Concurrent Guillain-Barré Syndrome and Myasthenia Gravis: The First Case in Taiwan

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Abstract- The concurrent development of Guillain-Barré syndrome (GBS) and myasthenia gravis (MG) is rare. It has been associated with molecular mimicry between infectious agents and self-antigens. Such antibodies may show cross-reactions against both myelin proteins of peripheral nerves and acetylcholine receptors of neuromuscular junctions. Thymoma-associated multi-organ autoimmunity may also play a role in initiating autoimmune process. We present such a case with the concurrent development of GBS and MG.

Key Words: Guillain-Barré syndrome, Acute inflammatory demyelinating polyradiculoneuropthy, Miller-Fisher syndrome, Polyneuropathy, Thymoma, Myasthenia gravis (MG)

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INTRODUCTION

Guillain-Barré syndrome (GBS) and myasthenia gravis (MG) are diseases of different entities. GBS is an acute post-infectious autoimmune disease mediated by autoantibodies against myelin proteins or axonal constituents of peripheral nerves, causing acute progressive weakness and areflexia. MG is a neuromuscular transmission disorder, initiated by autoantibodies against acetylcholine receptors (AchR), and is usually associated with thymoma or thymic hyperplasia. Pathological fatigability with fluctuating weakness is the cardinal symptoms of MG. The concurrent development of GBS and MG is rare. Only a few cases have been reported[1-4]. Both diseases share several common characters, including humoral autoimmunity, ptosis, oculobulbar paresis, muscle weakness and respiratory failure. Especially when GBS presents progressive muscle weakness with depressed tendon reflexes, fluctuating weakness and fatigued muscle strength suggesting a concurrent MG are easily overlooked. We report such a case with a close temporal coincidence between the two diseases.

CASE REPORT

A 36 year-old woman, who had no previous medical disorders, presented with dyspnea, diplopia, slurred speech and acute progressive general weakness within three days. One week prior to the onset of the above problems, she experienced symptoms of upper airway

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infection, including fever, sore throat, and cough.

On examination, abnormal findings of the cranial nerves include right partial ptosis, external ophthalmoparesis (paresis of the right medial rectus muscle), and facial diplegia. Weakness of the neck extensor and mild respiratory distress were observed in sitting position. In the limbs, the muscle power was grade 3 (Medical Research Council scale) in the proximal muscles and grade 4 in the distal ones. The tendon reflexes were globally absent. There were decreased pin-prick sensation at the wrist and mid-leg area, and decreased vibration sense on the fingers and toes.

The patient was admitted to the intensive care unit because of obvert respiratory distress. Nerve conduction studies showed a demyelinating polyneuropathy (Table and Fig. 1). The cerebrospinal fluid (CSF) was acellular with elevated protein level of 61.2 mg/dl. The Chlamydia antibodies and stool culture for campylobacter were negative. The diagnosis of GBS was established.

The patient experienced respiratory failure 12 hours after admission. Emergent intubation was performed with mechanical ventilation. On the same day of admission, she started to receive plasma exchange therapy with a regimen of 250 ml/Kg in 5 divided treatments on

Table. *Nerve conduction studies*

	Lat. (ms)*		Amp. (mV/μV)†		CV (m/s)*		FL (ms)*	
	R	L	R	L	R	L	R	L
Motor nerve								
	Conduction							
Median					47.7	31.0	40.3	*NR*
Wrist	8.7	11.0	6.1	5.2				
AE			6.3	3.7				
Ulnar								
Wrist	3.5	5.2	11.5	11.5				
AE			10.7	7.4				
Posteror tibial								
Ankle	9.5	8.1	2.0	1.1				
Knee			1.1	0.3				
Peroneal					36.6	31.5	56.8	66.9
Ankle	6.4	8.8	6.7	1.9				
BK			3.3	1.6				
Sensory nerve								
	Conduction							
Median	NR	4.3	NR	10.0	NR	32.6		
Ulnar	8.6	4.5	2.8	3.4	16.3	31.1		
Sural	4.3	NR	3.1	NR	52.3	NR		

Nerve conduction studies on the first day of admission.

Lat.: latency; Amp.: amplitude; CV: conduction velocity; FL: F-wave latency; R: right; L: left; AE: above-elbow; BK: below-knee; NR: no response. Bold entries represent abnormal values. *milliseconds (ms) for latency and F-wave latency and m/s (meters/second) for CV. †millivolts (mV) for compound muscle action potential and microvolts (μV) for sensory nerve action potential.

alternate days. The patient's muscle strength and sensory symptoms gradually improved after treatment.

