

SHORT COMMUNICATION

TIF1 γ -overexpressing, Highly Progressive Endometrial Carcinoma in a Patient with Dermatomyositis Positive for Malignancy-associated Anti-p155/140 Autoantibody

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Anti-p155/140 autoantibody-positive dermatomyositis is a distinct subgroup with internal malignancies and characteristic clinical features, e.g. prominent cutaneous manifestation and lack of interstitial pneumonia (1). The target antigens of p155/140 have recently been identified as transcriptional intermediary factor 1 γ (TIF1 γ) and TIF1 α , respectively (2). It is thus speculated that TIF1 γ is expressed in malignant tumour cells, leading to the development of anti-p155/140 autoantibody and the resultant occurrence of dermatomyositis. We report here the first case of anti-p155/140 antibody-positive dermatomyositis that shows the coexistence of a TIF1 γ -overexpressing malignant neoplasm.

CASE REPORT

A 52-year-old woman developed facial and palpebral oedema, erythema on the trunk, muscle weakness, and intermittent fever 2 weeks prior to our initial examination. Gottron's sign was positive and facial and palpebral oedema was observed. Nail-fold bleeding was not found. No swollen superficial lymph nodes were palpable. Serum examination revealed high levels of lactate dehydrogenase (LDH) (495 IU/l; reference values: 200–400 IU/l), C-reactive protein (CRP) (8.13 mg/dl, reference values: <0.1 mg/dl), creatine kinase (CK) (863 IU/l; reference values: 50–200 IU/l), and aldolase (8.6 U/l; reference values: 2.7–7.5 U/l). Antinuclear antibody titre was positive, at 1:40, with a homogeneous and speckled pattern.

The patient was positive for anti-p155/140 autoantibody, which is identical to anti-TIF1 γ autoantibody, as assessed by an immunoprecipitation study performed using extracts of the leukaemia cell line (2). Whole-body enhanced computerized tomography (CT) revealed neither visceral malignancy nor interstitial pneumonia. Head magnetic resonance imaging (MRI) showed no brain tumour. Upper gastrointestinal endoscopy and colonoscopy showed no malignancy. MRI revealed T2 high lesion in the upper arm, suggesting the involvement of muscle due to dermatomyositis. Skin biopsy from an erythematous lesion on the trunk showed a vacuolar change at the epidermal-dermal junction and a band-like infiltrate of lymphocytes in the upper dermis. Muscle biopsy from the quadriceps muscle disclosed

an infiltrate of lymphocytes between muscle fibres. The patient was diagnosed as having dermatomyositis. Because of the positivity of anti-p155/140 autoantibody, the coexistence of a malignancy was suspected, but was not detected at this time.

We started the patient on oral prednisolone, 60 mg daily, which was gradually tapered to 15 mg daily over a period of 9 weeks. The cutaneous manifestation and muscle weakness were improved, and serum LDH, CRP, CK and aldolase were normalized. Two months later, however, the patient had sudden genital bleeding. Endometrial biopsy revealed the presence of invasive endometrial carcinoma. Concomitantly with the tumour growth, the skin rash and facial and palpebral oedema recurred (Fig. 1A), with a high fever and disseminated intravascular coagulation. Total hysterectomy was performed, but lymph node dissection was not performed, due to massive bleeding during the operation. Considering the risk of post-operative complication, the dose of prednisolone (15 mg daily) was not increased. One week after the surgery, the palpebral erythema and oedema was improved dramatically (Fig. 1B). Currently, the patient's skin manifestation has deteriorated again with multiple lung metastases.

DISCUSSION

In our patient, the cutaneous lesions of dermatomyositis fluctuated strikingly along with the growth, removal, and regrowth of endometrial carcinoma. Since anti-

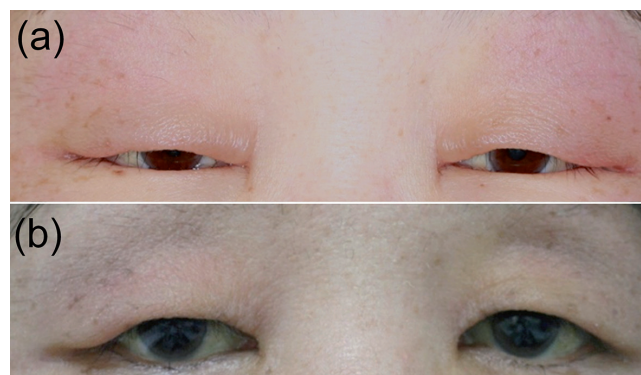


Fig. 1. Clinical features. (a) Severe palpebral oedema before hysterectomy. (b) Improvement in palpebral oedema after hysterectomy.

