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Thymoma-Associated Paraneoplastic Myositis, Presenting with Rapidly Progressive Muscle Contractures

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Dear Editor,

Thymic malignancy is associated with paraneoplastic neurological syndromes (PNSs). Myasthenia gravis (MG) is the most common PNS, and some thymomatous patients develop MG (25–40%) or paraneoplastic myositis (0.5–9%), which usually coexists with MG.[1,2] MG and myositis mostly occur simultaneously, or myositis develops later in myasthenic patients.[3] Here we report an atypical case of thymoma-associated paraneoplastic myositis presenting with rapidly progressive distal muscle contracture without apparent clinical weakness or symptoms of MG.

A 45-year-old female had developed painful swelling in her forearms without preceding trauma or infection 1 month previously. Two days later she could not extend the right third finger, followed by all fingers and both elbow joints after 1 week. She denied other symptoms such as myalgia or fever. At presentation her range of motion (ROM) was restricted in all metacarpophalangeal, both proximal interphalangeal, elbow, and knee joints, and had plantar flexed feet (Fig. 1A). A neurological examination revealed no remarkable weakness in unaffected muscles and even in affected muscles within acceptable ROM. There was also no evidence of atrophy or neuromyotonia. Serological results were normal except for mildly elevated muscle enzymes [creatinine kinase (CK) at 273 IU/L]. She was seropositive for anti-acethylcholine receptor (AChR) antibody (8.167 nmol/L) and titin (MG titin-30) antibody, but negative for anti-leucine-rich glioma inactivated-1 and anti-contactin-associated protein-2 antibodies.[4] Line immunoassays for myositis-specific antibodies and myositis-associated antibodies only revealed positivity for anti-polymyositis scleroderma antigen (PM/Scl) 75. Needle electromyographic studies revealed myopathic changes in paraspinal, proximal, and distal limb muscles, although a repetitive nerve stimulation test did not reveal any response decrements. MRI of the forearm and lower extremities demonstrated inflammation and fibrosis in all compartment muscles, suggestive of noninfectious inflammatory myositis involving both arms and legs, but no abnormalities were observed in joint capsules or tendons. A muscle biopsy demonstrated primary myopathy, with findings that were similar to but not diagnostic of polymyositis (Fig. 1B). Chest CT revealed a mediastinal mass, and video-assisted thoracoscopic surgery revealed thymoma (WHO type B2). She received intravenous methylprednisolone (500 mg) for 5 days, and 3 months later her ROM had improved considerably and the CK level had normalized to 52 IU/L. She subsequently received intravenous immunoglobulin intermittently as maintenance therapy.

This patient represents an atypical case of thymoma-associated paraneoplastic myositis with double seropositivity for anti-AChR and titin antibodies who presented with rapidly progressive distal muscle contracture without apparent clinical manifestations of myopathy or MG. The association of myositis with MG has been reported in patients with double seropositivity for anti-AChR and striational antibodies, and the presence of the striational antibodies may indicate concurrent MG and myositis.[2,3] However, the pathogenetic role of these