However, after the full therapeutic course of plasma exchange, the patient had difficulty weaning from mechanical ventilation on the 11th day of admission despite marked recovery of external ophthalmoparesis, limb muscle strength and tendon reflexes. Partial ptosis of the right eyelid and paradoxical weakness of the respiratory muscles comparing with marked restoration of limb muscle strength after plasma exchange suggested

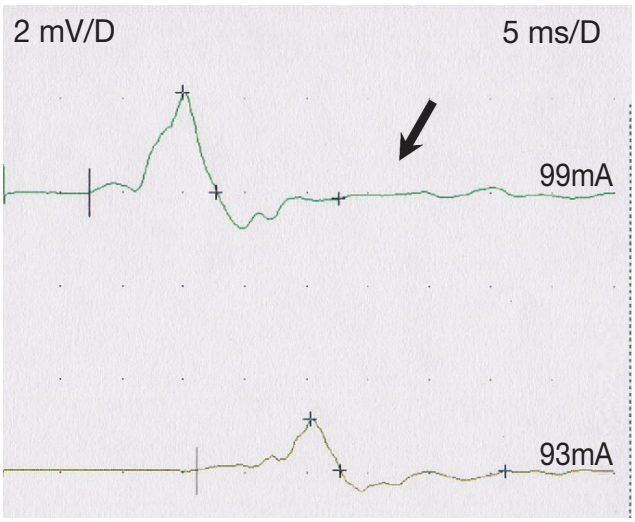

Figure 1. Temporal dispersion of the motor nerve conduction studies of the left posterior tibial nerve. The figure was the follow-up nerve conduction studies on third day of admission. There is a drop in CMAP area of more than 50% with increase in CMAP duration of more than 15%.

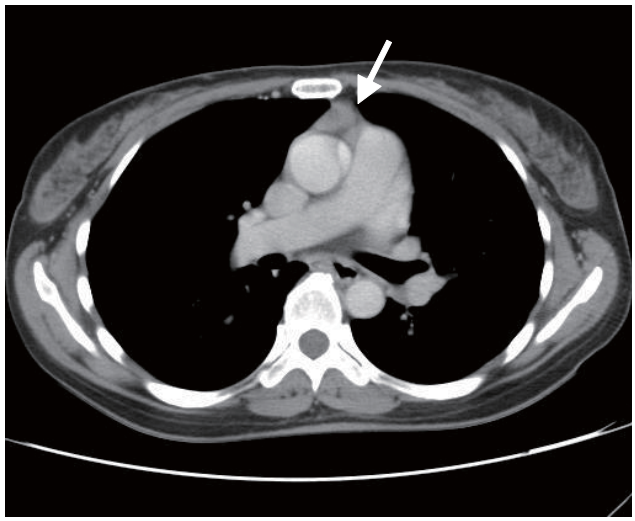

Figure 2. A thymic tumor on chest computed tomography. There is a lobulated nodule with enhancement with a size of 1.43 x 1.71 cm and central low density at the anterior mediastinum.

