A Case of Pleomorphic Carcinoma of the Lung Complicated by Anti-HMGCR Antibody-Positive Necrotizing Myositis

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A 72-year-old man presented with a four-month history of muscle weakness and pain. Serum creatine kinase level was markedly elevated at 22,720 IU/mL, and magnetic resonance imaging revealed high signal intensity in the thigh and upper arm muscles. The presence of an autoantibody against 3-hydroxy-3-methylglutaryl-coA reductase (HMGCR) in the serum confirmed the diagnosis of immune-mediated necrotizing myositis. Subsequent systemic examination revealed primary lung carcinoma in the right lower lobe. Despite the initial corticosteroid therapy, there was no improvement in muscle symptoms. Surgical resection of the tumor, followed by additional intravenous immunoglobulin therapy, controlled necrotizing myositis. The postoperative pathological diagnosis was pleomorphic carcinoma. Despite adjuvant chemotherapy, lung cancer recurred within six months, leading to the patient's death. This case suggests that while treatment of malignancy can be effective for tumor-associated syndromes, such as anti-HMGCR antibody-positive necrotizing myositis, immunosuppressive therapy used for myositis may be associated with an increased risk of cancer recurrence.

Key words: anti-HMGCR antibody-positive necrotizing myositis, pleomorphic carcinoma

INTRODUCTION

Among polymyositis cases, immune-mediated necrotizing myositis is classified as a form of myositis characterized by multiple necrotic and regenerative muscle fibers and complement deposition in muscle pathology [1]. Autoantibodies against signal recognition particles (SRPs) or 3-hydroxy-3-methylglutaryl-coA reductase (HMGCR) are often associated with this condition. While anti-HMGCR antibody-positive necrotizing myositis has been reported to be associated with oral statin therapy [2], 11.5% of patients with necrotizing myositis have malignant tumors [3], and the prognosis for these patients is poor [4]. This report describes a rare case of pleomorphic carcinoma of the lung associated with anti-HMGCR antibody-positive necrotizing myositis. We found that the patient's myositis-related symptoms improved following surgical resection of the primary tumor; however, there was no exacerbation of myositis despite early tumor recurrence.

CASE REPORT

A 72-year-old man with a history of hypertension and depression presented to his primary care physician with a four-month history of proximal muscle weakness in the lower extremities and muscle pain in the upper arms, shoulders, and thighs. The patient had a smoking history of 30 pack-years and no history of dyslipidemia or statin use. Blood chemistry revealed a significantly elevated creatine kinase (CK) level (22,720 IU/L). Myositis was suspected, and he was referred to our hospital for further evaluation.

On examination, his body temperature was 36.5°C, pulse rate was 75/min, and percutaneous capillary oxygen saturation was 99% on room air. He reported myalgia in the proximal limb muscles. Neurological examination of the cranial nerves revealed no abnormalities. Manual muscle testing showed symmetrical weakness (4/5) in the deltoid and iliopsoas muscles, whereas all distal leg muscles were normal. Laboratory results confirmed an elevated serum concentration of CK (19,533 IU/L), aldolase (163.1 IU/L), and an increased erythrocyte sedimentation rate of 32 mm/h. Magnetic resonance imaging revealed high-intensity short TI inversion recovery sequences in the deltoid, infraspinatus, and quadriceps femoris muscles, strongly suggesting myositis (Fig. 1A, B). Serologic testing for myositis-specific autoantibodies was positive for anti-HMGCR antibody but negative for anti-SRP, anti-aminoacyl-tRNA synthetase, anti-transcription intermediary factor 1 gamma, and anti-Mi-2 antibodies. Based on clinical, radiological, and serologic findings, the patient was diagnosed with anti-HMGCR antibody-positive necrotizing myositis. Concurrently, chest computed tomography revealed a 2-cm nodule in the

