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CASE REPORT

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Immune checkpoint inhibitor therapy in a patient with small cell lung cancer and anti-transcriptional intermediary factor 1-γ antibody-positive dermatomyositis: A case report

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Abstract

Autoimmune diseases (ADs) are closely related to cancers; 30% of dermatomyositis (DM) cases are associated with malignancy. In lung cancer patients accompanied by DM, the most frequent cancer type is small cell lung cancer (SCLC). Anti-transcriptional intermediary factor 1 γ (anti-TIF1γ) antibody is a promising marker for the assessment of cancer risk in DM patients. The recent use of immune checkpoint inhibitors (ICIs) for extensive-stage SCLC has improved patient outcomes. However, clinical trials of ICI excluded most patients with ADs because of the increased risk of toxicity. Nevertheless, recent evidences suggest that ICI may be appropriate for AD patients. A 76-year-old man diagnosed with extensive-stage SCLC and anti–TIF1γ Ab-positive DM developed limb weakness and typical skin manifestations of DM. Positron emission tomography-computed tomography showed diffuse uptake in all muscles. The results of a nerve conduction study and electromyography were consistent with acute myopathy. Electron microscopy showed tubuloreticular inclusions in endothelial cells. He was treated with corticosteroids for DM and chemotherapy with atezolizumab for SCLC. Despite concerns regarding the use of ICI because of DM, atezolizumab was administered under close observation. After treatment, tumor size decreased and his symptoms improved significantly. We believe that the response of SCLC to chemotherapy including ICI, had a positive effect on the improvement of DM. Clinicians should consider ICIs for SCLC patients with DM and carefully monitor the patient's symptoms during treatment.

KEYWORDS
anti–TIF1-γ antibody, dermatomyositis, immune checkpoint inhibitor, small cell lung cancer

INTRODUCTION

Autoimmune diseases (ADs) increase the risk of cancer by causing chronic inflammation, and conversely, cancers can cause ADs.[1,2] A total of 30% of dermatomyositis (DM), an idiopathic AD, cases are associated with malignancy.[3] DM is diagnosed in patients with typical skin lesions such as Gottron's sign, if three or more of the following symptoms are present: proximal and symmetrical muscle weakness, elevated serum levels of skeletal muscle enzymes, electromyography findings characteristic of myopathy, and evidence of myositis on muscle biopsy.[1,4]

In lung cancer patients accompanied by DM, the most frequent cancer type is small cell lung cancer (SCLC).[5] Immune checkpoint inhibitors (ICIs) for extensive-stage SCLC have improved patient outcomes. However, clinical trials of ICI excluded patients with ADs because of the increased risk of toxicity. Nevertheless, recent evidences suggest that ICI can be considered in patients with ADs.[2,6]

Yoojoo Kim and Dongil Park are co-first authors.

Anti-transcriptional intermediary factor 1 γ (anti-TIF1γ) antibody is a promising marker for the assessment of cancer risk in DM patients.[7] TIF1γ acts as a tumor suppressor and regulator of cellular proliferation, through the regulation of the transforming growth factor β (TGF-β) and Smad pathways.[8] Previous studies have confirmed an increased risk of cancer-associated dermatomyositis (CAD) in the presence of anti-TIF1γ autoantibody.[9–12] Clinicians should screen patients with anti-TIF1γ autoantibody for cancers even in the absence of suspicious symptoms.[13]

Although the incidence of immune-related adverse events (irAEs) is relatively high in patients with ADs, these irAEs are manageable in most cases.[14] Therefore, clinicians should carefully balance the risk of irAEs and the benefits of ICI for each patient.[2] Here, we present the case of a patient with extensive-stage SCLC and anti-TIF1γ antibody-associated DM who received chemotherapy including atezolizumab.

CASE REPORT

A 76-year-old man presented with dyspnea on exertion, productive cough, dysphagia, and neck pain. He was an ex-smoker with a 50-pack-year smoking history. The right cervical lymph nodes (LNs) were found to be enlarged. Chest computed tomography (CT) revealed a lung mass contacting the pericardium and multiple enlarged LNs in the neck and chest.

Excisional biopsy of the right-sided level III LN showed metastatic carcinoma suggestive of extensive-stage SCLC. During disease staging, his symptoms worsened rapidly. He also developed limb weakness and an inability to walk. Positron emission tomography (PET)-CT showed diffuse uptake in all muscles (Figure 1), and the laboratory investigations revealed elevated serum muscle enzymes, including creatine kinase (CK) (2122 U/L) and lactate dehydrogenase (LDH, 1382 U/L). A nerve conduction study and electromyography showed findings consistent with acute myopathy. A videofluoroscopic swallowing study was performed to assess upper gastrointestinal tract involvement and revealed a delayed swallowing reflex and severely impaired swallowing ability. He had an erythematous rash around his eyes, cheeks, and nasal bridge and hardened areas of skin on the finger joints (Figure 2(a),(b)). He was referred to a rheumatologist because of the suspicion of a systemic rheumatic disease, for which he underwent incisional biopsy of the left biceps brachii and anti-TIF1γ antibody testing. The biopsy findings were compatible with DM (Figure 3(a),(b)), and anti-TIF1γ antibodies were positive. He was diagnosed with cancer-associated dermatomyositis, a paraneoplastic syndrome caused by the SCLC.

