Gustatory rhinitis in multiple system atrophy

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ABSTRACT
Gustatory rhinitis is a type of nonallergic, noninflammatory rhinitis. A high incidence of rhinorrhea, including gustatory rhinitis, is reported in patients with Parkinson’s disease (PD). Herein, we report a case of gustatory rhinitis in a patient with a parkinsonian variant of multiple system atrophy (MSA-P). A 56-year-old man presented with gustatory rhinorrhea and bilateral copious nasal discharge while eating. Three years before visiting the ear, nose, and throat clinic, he developed Parkinsonism and was suspected of having MSA-P. He underwent posterior nasal neurectomy under endoscopic guidance, but it did not significantly reduce the rhinorrhea during eating. Pathological examination of the mucosa of the inferior turbinate demonstrated minimal inflammatory cellular infiltration. Severe (gustatory) rhinitis may also be a useful biomarker for the diagnosis of synucleinopathies, including PD and MSA, akin to anosmia, which is a well-known biomarker for the early diagnosis of PD.

Introduction

Gustatory rhinitis, a syndrome of food-induced nasal hypersecretion, is a type of nonallergic, noninflammatory rhinitis. Parasympathetic predominance is considered to be the underlying pathophysiological cause of gustatory rhinitis. However, the exact pathophysiology is still unclear [1].

Some reports suggest that rhinorrhea occurs more frequently among patients with Parkinson’s disease (PD) than among healthy controls [2–5]. However, these reports are based on questionnaire surveys; detailed findings of rhinorrhea in patients with PD have not yet been reported. Moreover, it is unclear whether other Parkinson-related disorders are also associated with excess rhinorrhea.

Herein, we report a case of gustatory rhinitis in a patient with a parkinsonian variant of multiple system atrophy (MSA-P), who underwent resection of the posterior nasal nerve.

Case presentation

A 56-year-old man was referred to our department with a chief complaint of bilateral copious nasal discharge while eating. His symptoms first appeared 3 years ago. The watery nasal secretion was so excessive that he lost his appetite. Endoscopic and CT examinations in the previous clinic revealed a left nasal polyp at the uncinate process and mild opacity in bilateral maxillary and ethmoid sinuses. He therefore underwent left nasal polypectomy, but his symptom did not improve. Oral administration of antihistamines, including d-chlorpheniramine maleate and azelastine hydrochloride, failed to improve his condition. A fixed-dose combination of fexofenadine hydrochloride/pseudoephedrine hydrochloride, which was prescribed for sympathetic stimulation, was temporarily effective. However, the symptom recurred within a month.

The patient’s past medical history included myocardial infarction, cerebral infarction of the caudate nucleus, hypertension, hyperlipidemia, and hyperuricemia. There was no history of allergies and nasal complaints. He developed parkinsonism 3 years before presenting to the ears, nose, and throat clinic. He was suspected of having MSA-P, because he developed Parkinsonism with poor levodopa responsiveness, while magnetic resonance imaging revealed atrophy of the...
putamen and the ‘putaminal slit’ sign, which is a hyperintense signal in the dorsolateral margin of the putamen (Figure 1(A)); furthermore, presynaptic nigrostriatal dopaminergic denervation was observed on single photon emission computed tomography (Figure 1(B)). He did not exhibit signs of autonomic failure such as urinary dysfunction and orthostatic hypotension.

Our endoscopic examination revealed atrophy of the nasal mucosa and good patency of the nasal cavity. The nasal mucosa was rather dry; there was no nasal discharge without food. Laboratory data showed that his peripheral blood eosinophils was 4.0% of total white blood cells.

We examined the increase in nasal secretion induced by eating food in two ways. First, we performed nasal endoscopy while he ate hot noodles. Nasal discharge was observed 90 s after he started eating. The inferior turbinate mucosa was not too thick; however, clear watery secretions were observed, which were the maximum at the nasal septum (Figure 2). Second, we measured the quantity of the secretions by weighing surgical sponges (Merocel®, Medtronic Xomed, Inc.), which were inserted into both nasal cavities for 10 min. We set this time length to collect measurable amount of nasal secretion and to prevent the saturation of the amount of nasal secretion in the

**Figure 1.** Brain imaging. (A) Magnetic resonance imaging showing atrophy of the putamen and the ‘putaminal slit sign’, a hyperintense signal on the dorsolateral margin of the putamen. (B) Single photon emission computed tomography showing decrease of 123I-ioflupane accumulation in the striatum.

