Neurology Asia 2026; 31(3) : 1191 – 1194

Co-occurrence of vitiligo and sweet ageusia in a post-thymectomy Myasthenia Gravis patient in remission: A case report

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Abstract

While several journals have published the co-existence of dysgeusia or vitiligo with Myasthenia Gravis (MG), none had described their co-occurrence with MG. Moreover, they usually precede the incidence of weakness, and they disappear several weeks after thymectomy. Here we present a case of a 37-year-old male post-thymectomy patient in remission who initially developed circumscribed depigmentation around the lips and fingers, before consulting us for loss of sweet taste sensation. Aside from elevated Acetylcholine Receptor Antibody (AChR Ab) (6.88 nmol/L; nv: <0.5nnmol/L), other work ups, including a repeat chest CT scan were unremarkable. A low dose prednisone resulted to slight improvement in sweet ageusia one month after initiation. In conclusion, co-occurrence of vitiligo and sweet ageusia may appear in an MG patient in remission even several years after thymectomy. While the decreased immune tolerance may have increased the risk of these non-MG symptoms, thymectomy should still be advocated among MG patients with indication as among the paraneoplastic syndromes associated with thymoma, it has relatively the worst prognosis.

Keywords: Vitiligo; sweet ageusia, myasthenia gravis

INTRODUCTION

Myasthenia gravis (MG) is an acquired autoimmune neuromuscular junction condition which usually manifests with fluctuating weakness of the eye, bulbar, and proximal body muscles.[1,2] Along with clinical signs and symptoms, a positive repetitive nerve stimulation (RNS), regardless of whether the patient has abnormal acetylcholine receptor antibody (AChR Ab) or anti- muscle specific kinase antibody (anti-MuSK Ab), usually confirms the diagnosis.[3,4] Around 5 to 25% have non-motor symptoms, while around 30% have thymoma.[5,6]

Among the non-motor symptoms associated with MG, pure red cell aplasia, alopecia areata, and dysgeusia were the most relatively common.[5] Other rare manifestations include Morvan syndrome, twenty nail dystrophy, and vitiligo.[7-9] Specifically, for dysgeusia and vitiligo, 2.5% and 1.7% of MG patients respectively may acquire these symptoms during their disease, usually during worsening of weakness or when AChR Ab titer is elevated.[5,6,9] They are believed to be caused by failure of tolerance of T-cell maturation leading to autoimmunity.[6,9] While several journals have published the co-existence of dysgeusia or vitiligo with MG, none had described their co-occurrence with MG together. Moreover, they usually precede the incidence of weakness, and they disappear several weeks after thymectomy. Here we present a case of a 37-year-old male post-thymectomy patient in remission who initially developed circumscribed depigmentation around the lips and fingers, before consulting us for loss of sweet taste sensation.

CASE REPORT

The patient is a 37-year-old Filipino male, diagnosed case of AChR Ab positive generalized MG, who underwent thymectomy 3 years ago. The patient was on remission with no

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Date of Submission: 4 February 2026; Date of Acceptance: 6 April 2026

https://doi.org/10.54029/2026jpu

medications until 3 months prior to consult, his doctor noticed depigmentation around his lips which also eventually involved his hands. No medications were given since the patient was unbothered. However, 7 weeks later, the patient started to complain inability to taste sweet foods with prominence of salty and bitter taste sensations leading to the current consult.

The patient had unremarkable vital signs and general physical examination. Upon examination of the oral cavity, no thrush, or any lesion or discoloration was seen in the mucosa and on the tongue. On skin inspection, well demarcated, irregularly shaped, depigmentation patches were noted in the upper and lower lips, and in the back of the fingers, posterior to the nails (See Figure 1a and 1b). Aside from mild bilateral ptosis which the patient claimed to be his baseline, no other signs of MG relapse like easy fatiguability, difficulty in breathing, dysarthria, diplopia, dysphonia and dysphagia were disclosed. The cranial nerves were normal except for difficulty in identifying sweet taste sensation in the anterior 2/3 of both sides of the tongue. The patient was able to identity salt. The process was done by applying a small pinch of either salt or sugar crystals on one side of the tongue by well moistened cotton bud, and instructing the patient not to retract his tongue for around 15 seconds so as not to spread the stimulus to the other side. The process was repeated on the other side. [10] The patient had 5/5 motor strength in all muscle groups and did not complain any sensory deficits. The gait and meningeal tests were normal.