He was treated with corticosteroids for DM and chemotherapy with carboplatin, etoposide, and atezolizumab for SCLC. Because of concomitant DM, we had concerns regarding the use of ICI. The rheumatologist suggested that the course of DM depends on the prognosis of the SCLC. Therefore, chemotherapy including atezolizumab was administered under close observation. After two cycles of chemotherapy with corticosteroids, the tumor size decreased (Figure 4(a)–(h)), and the DM-associated skin manifestations improved significantly (Figure 2(a),(b)). Muscle-related symptoms showed remarkable improvement and the

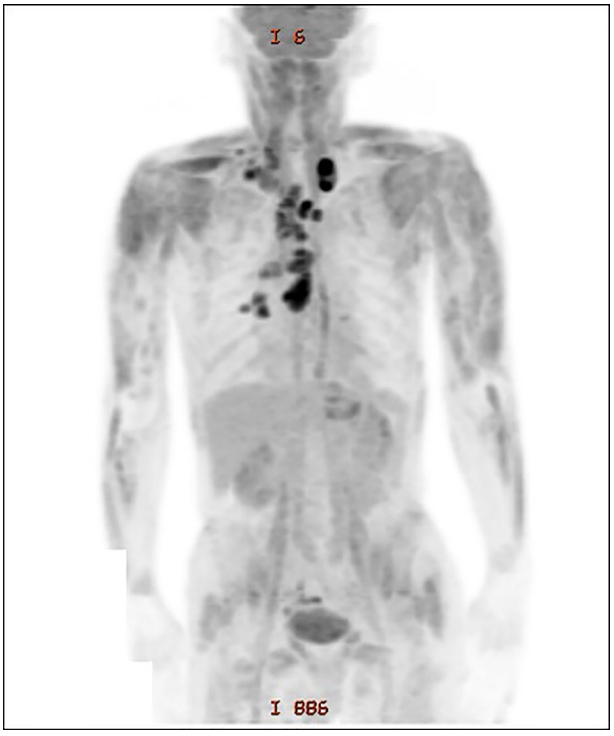

FIGURE 1 Initial positron emission tomography-computed tomography (PET-CT) scan. The PET-CT scan showed evidence of small cell lung cancer, mediastinal, and neck lymph node metastasis, and major and diffuse uptake in all muscles

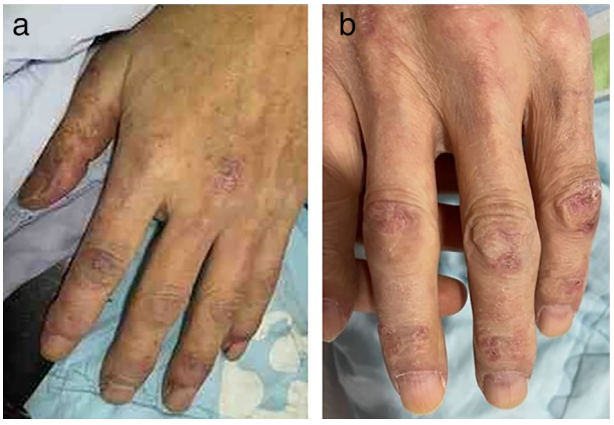

FIGURE 2 Representative photographs of hands of the patient, on hospital admission and after chemotherapy. (a) initial photograph of hands showing Gottron's papules; (b) healing of Gottron's papules after chemotherapy and steroid treatment

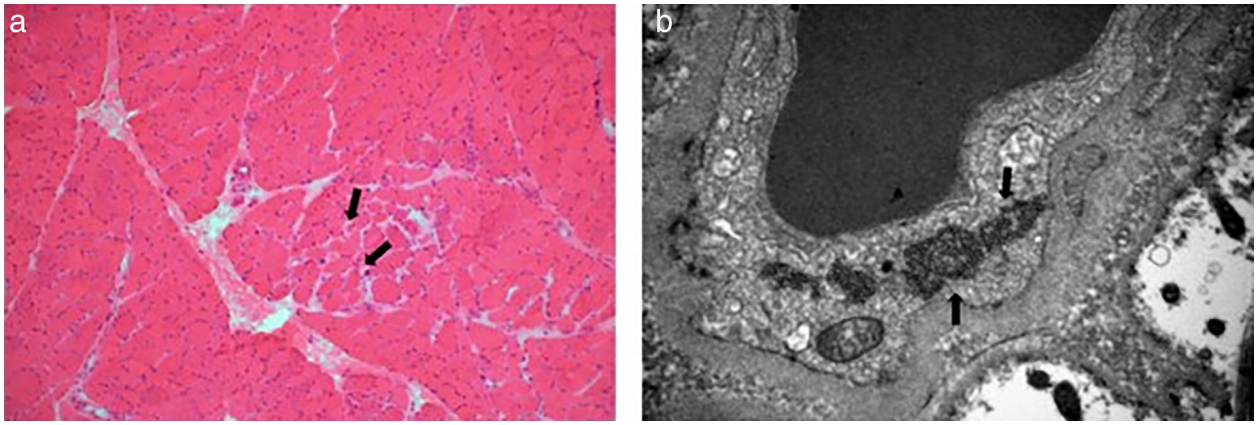

FIGURE 3 Pathological findings of biopsy of biceps brachii. (a) Hematoxylin and eosin staining showed some scattered atrophic muscle fibers (arrow) and occasional internal nuclei (100×); (b) electron microscopy showing tubuloreticular inclusions in endothelial cells, suggestive of dermatomyositis (arrow) (30,000×)

