Clinical Case Report

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Anti-TIF1γ antibody predicted malignancy of thymic tumor with dermatomyositis as an "autoimmune tumor marker"

A case report

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Abstract

Rationale: An association between inflammatory myopathy and malignancy has been recognized particularly in patients positive for anti-transcription intermediary factor 1γ (TIF1γ) antibody. We report a case of anti-TIF1γ antibody positive dermatomyositis (DM) associated with thymic carcinoma which radiographically mimicked benign tumor.

Patient concerns: A 72-year-old man presented typical characteristic cutaneous manifestations and proximal muscle weakness with elevated levels of myogenic enzymes. An anterior mediastinal tumor was detected by computed tomography (CT) scan and radiographically assessed to be benign with distinct borders and little enhancement.

Diagnoses: DM with anti-TIF1γ antibody and thymic carcinoma.

Interventions: Thymic carcinoma was completely resected by surgery. DM was induced into remission with glucocorticoid treatment.

Outcomes: The serum level of myogenic enzyme remained within normal range under low-dose glucocorticoid maintenance. No evidence of carcinoma recurrence with CT scan was observed at 1-year follow up.

Lessons: The present case indicated that anti-TIF1γ antibody would play a role as the "autoimmune tumor marker" in patients with inflammatory myopathy.

Abbreviations: CK = creatine kinase, CT = computed tomography, DM = dermatomyositis, TIF1γ = transcription intermediary factor 1γ.

Keywords: anti-TIF1γ antibody, dermatomyositis, malignancy

1. Introduction

Dermatomyositis (DM) is an idiopathic inflammatory myopathy, characterized by proximal skeletal muscle weakness, and specific cutaneous manifestations. High prevalence of malignant diseases in patients with inflammatory myopathy has been well recognized.[1–3] DM is diagnosed based on the classification criteria of Bohan and Peter. It includes clinical examinations such as myogenic enzymes, electromyography, and muscle biopsy in addition to clinical manifestations.[4,5] Recently a number of myositis-specific autoantibodies related with clinical characteristics of DM have been reported.[6] Among them, anti-transcription intermediary factor 1γ (TIF1γ) antibody is more prevalent in DM patients with malignancy than those without.[7,8]

Thymic tumors including thymoma and thymic carcinoma are diagnosed by histology. Thymic carcinomas show cytologic atypia, invasive margins, and loss of an organotypic appearance.[9] We report a case of anti-TIF1γ antibody positive DM associated with thymic carcinoma which radiographically mimicked a benign tumor.

2. Case report

A 72-year-old Japanese man presented with painful skin rashes on knuckles and eyelids. His medical history was notable for a 15-year history of diabetes mellitus and a stroke 5 years ago. His family history was unremarkable. Three months after his first visit, an elevated serum level of creatine kinase (CK) was detected in outpatient clinic and he was admitted to a nearby hospital. On physical examination, the following were noted: proximal muscle

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Written informed consent was obtained from the patient.

The authors have no conflicts of interest to disclose.

