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CASE REPORT



# Laryngeal myasthenia gravis following influenza vaccination: a case report and literature review

Feng Wang[a*], Tao Xiang[b*], Lanying He[a], and Jian Wang[a]

[a]Department of Neurology, Chengdu Second People's Hospital, Chengdu, Sichuan, China; [b]Department of Rehabilitation Medicine, Chengdu Jinniu District People's Hospital, Chengdu, Sichuan, China

**ABSTRACT**

**Background:** Myasthenia gravis (MG) is an autoimmune disease of acquired neuromuscular junction transmission disorder mediated by auto-antibodies. Extranophthalmic muscles are the most susceptible to MG, while the larynx muscle may also be affected. MG can be aggravated by various types of drugs. In the present study, a patient with laryngeal MG who received an influenza vaccination 5 days before onset was treated, which has not been previously reported.

**Case presentation:** A 58-year-old Asian woman developed mild dysphagia and severe dysarthria five days after receiving a trivalent inactivated influenza vaccine. The patient's quantitative MG score was 4 (1 for swallowing and 3 for speech), and the patient's neurological symptoms varied. The serum acetylcholine receptor (AChR) antibody titer was 0.67 nmol/L (normal range below 0.2 nmol/L), and other immunological and thyroid function tests were negative. As revealed by chest computed tomography (CT), there was no thymus abnormality. Based on the patient's history, clinical features, and examination results, the patient was diagnosed with laryngeal MG. The patient received pyridostigmine oral administration (60 mg/d) and steroid therapy (Prednisone, oral, 60 mg/d). The patient's symptoms began to improve after 7 days of treatment, and were significantly relieved after 2 weeks.

**Conclusion:** Influenza vaccination might cause an unexpected abnormal autoimmune response in MG as a very rare event. Further research is needed to assess the possible causal relationship between the influenza vaccine and neurological complications, also in addition to the safety of the vaccine.

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## Background

As indicated by prior research, influenza vaccination is the most effective preventive measure to reduce influenza virus infection, morbidity and mortality.[1,2] In China, influenza vaccines have been extensively used. In a previous study, the mean vaccination rate of urban regions in China from the 2009/10 influenza season to 2011/12 was examined, and the result was 9.0%.[3] As is common knowledge, the most common adverse reactions to influenza vaccination are influenza-like symptoms such as myalgia, fatigue or malaise, followed by headache, coryza, or cough. Gastrointestinal complaints such as anorexia, diarrhea, or constipation are also common after vaccination.[4] Cases of neurological disorders, such as optic neuropathy and Guillain-Barre syndrome, after influenza vaccination have also been reported.[5,6] However, there is a scarcity of reports on myasthenia gravis after influenza vaccination. In the present study, a case of laryngeal MG after influenza vaccination is presented, in which the patient's main manifestations were dysarthria and dysphagia. Said manifestations were exclusive initial and primary complaints.

Myasthenia gravis (MG) is an autoimmune disease of acquired neuromuscular junction transmission disorder mediated by auto-antibodies, with antibodies to acetylcholine receptors (AChR) being the most common pathogenic antibodies.[7] Extranophthalmic muscles are the most susceptible, presenting as symmetrical or asymmetrical ptosis and/or binocular diplopia, and are the most common first symptoms of MG, occurring in more than 80% of MG patients. Notably, MG can be aggravated by a variety of different drugs.[8]

## Case presentation

A 58-year-old Asian female with dysarthria and dysphagia was firstly admitted to the otolaryngology department. A fiberoptic laryngoscope was arranged to observe the pathophysiological changes of the pharynx and larynx, and the results revealed that there was no pathophysiological change. Subsequently, the patient was admitted to the department of neurology and underwent a thorough neurological examination. The muscular strength of the patient's upper and lower extremities was normal, and the deep tendon reflex of both sides was also normal. The patient's medical history was hypertension and cholesterol gallstone disease without smoking and alcohol consumption. The patient had been vaccinated against chickenpox many years ago, and received a trivalent inactivated influenza vaccination (Site and method of inoculation: intramuscular injection of deltoid muscle of left upper arm;

**CONTACT** Tao Xiang buaaqt@163.com Department of Rehabilitation Medicine, Chengdu Jinniu District People's Hospital, NO.300 Jinfu Road, Jinniu District, Chengdu, Sichuan, 610037, China

*These authors are equally contributed to this work

**Table 1.** Case reports of new-onset myasthenia gravis after vaccination.

| Author | Year | Age/ Sex | Vaccine type | Initial symptoms | Thymoma | Time to onset | Treatment | Prognosis (time to recovery) | MGFA class |
|---|---|---|---|---|---|---|---|---|---|
| Bahri[12] | 2003 | 46/F | HBV | Ocular, bulbar | - | 1 Mo after 2nd shot | Pyridostigmine, steroid | Improved (Not mentioned) | IIb |
| Biron[13] | 2010 | 48/M | HBV | Ocular | + | 1 Mo after 2nd shot | Edrophonium, plasma exchange, cyclophosphamide, steroid | Improved. (After 30 PE) | I |
| Takizawa[14] | 2017 | 69/M | BCG | Ocular | - | 6 Wks | Pyridostigmine | Improved (70 days) | IIa |
| Chung[15] | 2018 | 23/F | HPV | Ocular, bulbar | - | 3 d after 2nd shot | Pyridostigmine, steroid, IVIG | Improved (84 days) | V |
| Current case | 2020 | 58/F | FLU | Laryngeal | - | 5 d after shot | Pyridostigmine, steroid | Improved (28 days) | IIIb |

Mo months, Wks weeks, d days, HBV hepatitis B vaccine, BCG Bacillus Calmette-Guerin, HPV human papillomavirus, FLU influenza vaccine, IVIG intravenous immunoglobulin, MGFA myasthenia gravis foundation of America clinical classification.

