A 47-Year-Old Japanese Woman with Symptoms of Increased Salty and Reduced Sweet Taste Perception Preceding a Diagnosis of Thymoma-Associated Myasthenia Gravis

Patient: Female, 47-year-old
Final Diagnosis: Myasthenia gravis
Symptoms: Arm weakness • dysgeusia • left-side ptosis
Medication: —
Clinical Procedure: —
Specialty: Neurology

Objective: Unusual clinical course
Background: Myasthenia gravis (MG) is an autoimmune neuromuscular disorder, which is often accompanied by various complications. Partial dysgeusia is an uncommon nonmotor symptom of MG, and dysgeusia preceding typical MG symptoms is rare. Although ageusia and hypogeusia have been reported in patients with MG, increased perception of taste has not been reported.

Case Report: A 47-year-old Japanese woman presented with a reduced perception of sweet taste and an increased perception of salty taste. Meanwhile, she was diagnosed with thymoma-associated generalized MG and underwent extended thymectomy. Three months later, her anti-acetylcholine receptor (AChR) antibody (Ab) titer increased to 70 nmol/L, when she had completely lost perception of sweet taste and had developed a markedly increased perception of salty taste. Prednisolone and tacrolimus were then added to the medication, and her partial dysgeusia gradually improved. As the AChR Ab titer decreased, disturbance of sweet taste resolved, although a slight decrease persisted. The increased perception of salty taste returned to normal.

Conclusions: This is a rare case of a patient with MG who developed an increased salty taste perception with a reduced sweet taste perception 3 months before the onset of her motor symptoms. We suggest that MG should be considered as a differential diagnosis in patients with partial dysgeusia but no motor symptoms.

Keywords: Angiotensin II • Dysgeusia • Myasthenia Gravis • Thymoma

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Background

Myasthenia gravis (MG) is an organ-specific autoimmune disorder that is mediated primarily by anti-acetylcholine receptor (AChR) antibodies (Abs) or, less frequently, by anti-muscle-specific receptor tyrosine kinase (MuSK) Abs at the neuromuscular junction [1]. It is frequently accompanied by various complications, known as nonmotor symptoms. These symptoms occur in approximately 25% of patients with MG and include alopecia areata, pure red cell aplasia, and dysgeusia [2]. In MG-associated dysgeusia, not all tastes are necessarily affected. Patients with MG-associated dysgeusia most often experience a decrease in or loss of sweet taste perception; this might be associated with an autoimmune mechanism [3]. The number of patients with MG in whom partial dysgeusia preceded the motor symptoms is limited [4-8]. Although ageusia and hypogeusia have been reported in patients with MG, increased perception of taste has not been reported. Here, we report the case of a 47-year-old Japanese woman with MG who developed not only a reduced perception of sweet taste but also an increased perception of salty taste 3 months before the onset of her motor symptoms.

Case Report

A 47-year-old Japanese woman with no past medical history noticed a reduced perception of sweet taste and an increased perception of salty taste in December 2018. The serum zinc level and thyroid function had been found to be in the normal range at another hospital. She visited our hospital in April 2019 after having left-side ptosis that worsened in the mornings and arm weakness with circadian variation from March 2019. Upon physical examination, her body temperature was 36.6°C, heart rate was 106 beats per min, blood pressure was 128/61 mmHg, and percutaneous oxygen saturation was 99%. The interior of her mouth, including the tongue, was noted to be normal. Neurological examination revealed left-side ptosis, impaired upward gaze of the left eye, symmetric pupils (both 3 mm in diameter), and a normal manual muscle testing score of the extremities.

The left-eye ptosis worsened in the sustained upward gaze test and improved in the ice pack test. Enhanced ptosis was observed, suggesting that her ptosis was bilateral. The result of the edrophonium test was positive. A repetitive nerve stimulation test of the left orbicular muscle of the eye, trapezius muscle, and abductor muscle of the little finger at 3 Hz indicated abnormal amplitude decrement results of 15.6%, 22.7%, and 12.4% respectively. Immunoassay results showed a high titer of AChR Abs (35 nmol/L) but no MuSK Abs (<0.02 nmol/L). A chest X-ray and whole-body computed tomography scan revealed a calcified anterior mediastinal tumor, indicating thymoma and no ectopic thymoma. Thus, a diagnosis of MG was made. The quantitative MG score was 9, and her MG activities of daily living profile was 5. The disease was classified as class IIa MG, according to the criteria set by the MG Foundation of America.

The common causes of dysgeusia were examined. The hemoglobin level was 10.0 g/dL; serum iron level, 33 μg/dL; ferritin level, 5.2 ng/dL; total iron-binding capacity, 423 μg/dL; vitamin B₁₂ level, 241 pg/mL; and zinc level, 81 μg/dL. The thyroid function test results were in the normal range, as were the levels of serum creatinine, liver enzyme, and blood glucose; anti-SSA/Ro antibody results were negative. Because iron-deficiency anemia and vitamin B12 deficiency were suspected, iron and mecobalamin supplememtations were administered, but her dysgeusia showed no improvements. For the treatment of MG, pyridostigmine was initiated, and the

Figure 1. Photomicrographs of the surgical specimen. (A) Low-power image demonstrated lymphocyte-rich thymoma (hematoxylin and eosin [H&E] stain, ×4). (B) High-power image showed tumor composed of polygonal epithelial cells set in a background of numerous lymphocytes indicating type B2 thymoma (H&E stain, ×60).
surgeons performed an extended thymectomy in June 2019. Pathological findings confirmed a type B2, noninvasive thymoma (Masaoka stage I; Figure 1). At 3 months after the surgery, the AChR Ab titer increased up to 70 nmol/L. Her weakness slightly worsened and her perception of sweet taste was lost completely; however, her salty taste perception was markedly increased. Prednisolone and tacrolimus were added to the treatment regimen in September 2019, and her weakness and partial dysgeusia gradually improved. As the AChR Ab titer decreased, disturbance of sweet taste resolved, although a slight decrease persisted. The increased perception of salty taste returned to normal.