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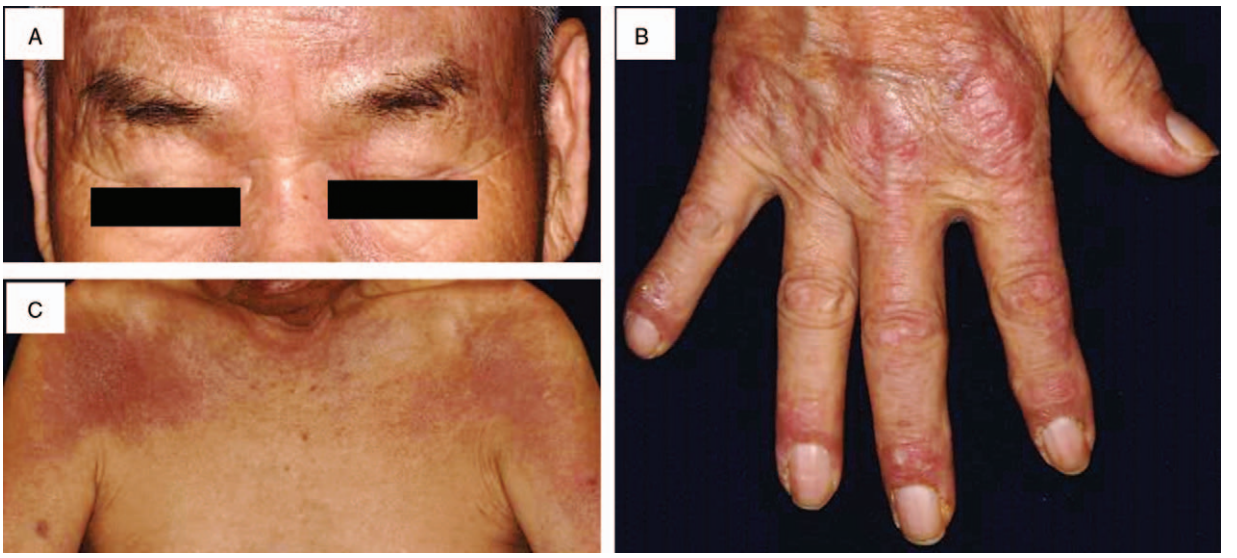

Figure 1. Cutaneous manifestations of patient. (A) Heliotrope rash over the upper eyelids. (B) Gottron's papules overlying knuckles. (C) Erythematous rash on shoulders.

weakness, heliotrope rash of the eyelids, erythematous rashes on elbows, shoulders, and right thigh, and Gottron's sign over his knuckles (Fig. 1). Laboratory tests showed elevated serum levels of CK (1576 IU/L) and aldolase (8.2 U/L), and the antinuclear antibody was positive (1:1280, speckled and nucleolar pattern). He was diagnosed with DM and was referred to our hospital for further investigation and treatment. While autoantibodies including anti-aminoacyl tRNA synthetase antibody, anti-Mi-2 antibody, and anti-melanoma differentiation-associated gene 5 antibodies were negative, anti-TIF1γ antibody was positive (107 indexes). Magnetic resonance images showed high-intensity areas on whole-body muscles with short-tau inversion recovery images, suggesting the presence of muscular inflammation. A skin biopsy specimen revealed mononuclear cell infiltrations around vessels at the dermal-epidermal interface. The result of electromyogram of the proximal muscles was compatible with inflammatory myopathy.

Computed tomography (CT) scans showed an anterior mediastinal mass with diameter of 23 mm. It had homogenous density with little contrast effect and well-defined borders (Fig. 2), leading to the radiographic diagnosis as non-invasive thymoma or thymic cyst. Knowing that anti-TIF1γ antibody has been related to malignancies in DM patients, we performed thoracoscopic thymectomy to further confirm the diagnosis. Based on the