**Figure 2.** (A) Appearance of clear watery secretions at inferior turbinate mucosa and nasal septum after eating hot noodles. (B) The quantity of clear watery secretions was the maximum at the nasal septum.
sponge. We measured the secretions 1 h before, during, and 1 h after dinner. The secretions weighed 90.8 mg on the right side and 34.4 mg on the left sides, before dinner. They increased to 2269 mg on the right side and 1570 mg on the left side, during dinner. One hour after dinner, the secretions weighed almost 244 mg on the right side and 200 mg on the left sides (Figure 3).

Because the previous medication was ineffective, surgical treatment to reduce the nasal secretion was considered. As he had history of myocardial infarction and cerebral infarction, we chose selective posterior nasal neurectomy under endoscopic guidance as a minimally invasive surgery. The surgery was completed without incidence. Pathological examination of the mucosa sample at the inferior turbinate along the incision for posterior nasal neurectomy demonstrated minimal inflammatory cellular infiltration (Figure 4), which suggested that the rhinorrhea occurred through non-inflammatory process.

After surgery, the patient reported that the quantity of nasal discharge had decreased subjectively by half. However, the measurement of nasal secretion at dinner at home failed to show the decrease; at 1 month after surgery, the nasal secretion on the left side weighed 1314 mg (the sponge on the right side accidentally fell into soup). At 1 year after surgery, the secretions weighed 1840 mg and 1740 mg in the right and left sides, respectively (Figure 3).

Discussion

Previous studies have reported that rhinorrhea is more prevalent in patients with PD (24–50%) than in normal controls (6–26%) [2–5]. Furthermore, 38% of patients with PD with rhinorrhea reported worsening of rhinorrhea while eating [4]. Despite these reports, there is no report of excess rhinorrhea in other parkinsonism-related disorders. To the best of our knowledge, this is the first detailed case report of rhinorrhea in patients with MSA.

PD, MSA, dementia with Lewy bodies, and pure autonomic failure are categorized as synucleinopathies, a group of neurodegenerative diseases caused by an abnormal accumulation of misfolded phosphorylated α-synuclein in the neurons, glia, or both [6,7]. Autonomic dysfunction is observed in synucleinopathies [8]. The sympathetic nervous system tends to be affected more than the parasympathetic system, which is indicated by the higher rate of orthostatic hypotension [8] and cardiac sympathetic denervation [9]. Therefore, the majority of autonomic nervous symptoms in these patients are based on the deficiency of sympathetic tone and relative predominance of parasympathetic tone. The observation of rhinorrhea is in line with this rationale, because it is caused by parasympathetic nerve hyperactivity in the nasal glands.

Although there is no direct evidence that the pathology of MSA causes gustatory rhinitis in our patient, the time lapse between the two events suggests a
strong relationship. Pathological examination of the nasal mucosa revealed little inflammatory cellular infiltration in the mucosa, suggesting that rhinorrhea is more likely to be associated with autonomic dysfunction rather than with inflammation. However, the measured amount of nasal secretion during eating was not reduced after posterior nasal neurectomy. This may be because parasympathetic fibers innervating the anterior region of the nasal mucosa are involved in this pathophysiology.

Our patient complained of rhinorrhea only during eating. The central gustatory pathway ascends from the solitary tract nucleus in the medulla, up to the parvicellular part of the posteromedial ventral thalamus [10]. Moreover, collateral pathways project to the hypothalamus, which controls autonomic nerve reaction, through the parasympathetic nucleus of the brainstem, superior/inferior salivary nucleus, and dorsal nucleus of the vagus nerve [11]. Synucleinopathies present with severe neurodegeneration of the dorsal nucleus of the vagus nerve [7,12]. It can be assumed that parasympathetic dysfunction of the dorsal nucleus of the vagus nerve provides positive feedback to the hypothalamus, which stimulates the salivary nucleus simultaneously, leading to gustatory rhinitis.

Recent studies have focused on the role of nonmotor facets for the early diagnosis of synucleinopathy. Olfactory dysfunction is a well-known rhinologic biomarker for PD [12]. The low specificity of the symptoms is a disadvantage such biological markers; therefore, we need to evaluate several symptoms together to make a reliable diagnosis. Our report, along with previous studies, [2–5,12] suggests that severe (gustatory) rhinitis may be a useful biomarker for the diagnosis of synucleinopathy. We should keep the possibility in mind when treating patients with gustatory rhinitis.

**Informed consent**

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

**Ethical statement**

This study was approved by the Human Ethics Committee of the University of Tokyo (No. 2487).

**Disclosure statement**

The authors have no conflict of interest related to this article.

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