CASE REPORT

Thymectomy Cures Diabetes Mellitus and Ameliorates Myasthenia Gravis in a Patient with Thymus Hyperplasia and Hyperthyroidism: Report of a Case

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Received: 2 July 2014 / Accepted: 2 September 2015 / Published online: 12 September 2015
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Abstract Myasthenia gravis (MG) is a devastating autoimmune disease that involves the acetylcholine receptor (AChR) in the postsynaptic membrane of the neuromuscular junction. It is not uncommon for MG to accompany with other autoimmune diseases and complicate with multiple organ dysfunction. Here, we report on an 18-year-old female patient with a rare case of MG concomitant with thymus hyperplasia, diabetes mellitus, and hyperthyroidism. After full excision of the hyperplastic thymus gland, the patient's muscle weakness was greatly improved and her blood glucose level was restored to normal at the 6-month follow-up.

Keywords Myasthenia gravis · Diabetes · Thymus hyperplasia · Hyperthyroidism · Thymectomy

Case

An 18-year-old female, without positive family history, complained of right eyelid drooping, diplopia, and masticatory muscle weakness for 3 months. Her symptoms were alleviated with pyridostigmine bromide (120 mg/day). She was admitted with a 3-day history of dyspnea and myasthenia of the limbs. Physical examination revealed tachycardia (139/min), reduced muscle tension of her limbs (level IV), abated

tendinous reflex, and a positive fatigue test and a neostigmine test. Her Osserman classification was myasthenia gravis (MG) type IIB. Pyridostigmine bromide (120 mg/day) and methylprednisolone (500 mg/day) helped reduce her symptoms. Laboratory analyses indicated that her serum potassium was 4.62 mmol/L (reference interval [RI], 3.5–5.5 mmol/L), fasting plasma glucose was 8.0 mmol/L, urinary glucose was (++) , her 75 g/2 h oral glucose tolerance test (OGTT) was 14.2 mmol/L, thyroid-stimulating hormone (TSH) was 0.007 μ IU/mL (RI, 0.27–4.2 μ IU/mL), free T4 was 63.59 pmol/L (RI, 12.0–22.0 pmol/L), free T3 was 11.60 pmol/L (RI, 3.1–6.8 pmol/L), thyroid globulin antibody was 30.45 IU/mL (RI <115.0 IU/mL), anti-thyromicrosomal antibody (ATM-Ab) was 61.73 IU/mL (RI <35.0 IU/mL), thyroid peroxidase antibodies (TPO-Ab) were 396.98 IU/mL (RI <300.0 IU/mL), and TSH receptor antibody (TR-Ab) was 17.2 IU/mL (RI <9.0 IU/mL). In addition, she was positive for acetylcholine receptor antibodies (AChR-Ab), serum antibodies of glutamic acid decarboxylase (anti-GAD) and islet cell antibodies (ICA), and negative for insulin autoantibody (IAA). The thyroid ultrasound revealed multiple small follicles in both lobes. Chest computed tomography (CT) depicted a soft tissue in the thymus area of the anterior-superior mediastinum, which was considered thymus hyperplasia (Fig. 1a). The electromyogram suggested decreased muscle contraction and inconsistent or blocked fiber transmission. After a multidisciplinary round, the patient was treated with a full thymectomy under general anesthesia. Histological examination confirmed thymus hyperplasia (Fig. 2). The patient was finally diagnosed with MG accompanied with thymus gland hyperplasia, type I diabetes mellitus (DM), and hyperthyroidism.

The patient had a MG crisis after surgery, which was managed with tracheotomy/ventilator-assisted breathing, pyridostigmine bromide, and glucocorticoids. Her muscle weakness disappeared rapidly, and 10 days later, her fasting

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Fig. 1 Chest CT image of pre-operation (a) and post-operation (b)

plasma glucose and urinary glucose were back to normal. The patient was discharged with pyridostigmine bromide at a maintenance dose of 90 mg/day. The 6-month follow-up chest CT was not significant (Fig. 1b), the thyroid ultrasound showed that the small follicles were slightly reduced, and her fasting blood glucose was normal.

Discussion

MG often accompanies with other autoimmune diseases, and hyperthyroidism is the most common. Both MG and thyroid diseases are related to human leukocyte antigen gene loci DR3. In addition, MG and thyroid disease are associated with immune abnormalities and autoantibody production. For example, AChR-Ab cross reacts with thyroglobulin in MG and Graves's disease patients due to their similarities in molecular sequence and structure, as well as possible common antigen epitopes between cholinesterase and thyroglobulin [1]. In our case, various autoimmune antibodies, such as AChR-Ab, ATM-Ab, TPO-Ab, and TR-Ab, were positive.

Physiologically, thymus stromal cells ectopically express a variety of tissue-specific genes controlled by an autoimmune regulator, which also regulates the expression of many peripheral proteins, including insulin in the thymus gland [2].

Fig. 2 Postoperative pathology confirmed thymus gland hyperplasia (HE staining, scale bar=50 μ m)

Thymus cell dysfunction may impair central immune tolerance, destruct islet β cells, and eventually lead to type 1 DM. Interestingly, the thymus microenvironment alters frequently in DM patients [3]. In this case, the patient was positive for anti-GAD and ICA, which supported the diagnosis of MG accompanied with type 1 DM.

Thymus resection has been widely used in the treatment of MG ever since Blalock et al. reported that a MG patient dramatically improved after thymus resection due to a thymus cyst in 1939 [4]. Thymectomy may terminate continuous antigen stimulation, reduce secretory β cells that release AChR-Ab, and terminate autoreactive T-cell production. In our case, DM was cured after thymectomy, which is consistent with an animal study demonstrating that full excision of the thymus could prevent DM [5].

Acknowledgments We thank Medjaden Bioscience Limited for assisting in the preparation of this manuscript.

Conflict of interest The authors declare that they have no competing interests

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