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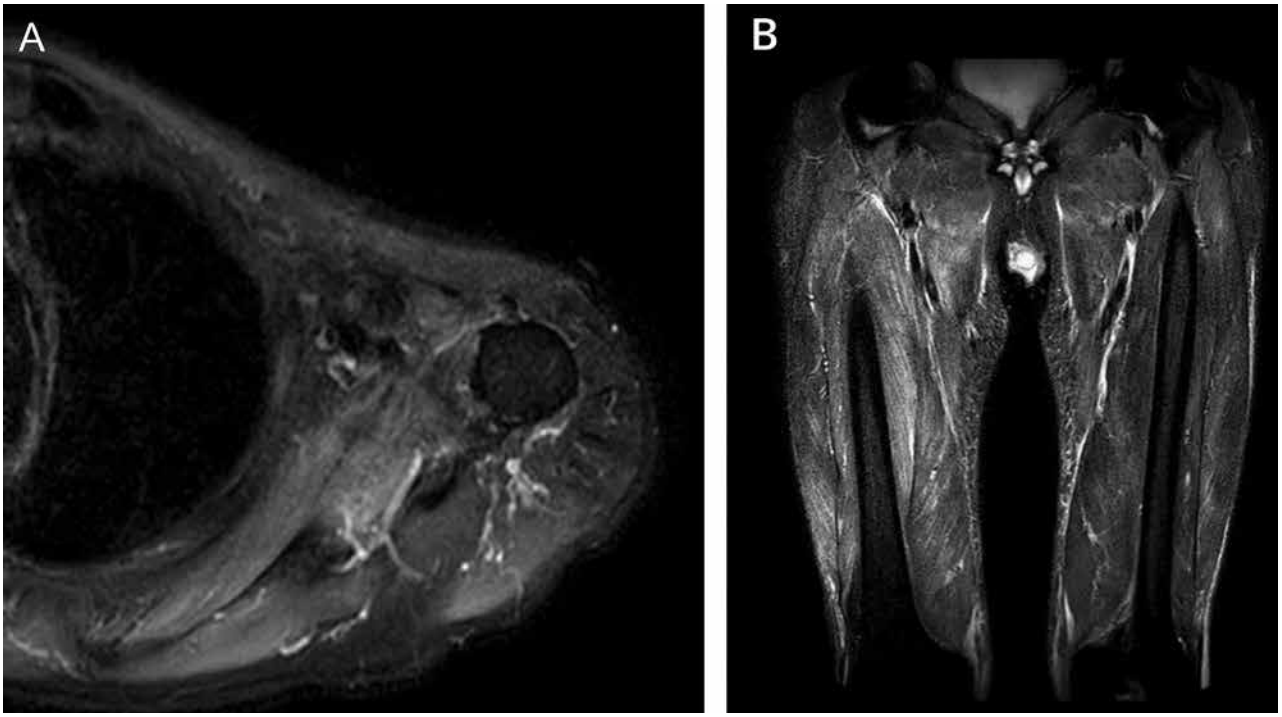

Fig. 1 Short TI Inversion Recovery (STIR) sequences show high signal intensity in the muscle groups from the left shoulder joint to the upper arm (A) and in the left thigh (B).

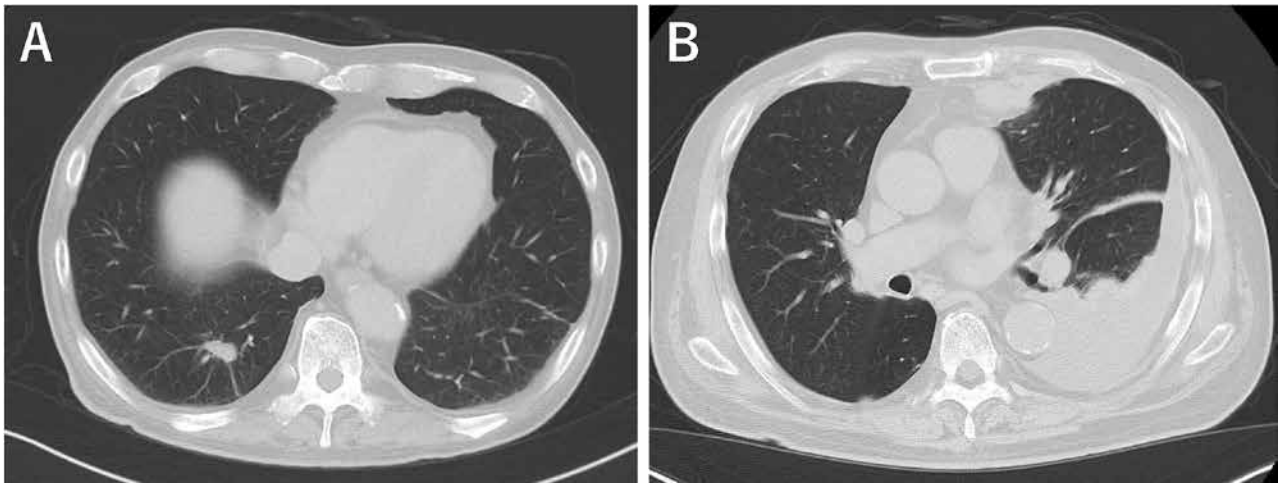

Fig. 2 Chest computed tomography findings at the time of lung cancer diagnosis (A) and at the time of recurrence (B).

lower lobe of the right lung (Fig. 2A). Bronchoscopy was performed, and pathological examination confirmed lung carcinoma with no detectable driver mutations; the tumor proportion score for programmed cell death ligand 1 was 60%. Subsequent whole-body evaluation showed no evidence of metastasis, resulting in clinical stage T1bN0M0.