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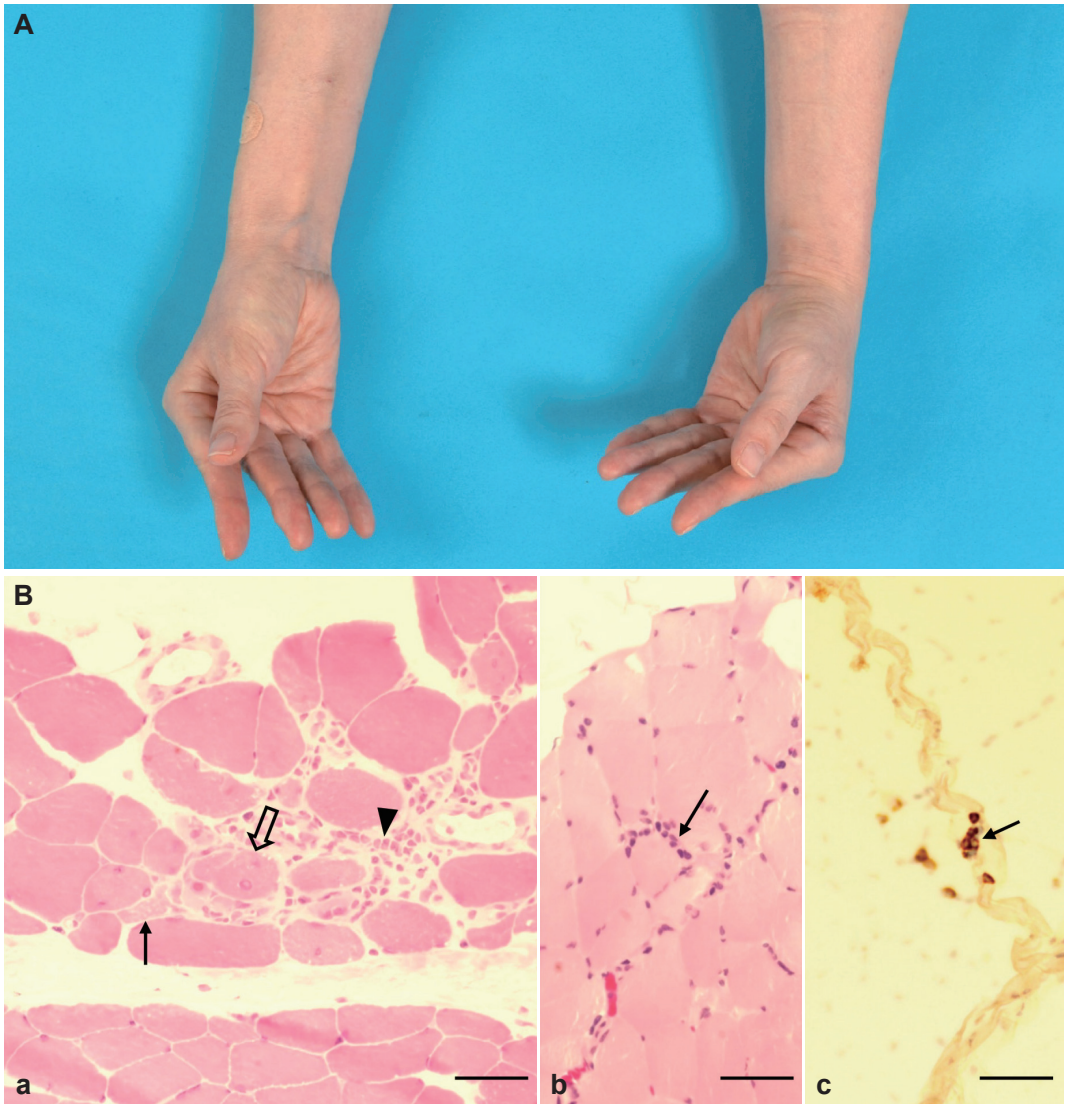

Fig. 1. Clinical and pathologic findings of the patient. A: Photograph of the patient's hands. She had restricted ROMs in all metacarpophalangeal and both proximal interphalangeal joints. B: Pathological findings of the vastus lateralis muscle biopsy. (a) Muscle fiber necrosis (solid arrow) and regeneration (open arrow), and interstitial inflammatory cell infiltration (arrowhead) are evident (HE ×400, frozen section). (b) Necrotic muscle fibers (arrow) with lymphocytes (HE, ×400). (c) Immunohistochemical staining of the same area in panel B (b) reveals predominantly CD8-positive T cells (arrow) (×400). (Scale bar=100 micrometers). ROM: range of motion.

antibodies has not been demonstrated.[3] A recent review of 13 cases with MG and myositis found that all patients had mild-to-moderate MG symptoms, while thymoma was found in 10 patients (8, 1, and 1 with WHO types B2, AB, and B3, respectively), all of whom were positive for anti-RyR1 (ryanodine receptor) and titin antibodies.[3] The extent of muscle involvement varied, including isolated focal, distal predominance, or proximal predominance. MG and myositis occurred simultaneously in 10 patients, and myositis subsequently developed in 2 myasthenic patients. However, MG developed 4 years after the occurrence of myositis in only one patient, who had proximal weakness with high CK (2500 IU/l). This suggests that close observation is needed to recognize newly developing MG, since symptoms of MG might not be obvious and could be missed in myositis.[2] The management of PNS in thymomatous patients includes treatment of the thymoma, immunosuppressive drugs, and symptom-specific management1. Our patient received complete thymectomy for thymoma, immunotherapy, and rehabilitation. This case suggests that unexplained muscle contractures can be atypical symptoms of paraneoplastic myositis, warranting further evaluation and proper management.

This article does not require IRB/IACUC approval because there are no human and animal participants.

Author Contributions

Conceptualization: Jin Hee Kim, Hyemin Jang, Ju-Hong Min. Visualization: Hee Jung Kwon, Yeon-Lim Suh. Writing—original draft: Jin Hee Kim. Writing—review & editing: Ju-Hong Min.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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