Dosage: 0.5 ml; Manufacturer: Hualan Biological Vaccine Co., LTD) 10 days before being admitted, and the symptoms of dysarthria and dysphagia occurred on the fifth day after vaccination.

The patient had severe dysarthria and mild dysphagia, her quantitative MG score was 4 (1 for swallowing and 3 for speech), and the patient's neurological symptoms varied. The serum AChR antibody titer was 0.67 nmol/L (normal range below 0.2 nmol/L). The patient's dysarthria and dysphagia temporarily improved with the pyridostigmine test. Repeated nerve stimulation (RNS) did not indicate a significant reduction in the compound muscle action potentials (CMAP) of the orbicularis oculi, deltoid, quadriceps femoris, and intercostal muscles. Other immunological and thyroid function tests were negative. As revealed by chest computed tomography (CT), there was no thymus abnormality. Other possible intracranial lesions, such as hemorrhage, infarction, and tumor, were excluded by craniocerebral magnetic resonance imaging (MRI). According to the anti-acetylcholine receptor antibody tests and pyridostigmine test, the patient was diagnosed with laryngeal myasthenia gravis and received pyridostigmine (60 mg/d), which was administered orally, and steroid oral therapy (Prednisone, 60 mg/d). The patient's symptoms began to improve after 7 days of treatment, and were significantly relieved after 2 weeks. Later, the patient was discharged. The patient took pyridostigmine for four weeks, and the prednisone was tapered off to stop within six months. A 6-month follow-up was conducted after discharge, and the patient's symptoms were completely resolved without exacerbation or recurrence. The patient was pleased with the treatment plan and the results.

## Discussion and conclusion

MG is a relatively uncommon disorder with an annual incidence of 10–20 new cases per million.[9] MG manifests as fluctuating skeletal muscle weakness and fatigue, and although the ocular muscles are most commonly affected, any muscle is susceptible to MG. If the larynx muscle is affected, dysarthria, dysphagia, slurred speech and dysphonia may occur. The classification of MG by the Myasthenia Gravis Foundation of America (MGFA) was provided to evaluate the severity of the disease for better treatment and prognosis evaluation. MG is divided into Class I, Class II (II a and II b), Class III (IIIa and IIIb), Class IV (IVa and IVb) and Class V. The oropharyngeal and respiratory muscles are predominantly affected, with both being classified as IIIb.[10]

Influenza vaccines are widely used every year. The common neurological side effects after influenza vaccination are neuralgia, paresthesia, and neuritis, which are usually described in the drug instructions. Several serious adverse events have been reported that are suspected to be associated with influenza vaccination, such as Guillain-Barré syndrome, acute disseminated encephalomyelitis, and febrile convulsions.[11] After conducting a literature review, no reports on myasthenia gravis in patients after influenza vaccination were found, but cases of myasthenia gravis caused by hepatitis B vaccine, human papillomavirus vaccine and Bacillus Calmette-Guerin vaccine have been reported (Table 1).[12–15] In said case reports, the mechanism of MG induced by inoculation was not clear, but was speculated to be related to an unusual autoimmune response.

Dysarthria and dysphagia are the most common major symptoms of MG in the larynx[16]. Larynx weakness is a significant challenge for doctors, and even though most patients have fiber laryngoscopy, there still can be misdiagnosis problems. As such, patients with laryngeal weakness should be evaluated for fluctuating weakness. For the majority of patients with laryngeal MG, the neostigmine/fluoride test is positive, suggesting that such result could be a diagnostic criterion. Approximately half of patients with laryngeal MG have positive ACRs and decreased RNS response, which can also lead to early diagnosis of laryngeal MG.[16]

Despite the present case indicating that there may be a link between vaccination, auto-immunity, and the development of MG, there are limitations to the present study. The belief of the present authors is that further research is needed, not only to assess the safety of influenza vaccines, but also to determine the association of MG with influenza vaccines.

## Abbreviations

| | |
|---|---|
| MG | Myasthenia gravis |
| AChR | Acetylcholine receptor |
| RNS | Repeated nerve stimulation |
| CMAP | Compound muscle action potentials |

| | |
|---|---|
| CT | Computed tomography |
| MRI | Magnetic resonance imaging |
| MGFA | Myasthenia Gravis Foundation of America |
| HA | Hemagglutinin |
| NA | Neuraminidase; |
| SCID | Severe combined immunodeficiency |

## Authors' contributions

FW and TX participated in the design of this research. FW, LYH, and JW collected and analyzed the raw clinical data. FW, TX, LYH, and JW carried out computational studies and wrote the manuscript. FW and TX contributed equally to this work as co-first authors. All authors have read and approved the final manuscript.

## Disclosure of potential conflicts of interest

No potential conflict of interest was reported by the author(s).

## ORCID

Tao Xiang http://orcid.org/0000-0002-2397-0531

## Data availability statement

All data and material supporting our findings are contained within the manuscript.

## Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor of this journal.

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