Severe Myopathy in Patients with Thyrotoxicosis

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Myopathy, including muscle weakness, is not rare in patients with thyrotoxicosis (1). While the precise mechanism of the myopathy associated with Graves’ disease is not known, several hypotheses are reported. Some patients show myoskeletal disorders from an autoimmune mechanism. One of the most important states is disorder of neuromuscular junction, observed in the patients with myasthenia gravis and Eaton-Lambert syndrome. It is reported that the anti-acetylcholine receptor antibodies that occur in myasthenia gravis are comparable to the anti-TSH receptor antibodies found in Graves’ disease. It has been found that thyroglobulin and acetylcholinesterase share epitopes recognized by B cells, and that antibodies to either antigen cross-react with the other. Some patients who suffer from non-organ-specific autoimmune diseases, such as systemic lupus erythematosus (SLE) and progressive systemic sclerosis (PSS), show inflammatory damages of neural junctions in central nervous system, resulting in the neurological asthenia, which is accentuated in the presence of Graves’ hyperthyroidism (2). However, whether the anti-TSH receptor antibodies, immunoglobulins which interact not only with TSH receptor but also with other components of nervous system, directly affect the neuronal and neuro-muscular junction is not known (3). Another mechanism of abnormal muscle function is a setting disorder of cell membrane potential, which comes from an abnormal electrolyte metabolism in the patients with Graves’ disease. In Asia, periodic paralysis observed in patients with Graves’ disease is lmore common (4). It has been speculated that the augmentation of synthesis of membrane Na⁺-K⁺ activated ATPase is related to the mechanism of paralytic myopathy. However, the exact mechanism of this type of myopathy is not certain(5). Some patients with Graves’ hyperthyroidism show hypercalcemia and hypomagnesemia. These electrolyte disorders may also be related to the occurrence of muscle weakness and myopathy through the disturbance of cell membrane potential setting. However, the patients who have abnormal levels of these electrolytes do not necessarily show myopathy. Thus, the mechanism of this myopathy could be induced by the combination of other factors which are generated in Graves’ hyperthyroidism.

As is well known, neurological disturbances are frequently observed in patients with thyrotoxicosis. Myopathy, independent from neurological disorder, also is known as one of the symptoms of thyrotoxicosis. Noto and his coworkers reported a case with dysphagia associated with thyrotoxicosis (6). They speculated that this symptom is thyroid hormone dependent but does not depend on the neurological or electrolyte disorders, because the symptom is dramatically improved by treatment with thimazole, during which the serum levels of thyroid hormone are decreased without changes in electrolyte metabolism. Severe myopathy resulting in cardiac and respiratory episodes can often be observed in certain patients with marked disorders of serum levels of electrolyte. In contrast, this severe myopathy is not frequent in patients who do not show electrolyte abnormalities (7). The authors supposed that the symptom is accentuated by the presence of basic multiple risk factors for stroke including age, hypertension, atrial fibrillation and lacunar infarctions in the past. This suggestion is clinically important because the prominent thyrotoxic myopathy may clearly emerge by the presence of latent hypoxic state in the central nervous system. Graves’ hyperthyroidism is clinically found not only in young but also in the aged subjects, and the number of aged patients who have mild cerebral hypoxia without magnified symptoms. In these subjects, the focus of hypoxic lesion is not confirmed by CT or MRI scan. The report of Noto and his coworkers indicates that not only dysphagia but also circulatory and respiratory accidents could potentially be introduced in the aged patients with Graves’ hyperthyroidism.

The relationship between hypoxia in the central nervous system and thyrotoxic myopathy is not certain. As is observed in patients with hyperthyroidism, the hypersensitive state is common. Particularly, the sensitivity in the autonomous nervous system is increased. Not only mental irritability (including anxiety) but also excess sweating, tachycardia, tremor, and accelerated bowel movement are frequently observed in these patients. The disorders which are similar to hypersensitivities found in thyrotoxicosis are also observed in patients with severe hypoxia in the central nervous system. The combination of mild hypoxia in the central nervous system with hypersensitivity induced by hyperthyroidism may permissively accelerate the symptoms. As suggested by Noto and his coworkers, it should be emphasized that possible hyperthyroidism must be considered in patients with an unexplained neuro-muscular abnormal state in aged people, even though the clinical manifestation could be identified as a result of a minor cerebral hypoxic event alone.

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References