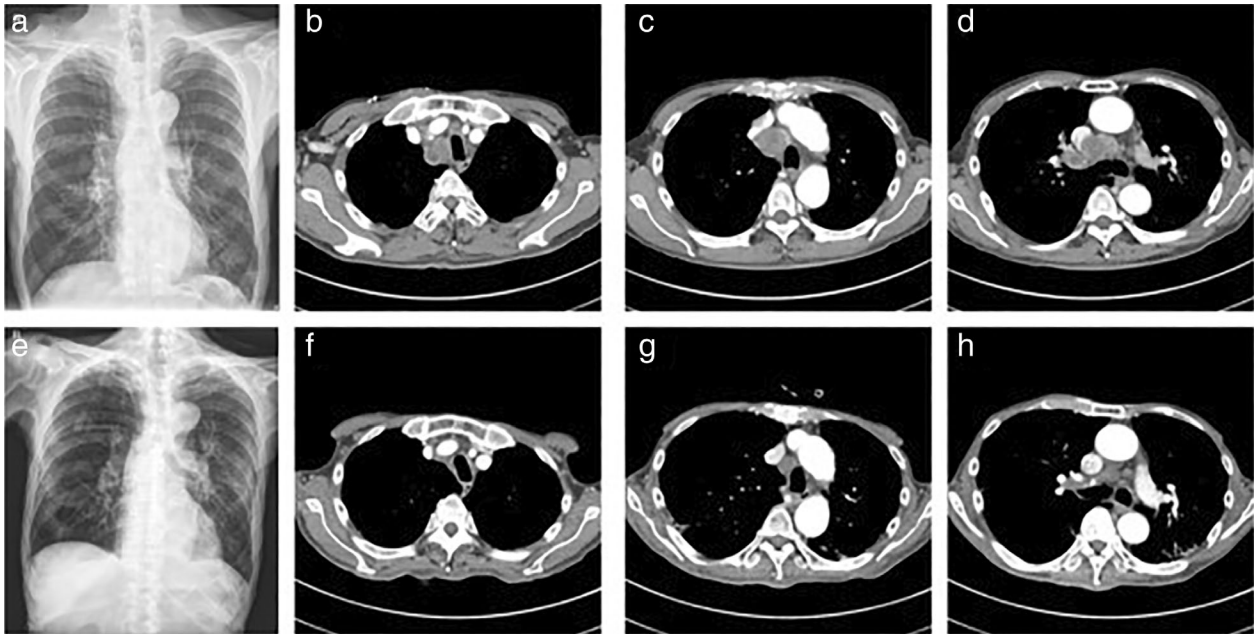

FIGURE 4 The posterioanterior (PA) chest X-ray and chest computed tomography (CT) scan. (a) Initial chest PA showed mediastinal widening and thickened paratracheal stripe; (b)–(d) initial chest CT scan revealed enlarged mediastinal lymph nodes (LNs) and mass; (e) chest PA after two cycles of chemotherapy demonstrated decreased sizes of LN and mass; (f)–(h) follow-up CT scan showed remarkable response of tumor after chemotherapy

serum CK level was normalized. Moreover, there was no significant irAE.

DISCUSSION

Patients with CAD have worse symptoms and a poorer prognosis.[8] They have a distinct autoantibody pattern, with negative DM-specific autoantibody and positive anti-TIF1γ antibody, suggesting that anti–TIF1γ plays a role in the development of CAD.[3,15]

The main treatment of DM is corticosteroids,[16] but treatment of malignancy also improves the symptoms of paraneoplastic DM.[17,18] There are concerns that ICI may exacerbate ADs because most patients with ADs were excluded from clinical studies of immunotherapy. However, recent cases show that the combination therapy with ICI and chemotherapy significantly improve the survival of SCLC patients,[19] and the prognosis of DM depends on the treatment response of the underlying malignancy.[20] Therefore, clinicians should consider ICIs for SCLC patients with DM and carefully monitor the patient's symptoms during treatment.

Because this patient was transferred to another hospital after three cycles of treatment for personal reasons, we could not confirm the long-term survival and symptoms. Instead, we presented tumor shrinkage on CT and improvement of symptoms as treatment outcomes, which is a limitation of this study.

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CONFLICT OF INTEREST

Not applicable.

PATIENT CONSENT

All included patients provided written informed consent.

CONSENT FOR PUBLICATION

Written consent to publish this information was obtained from study participant.

DATA AVAILABILITY

Not applicable.

ETHICS APPROVAL

The study was completed and approved by our local ethics review board in accordance with the declaration of Helsinki.

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