He had positive 3 Hertz repetitive nerve stimulation (RNS), AChR Antibody, and thymoma 3 years ago. Since no MG symptoms were present in the current consult, a repeat RNS was not done. Nevertheless, present AChR Ab (6.88 nmol/L; nv: <0.5nnmol/L) titers showed elevated results. Repeat chest CT scan to rule out thymoma recurrence however and other laboratory tests, including complete blood count, erythrocyte sedimentation rate, c-reactive protein, thyroid function test, Zinc levels, fasting blood sugar, and HbA1C among others were unremarkable. Tests for lupus, Sjogren disease, and thyroid antibody tests were not done. The patient refused to undergo skin biopsy and further

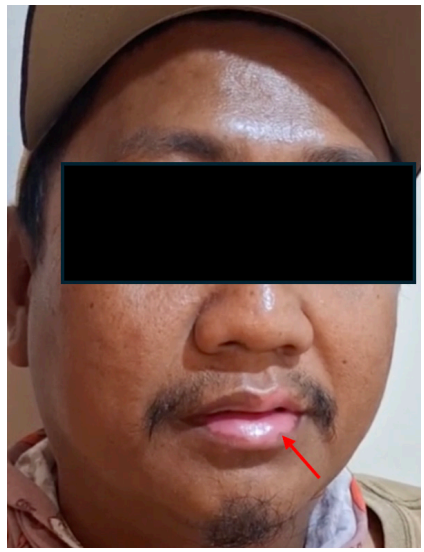

Figure 1a. Vitiligo at the upper and lower lips. (red arrow)

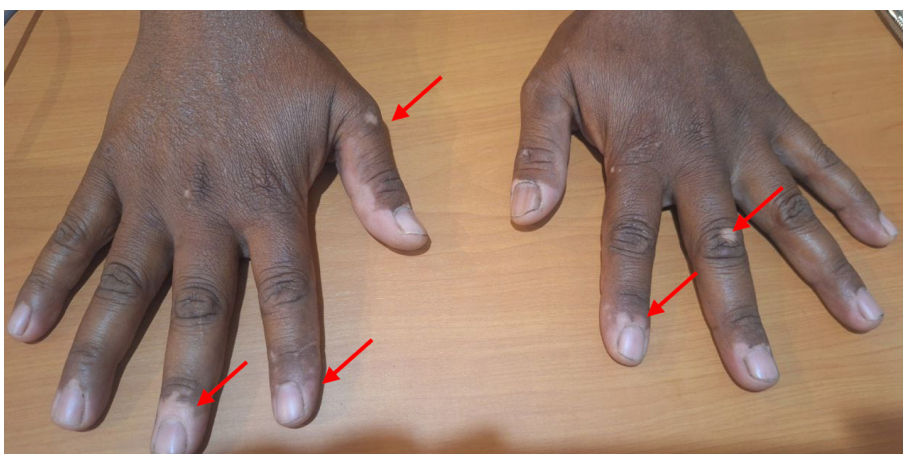

Figure 1b. Vitiligo at the dorsal posterior portion of the fingernails. (Red arrows)

workups for the ageusia. Due to this, the patient was diagnosed as a case of post-thymectomy generalized MG in remission with vitiligo and sweet ageusia.

Due to the autoimmune nature of the patient's condition, a low dose prednisone at 10 mg once a day with calcium supplement, without resumption of pyridostigmine bromide, was started. One month after steroid initiation, there was slight improvement in sweet ageusia, with no obvious reduction in vitiligo.

DISCUSSION

Although in remission, the previous history of abnormal RNS, the response to usual treatment for MG and thymectomy, and the currently elevated AChR Ab confirmed the diagnosis of MG in our patient. No skin biopsy was done, however, the obvious patches of depigmentation around the lips and the fingers suggest concomitant vitiligo. Taste strips may be ideal to test sweet or salty sensation, nevertheless, abnormal gross examination by intermittent administration of sugar and salt with water cleansing, in taste areas for chorda tympani, may support our patient's claim of sweet ageusia. Hence, we treat our patient as a case of post-thymectomy MG in remission with co-occurrence of vitiligo and sweet ageusia.