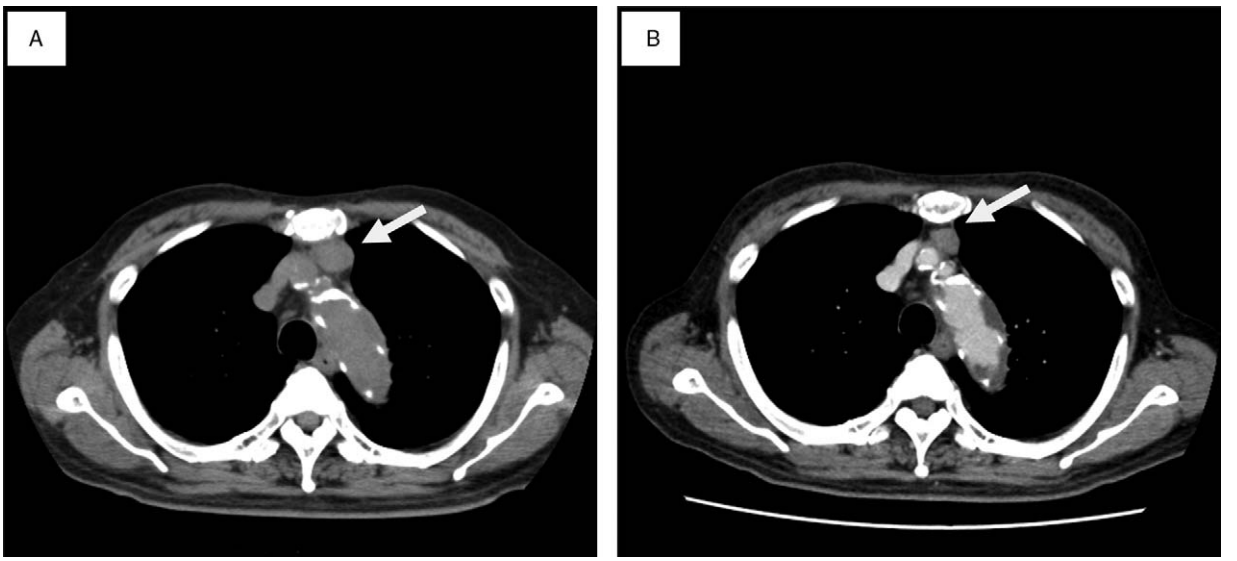

Figure 2. Chest computed tomography scans showed a mass in anterior mediastinum (arrows) (A; plain, B; enhanced). It had well-defined borders with little contrast effect.

histologic findings, this tumor was ultimately diagnosed as squamous cell carcinoma of the thymus. Two weeks after the surgery, oral glucocorticoid (1.0 mg/kg/day) was administered followed by immediate disappearance of his skin involvement and by gradual improvement in muscle weakness. Under low-dose glucocorticoid maintenance, there is no feature of disease relapse at least for 1 year.

3. Discussion

The prevalence of malignancy in patients with DM has been estimated approximately 30%. [2,10,11] A type and site of cancers occurring in DM patients are mostly comparable in the general population. [10,12] Although DM are usually treated with combination of glucocorticoid and immunosuppressive agents, some cases of paraneoplastic DM achieved remission without such treatment after the cure of underlying malignancy.[13] In our case, however, immunosuppressive treatment was needed, indicating that paraneoplastic immune response had been established and did not need sustained antigen presentation from cancer cells. Anti-TIF1γ antibody is identified in about 20% of adult DM patients.[6,14,15] Among them, 60% to 80% have malignant diseases. [12] Despite such strong correlation between anti-TIF1γ antibody, malignancy, and myositis, the pathogenesis of the interaction between them remains unclear. TIF1γ has been known as a tumor suppressor by preventing TGF-β pathway, [16,17] while overexpression of TIF1γ has been reported to be associated with oncogenesis and poor prognosis in some cancers.[18,19] It has been hypothesized that mutations of TIF1γ genes in tumors provoke a specific anti-tumoral immune response which secondarily causes a cross-reactivity to the target organs of myositis, including muscle, and skin.[12]

The occurrence of thymic carcinoma is extremely rare in DM[20] and, vice versa, the incidence of paraneoplastic syndrome with thymic carcinoma is very low.[20,21] The prognosis of thymic carcinoma is, however, obviously poorer compared with that of thymoma. Surgery should be considered in the management of thymic carcinoma. Complete resection is extremely important, and delay of diagnosis would result in poor outcome.[22] In addition, the diagnostic accuracy of radiography for thymic tumors is advanced but still has limitation to some extent.[23]

In our case combined assessment using anti-TIF1γ antibody and conventional screening for malignancy, although the latter had failed to present malignant aspect, ultimately lead to curative treatment. Anti-TIF1γ antibody played a role as "autoimmune tumor marker" in the management of our patient.

Author contributions

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Writing – review & editing: Yuichiro Fujieda, Takuya Kawamura, Nobuya Abe, Shuhei Shimoyama, Michihito Kono, Masaru Kato, Shinsuke Yasuda, Tatsuya Atsumi.

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