy, submandibular gland surgery and diabetic autonomic neuropathy (3). The reported incidence differs greatly depending on the method of diagnosis. The pathophysiology of Frey’s syndrome is explained by the theory of abnormal regeneration. Cholinergic secretomotory parasympathetic fibers from n. glossopharyngeus, innervating the parotid gland pass through the otic ganglion to the auriculotemporal branch of the mandibular nerve. They are cut in parotid operations. Frey’s syndrome is caused by their abnormal regeneration, resulting in misdirected innervation of the sweat glands and the facial skin (1, 6).

The latency period of Frey’s syndrome is explained with the time required for nerve fibers regeneration. According to the literature it ranges from two weeks to two years, but delay of 40-50 years has also been reported (7, 8). In our case the latency period was 5 years.

Various surgical techniques have been described for the prevention of Frey’s syndrome. (3, 9), among which the most important are development of a thick skin flap and accomplishment of partial superficial parotidectomy whenever possible. An alternative is the use of superficial musculoaponeurotic (SMAS) flap, which is placed in the bed of the resected parotid gland, and serves as a barrier against the anastomoses between the postganglionic fibers and the sweat glands (10). The ideal barrier must either remain in place permanently, or be replaced by dense fibrous tissue, which makes polytetrafluoroethylene (PTFE) implants an ideal solution, because of their good biocompatibility, low tissue reactivity and lack of absorption.

Another option is the use of topical antiperspirants (aluminum hydroxide) and systemic and topical anticholinergic drugs, as scopolamine, and glycopyrrolate. Their use is limited by the poor effectiveness, anticholinergic side effects and local irritation (3).

In literature is described a block of ganglion stellatum (11), which leads to partial relief in patients with diabetic autonomic neuropathy. It is ineffective in Frey’s syndrome, because the parasympathetic nerve fibers of the auriculotemporal nerve remain unaffected (12).

Our treatment of choice is the intracutaneous injection of botulinum toxin. Its use was introduced in 1995 by Drobik and Laskawi. By receptor-mediated endocytosis in neurons, Botulin toxin destroys the synapse-associated protein (SNAP-25), which is responsible for exocytosis of acetylcholine vesicle (3). Gustatory sweating usually stops in 48 to 72 hours (13). Possible complication is a transient paresis of the orbicularis oris muscle (14). Significant side effects have not been reported. There are very few studies to track the duration of the effect of botulinum toxin. Jens et al observed no recurrence of symptoms for up to 23 months in a series of 7 patients with Frey’s syndrome, treated with botulinum toxin (1), while Rainer et al reported recurrence in 12 of 19 patients after an average of 17.3 months (13). They were effectively treated with repeated injections.

Conclusion
The severity of Frey’s syndrome varies from asymptomatic to socially debilitating. The patients must be informed that it occurs in about 10% of the cases. This complication is difficult to prevent and treat and its onset can be years after the operation. Some modifications in the surgical technic, as elevation of a thicker skin flap can decrease its incidence. Botulin toxin injection may be proposed as a minimally invasive method of treatment.

Bibliography