Several reports have been published about the presence of vitiligo or sweet ageusia, and MG, but none has reported the presence of the two symptoms together in this condition. For vitiligo, a 46-year-old female with mild eye signs started to develop depigmentation 27 years after her initial MG symptoms.[9] This patient had no thymoma and was managed only with ointment and steroid cream.[9] In contrast, a 53-year-old male had vitiligo, alopecia, and oral lichen planus which only improved several months after thymectomy.[11] For sweet ageusia, most patients reported were in the 30 to 50 age group, who complained of taste abnormalities way before MG symptoms appear. Most of these patients had severe MG symptoms and highly elevated AChR Ab titers. Post thymectomy, as titers decreased and MG signs improved, so as the dysgeusia.[5,6] In contrast, our patient had concomitant vitiligo and dysgeusia which appeared several years post thymectomy and during remission. Aesthetically, vitiligo may lead to anxiety and low self-esteem. Our patient however wasn't bothered by the skin changes, as no sensory abnormalities were felt. He only consulted for the sweet ageusia as it led to noticeable weight loss.

Among neoplasms, thymoma has the highest proportion of patients who develop paraneoplastic syndromes. Accordingly, among this cohort, 30% will develop MG, while 10 to 15% will manifest with other paraneoplastic diseases, mostly autoimmune conditions.[9] For vitiligo, while the etiology is still unclear, many journals suggest development of autoantibodies against melanin receptors, causing its destruction. Similarly, antibodies against alpha-gustducin receptors which are G-protein cell receptors (GPCR), are suspected to induce sweet dysgeusia among MG patients. Unlike salty and sour tastes, which are served by ion channels, sweet, umami and bitter tastes are activated by GPCR.[5,6] Nevertheless, concrete studies were yet to be done to explain why sweet taste is affected while others are spared. As 28% of MG patients have muscarinic type AChR Ab and since muscarinic receptors are also found in taste receptors, some believe that affection of the said receptors by the antibodies may result to activation of PLC/IP3 pathway leading to their destruction. As all MG patients with dysgeusia and most patients with vitiligo also have thymoma, it is hypothesized that failure of tolerance of adult T-lymphocytes in the thymic tissue may have increased the chance of autoimmunity, not only for vitiligo and sweet ageusia but also for non-MG symptoms.[5,6]

If thymoma is the possible source of antigens leading to development of autoantibodies against the melanin, alpha-gustducin, and acetylcholine receptors in our patient, then why he still developed vitiligo and sweet ageusia despite the post-thymectomy state? While presence of left-over thymic tissue may be possible, the negative repeat chest CT-scan may render this less likely but can't be ruled out. Previously, we reported a post thymectomy patient in remission who suffered from autoimmune Morvan Syndrome (MoS).[8] In a larger study, they noted that removal of the thymus may result to increased risk of all cause-death, cancer, and autoimmune disease like MoS. They argued that thymic tissue is needed for immune surveillance, differentiation, selection, production of mature T-cell cells and CD4+ and CD8+ lymphocytes, even among adult population. [12] Moreover, manipulation of the thymus during thymectomy may have also resulted to the release of harbored antigenic targets, in this case antigens for melanin and alpha gustducin receptors. Looking at another perspective, the loss of immune tolerance may have lessen the resistance of acquiring extra-thymic internal pathological and infectious

pathogens that may serve as antigens for molecular mimicry. Nevertheless, we believe that regardless of thymectomy state, the chance for harboring non-MG symptoms is still possible. We still advocate thymectomy however, as among the 3 (sweet ageusia, vitiligo, and MG), MG has the worst prognosis. Accordingly, thymectomy reduces the risk of prolonged hospitalization, exacerbation and myasthenic crisis.

In conclusion, **c**o-occurrence of vitiligo and sweet ageusia may appear in an MG patient in remission even several years after thymectomy. While the decreased immune tolerance may have increased the risk of these non-MG symptoms, thymectomy should still be advocated among MG patients with indication as among the paraneoplastic syndromes associated with thymoma, it has relatively the worst prognosis. Further studies are needed to clarify the immunological mechanisms underlying post-thymectomy autoimmunity and to determine whether such associations are coincidental or part of a broader syndrome spectrum.

DISCLOSURE

Ethics: The patient has provided consent for data collection and publication of this paper.

Financial support: None

Conflict of interests: None

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