Intravenous methylprednisolone (1,000 mg/day) was administered for three days, followed by oral prednisolone (PSL) at 60 mg/day (1 mg/kg/day), which was tapered every 2–4 weeks. Despite these treatments, no improvement in muscle symptoms was observed; however, serum CK level decreased. To facilitate surgical resection of the lung tumor, the PSL dose was reduced to 10 mg/day, and intravenous immunoglobulin (IVIg) was initiated, anticipating symptomatic improvement with tumor resection, which resulted in improvement of muscle weakness. The patient underwent right lower lobectomy, and the postoperative pathological diagnosis was pleomorphic carcinoma of the lung at pathological stage T1bN0M0 (IA2). Following surgery, there was further improvement in myositis symptoms with normalization of serum CK and aldolase levels. Necrotizing myositis remained controlled with PSL at 10 mg/day without additional IVIg.

The patient underwent postoperative adjuvant platinum-based chemotherapy. Six months after surgery, a left pleural effusion was observed (Fig. 2B). Pleural biopsy confirmed pleural dissemination of pleomorphic carcinoma. Interestingly, there was no recurrence of myositis symptoms such as myalgia, muscle weakness, or elevated serum CK levels, despite tumor recurrence. At the time of tumor recurrence, the patient's overall clinical status was significantly poor, requiring palliative care due to respiratory failure. Consequently, further anti-cancer therapy, including immune checkpoint inhibitors, was deemed inappropriate. The patient died 13 months after being diagnosed with necrotizing

myositis due to respiratory failure and systemic deterioration caused by cancer progression.

DISCUSSION

Here, we present a rare case of anti-HMGCR antibody-positive necrotizing myositis associated with pulmonary pleomorphic carcinoma. Necrotizing myositis significantly improved after IVIg administration and surgical resection of the primary tumor; however, we did not observe exacerbation of myositis upon cancer recurrence. This case is characterized by the entire clinical course, from the diagnosis of cancer associated with HMGCR antibody-positive myositis to death, and by its rapid recurrence and progression leading to death shortly after surgery.

The rate of malignancy associated with necrotizing myositis was higher in anti-HMGCR antibody-positive cases (17.3%) than in anti-SRP antibody-positive cases (8.1%) [3]. These findings suggest a specific link between anti-HMGCR antibodies and cancer development. Studies have shown that HMGCR expression is higher in tumor tissues than in normal tissues, and a correlation has been reported between tumor progression and anti-HMGCR antibody titers [5]. These findings support the hypothesis that anti-HMGCR antibodies, driven by HMGCR expression in tumors, contribute to paraneoplastic pathology. Therefore, cancer screening is strongly recommended for patients with anti-HMGCR antibody-positive myositis [6, 7]. In our case, cancer screening was performed at the time of diagnosis of HMGCR-positive myositis, leading to the diagnosis of early-stage lung cancer. Many reports have suggested an association between cancer and myositis onset. However, it remains unclear whether myositis symptoms worsen with cancer recurrence. While some reports indicate that myositis symptoms worsen during recurrence [5, 8], our patient did not show exacerbation of myositis at recurrence, either in subjective symptoms or laboratory findings, despite the recurrence of pulmonary pleomorphic carcinoma. This suggests that although cancer may be a causative factor, it may not be an aggravating factor for myopathy. Further case studies are required to clarify this complex relationship.

Although the patient had stage IA2, early-stage lung cancer, rapid recurrence within six months of surgery and adjuvant chemotherapy, followed by swift progression to death, may have been influenced by pleomorphic carcinoma itself [9]. Pleomorphic carcinoma with an adenocarcinoma component may have an increased risk of recurrence [10]; however, immunosuppressive therapy for necrotizing myositis may hinder tumor immunity. Immunosuppression using corticosteroids is a known risk for tumor progression [11]. Although there are no clear reports of IVIg exacerbating cancer, it may have influenced tumor progression in this case. The appropriate management of immune-mediated necrotizing myositis with co-occurring cancers remains challenging. Additionally, the efficacy of immune checkpoint inhibitors has been reported in pleomorphic carcinoma [12]. In the present case, although anticancer therapy was considered at the time of recurrence, the patient's rapid deterioration prevented its use. Although there are no reports of immune checkpoint inhibitor administration for cancer complicated by necrotizing myositis, these agents are generally considered difficult to administer because of the high risk of immune-related adverse events.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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