p155/140 antibody react with TIF1 γ (2), it is possible that TIF1 γ expressed by the endometrial cancer cells induced the autoantibody. Furthermore, TIF1 γ down-regulates Smad4, which inhibits cell proliferation and promotes apoptosis (3). We therefore investigated the expression of TIF1 γ and Smad4 in the patient's endometrial carcinoma by immunohistochemistry with specific antibodies (anti-TIF1 γ and anti-Smad4 rabbit polyclonal antibody, Santa Cruz Biotechnology Inc., CA, USA; 1:50). The tumour cells were positive for TIF1 γ and negative for Smad4 in the nuclei, while the normal endometrial epithelial cells were TIF1 γ ⁻ Smad4⁺ (Fig. 2).

This is the first report to show the presence of a TIF1 γ -bearing neoplasm in anti-p155/140 antibody-positive dermatomyositis. Given the antigenic role of the overexpressed TIF1 γ for the induction of autoantibody, the TIF1 γ ⁺ malignant tumour might be a cause of dermatomyositis. In addition, the TIF1 γ -depressed Smad4 expression might lead to the highly progressive behaviour of the cancer, as reported in colorectal carcinoma showing a correlation of Smad4 loss with

poor prognosis (4). Our finding suggests that TIF1 γ expression in neoplasms not only determines the tumour activity but also causes dermatomyositis.

The authors declare no conflicts of interest.

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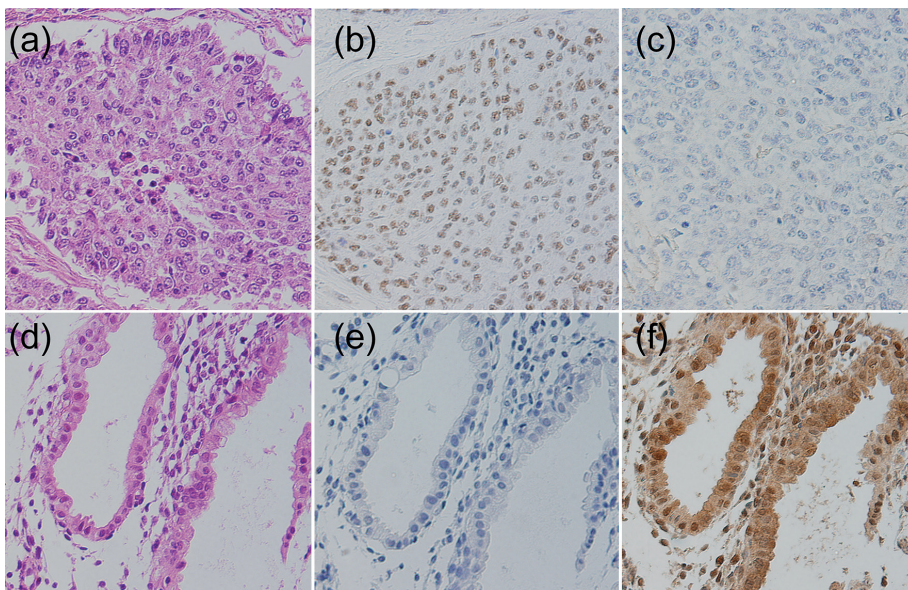


Fig. 2. Histopathology and immunohistochemistry of endometrial carcinoma (original magnification $\times 200$). (a) H&E stain; (b) immunostaining for transcriptional intermediary factor 1 γ (TIF1 γ); (c) immunostaining for Smad4 in the endometrial carcinoma of our case. In our case, TIF1 γ was positive, while Smad4 was negative. (d) HE stain; (e) immunostaining for TIF1 γ ; (f) immunostaining for Smad4 in a normal endometrial tissue of another patient. TIF1 γ was negative, while Smad4 was positive in normal endometrial tissue.