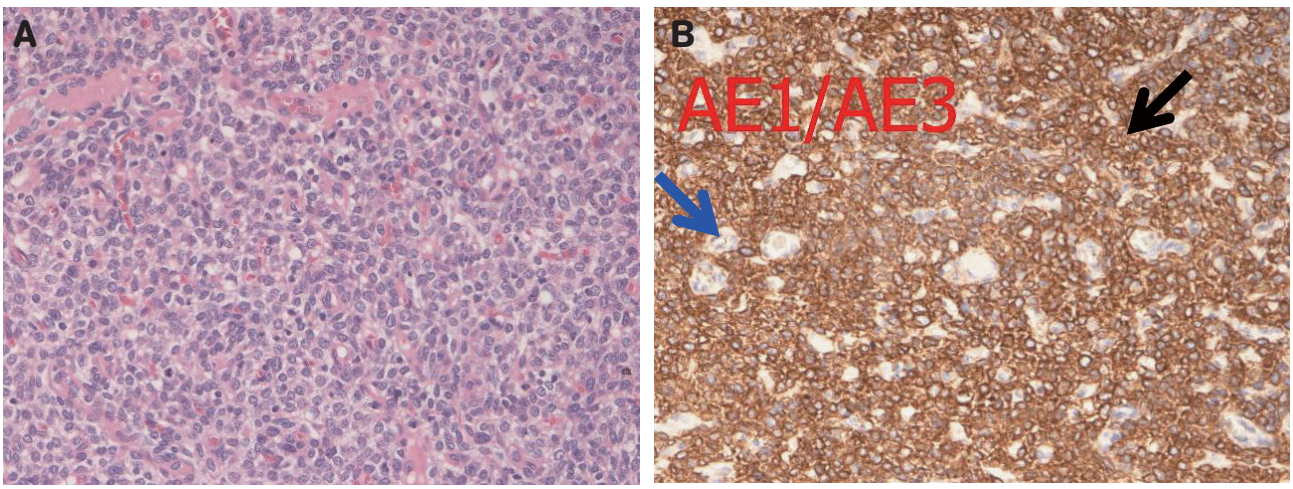

Figure 3. Microscopic examination of the resected thymoma: Thymic tissue with solid tumor mass consists of small blue cells in sheet growth. Cytokeratin AE1/AE3 positive epithelial cell are in brown color (black arrow); Lymphocytes are AE1/AE3 negative (blue arrow).

the possibility of a neuromuscular junction disease. Complete ptosis of the right eyelid and partial left ptosis were provoked by sustained upward gaze for about 50 seconds. Low-frequency (3Hz) repetitive nerve stimulation showed decremental changes (18%~30%) in both the abductor pollicis brevis and trapezius muscles. Single-fiber electromyography demonstrated markedly increased jitter with blocking in the right orbicularis oculi. Serum AchR antibody was markedly elevated (126.82 nmole/L). Thyroid function was normal. The chest computerized tomography (CT) revealed a lobulated enhanced thymic tumor in the anterior mediastinum (Fig. 2). The patient successfully weaned from mechanical ventilation after treated with pyridostigmine and corticosteroids.

Two weeks later, the patient received surgical removal of the thymic tumor. Thymoma was confirmed by histopathological examination (Fig. 2). Five months after surgery, corticosteroid was gradually tapered down. The patient was treated with pyridostigmine (60 mg for 3 times a day) and was in good physical status except for occasional mild right ptosis.

DISCUSSION

The diagnosis of GBS of the patient was established on basis of the acute clinical course, nerve conduction studies of demyelinating polyneuropathy and a finding of albumino-cytologic dissociation in CSF. A thymoma-related generalized myasthenia gravis was also confirmed by the typical neurophysiological, immunological and radiological findings.

The incidence of GBS and MG has been reported 0.4 to 1.7 and 10 to 20 per million persons per year accordingly[5,6]. It has been statistically estimated an incidence of temporal coincidence of less than 1 to 10 billions[2]. Only a few cases have been reported[1-4]. In 2005, Farah et al.[3] reported a 71 year-old man with MG diagnosed in 1980 developed acute motor sensory axonal neuropathy (AMSAN) in 1992. In Kizilay's (1) and Kraus's(2) reports, postinfectious GBS was followed by the development of MG 3 weeks and 10 weeks later, respectively. Carlander et al described a patient with past history of possible GBS developed MG 16 years later. The patient died of another episode of GBS, respiratory failure complicated with massive gastrointestinal bleeding another 11 years later. The most remarkable features of our case is the close relation between the development of GBS and MG.

Autoimmunity plays an important role in both GBS and MG. Molecular mimicry between the infectious agents and self-antigen has been postulated to initiate MG and GBS concurrently, in which case GM1, GQ1 and Campylobacter jejuni antibodies were positive[2]. Some theories hold that a common infectious event may be able to produce cross-reacting antibodies against both the myelin proteins of peripheral nerves and the AchR of neuromuscular junctions. An experimental study showing the antibodies from the patient with GBS cross-react against AchR from the mice strongly supports this theory[7].

Thymoma can be a common cause of MG and other autoimmune neurological diseases as well, including polymyositis, dermatomyositis, multiple sclerosis, stiff-person syndrome and limbic encephalitis[8-11]. Thymoma-associated multi-organ autoimmunity is considered to be similar to graft-versus-host disease[12], proved by identical histological findings of the skin or bowel mucosa. However, to the best of our knowledge, no association has yet been make between thymoma-associated multi-organ autoimmunity and GBS. We propose another hypothesis for the concurrent development of GBS and MG in our patient. With the existence of a thymoma, there may be low-titered antibodies not sufficient to cause clinical symptoms of MG. However, if an infectious event occurs, it may not only induce antibodies causing GBS, but also enhance the production of anti-AchR antibody leading to development of MG.

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