Discussion

Among the patients with MG, 2.5% have been reported to develop partial dysgeusia and only 1.4% to develop dysgeusia preceding the motor symptoms [3], with only a few cases reported [4-8]. According to the previous reports, in all patients who developed MG-associated dysgeusia, both AChR Abs and thymoma were present, and dysgeusia developed as the AChR Ab titer increased [9]. Although the dysgeusia was most commonly limited to sweet taste, disturbances of sweet and salty tastes [7] or other tastes have also been reported [8,10]. In all cases previously reported, ageusia and hypogeusia developed, and an increased perception was not reported in any cases. Our present patient, however, had a reduced perception of sweet taste and an increased perception of salty taste. Whereas the hypogeusia to sweet taste persisted, the increased perception of salty taste completely improved, suggesting that the disturbance might not be attributable to the relative change in her taste perception.

The dysgeusia in our patient did not improve with the intake of iron and mecobalamin supplementations; rather, it exacerbated after thymectomy, until it improved when prednisolone and tacrolimus were added to the medication. Because the dysgeusia correlated with the change in the AChR Ab titer, we suspected thymoma-associated generalized MG with hypogeusia to sweet taste and hypergeusia to salty taste and non-motor symptoms preceding the motor manifestations.

Hypogeusia to sweet taste has been reported in patients with MG [3] and Guillain-Barré syndrome [11], and hypogeusia to sweet and salty tastes has been reported in those with Fisher syndrome [12]. All of these are autoimmune diseases, and the frequency of accompanying dysgeusia is low. Regarding MG, partial dysgeusia in the patients might be associated with an autoimmune mechanism because both AChR Abs and thymoma were present in all patients with MG-associated dysgeusia, and the degree of dysgeusia changed in parallel with the AChR Ab titer [9].

In our patient’s case, the AChR Ab titer increased to 154% at 4 months after an extended thymectomy. It has been reported that an AChR Ab titer at 1 year after thymectomy ranged from 27.5% to 150%. An AChR Ab titer at 1 year after thymectomy had a significant inverted correlation with the number of the germinal center B lymphocytes in the thymus [13]. We thought that the AChR Ab titer increased after thymectomy because the number of the germinal center B lymphocytes was small in our case.

Humans can recognize 5 basic tastes: sweet, sour, salty, bitter, and umami. The taste receptors are categorized into 2 types: ion channels and G protein-coupled receptors. Sour and salty tastes are associated with the ion channels, whereas sweet, bitter, and umami tastes are associated with the G protein-coupled receptors. A likely mechanism of dysgeusia in patients with MG is the production of antibodies by the thymus against particular taste receptors [4]. Another likely mechanism of dysgeusia is that the thymus produces not only nicotinic receptors at the neuromuscular junction but also muscarinic receptors on taste receptor cells [6]. Abs against the muscarinic AChRs have been detected in 28% of patients with MG [14]. Acetylcholine binds to the muscarinic AChRs on taste receptor cells and activates the PLC/IP3 pathway, leading to the adjustment of the responses to various tastes [15]. The PLC pathway mediates taste responses to bitter, sweet, and umami substances [16]; however, the latter hypothesis failed to explain the dysgeusia of our patient, particularly the increased perception of salty taste.

An increasing amount of evidence suggests that taste function is modulated by hormones. Angiotensin II suppresses amiloride-sensitive taste responses to sodium chloride and increases nerve responses to sweeteners. It has no effect on the responses to potassium chloride, sour, bitter, or umami tastants [17]. A slight to moderate increase in the urinary excretion of aldosterone has been reported during the period with extremity weakness in patients with generalized MG, and the value returned to the normal range during the period without extremity weakness [18]. Because dysgeusia and weakness changed in parallel with the titer of AChR Abs in our patient, increased aldosterone might have decreased the level of angiotensin II via negative feedback, leading to the hypogeusia to sweet taste and hypergeusia to salty taste. We hypothesized that the hypogeusia to sweet taste was caused by immunologic and endocrinologic mechanisms and the hypergeusia to salty taste was caused by only an endocrinologic mechanism. Therefore, the degree of dysgeusia to salty taste might be less than that to sweet taste when the AChR Ab titer reached the maximum, while the dysgeusia to sweet taste persisted after the dysgeusia to salty taste disappeared as a result of MG treatment. Another hypothesis we considered was that decreased sweet taste for a long time may eventually sharpen salty taste in the central nervous system and tongue level,
and normalization of salty taste may be concomitant with subclinical improvement of sweet taste. Nevertheless, the exact mechanism underlying the hypogeusia to sweet taste and hypergeusia to salty taste in our patient remains unclear.

There are 2 major limitations in this report that could be addressed in future research. First, we did not assess her dysgeusia by an objective test. Second, we could not measure angiotensin II and aldosterone values. Further studies are warranted to clarify the mechanism of dysgeusia in patients with MG.

Conclusions

This is a rare case of a 47-year-old Japanese woman with MG who developed an increased salty taste perception with a reduced sweet taste perception 3 months before the onset of motor symptoms. The increased perception of salty taste might be linked to only an endocrinologic mechanism, and the decreased perception of sweet taste might be associated with immunologic and endocrinologic mechanisms. This report suggests that MG should be considered as a differential diagnosis in patients with partial dysgeusia if they do not present with any motor symptoms.

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Declaration of Figures’ Authenticity

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