Use of Etanercept in the Treatment of Dermatomyositis: A Case Series

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ABSTRACT. ***Objective.*** To evaluate the efficacy of etanercept, a recombinant human soluble fusion protein of tumor necrosis factor-α (TNF-α) type II receptor and IgG1, in patients with adult dermatomyositis (DM).

Methods. Five patients with active DM were studied. All patients reported muscle weakness and had elevated muscle enzymes creatine kinase and lactate dehydrogenase. Because of lack of response to steroid and cytotoxic therapy, etanercept was given at a dose of 25 mg subcutaneously twice a week for at least 3 months.

Results. All patients experienced an exacerbation of disease, with increase of muscle weakness, elevation of muscle enzyme levels, and unchanged rash. Treatment with etanercept was stopped. After receiving a combination of methotrexate (MTX) and azathioprine, disease manifestations improved in all patients.

Conclusions. In our case series, TNF-α inhibition by etanercept was not effective, suggesting that a broad immunosuppressive therapy is needed to treat DM. (J Rheumatol 2006;33:1802–4)

Key Indexing Terms:
DERMATOMYOSITIS ANTI-TUMOR NECROSIS FACTOR-α ETANERCEPT

Polymyositis/dermatomyositis (PM/DM) is essentially treated with steroids and cytotoxic drugs[1,2].

Tumor necrosis factor-α (TNF-α) may play a role in the pathogenesis of PM/DM. It was found to be overexpressed in muscle from patients with PM/DM and its expression is decreased following steroid therapy, suggesting that TNF-α is a key factor in activating muscle inflammation[3]. Polymorphism in TNF-α-308 promoter region has been found associated with juvenile DM. Children with DM with the TNF-α-308A allele had more prolonged disease and higher production of TNF-α than children with DM with the common TNF-α-308G allele[4].

Recently, response to therapy with TNF-α blockers has been reported in patients with PM/DM[5-7]. We assessed the efficacy of etanercept in a series of our patients with DM.

MATERIALS AND METHODS

Study protocol. All 5 patients had definite DM according to the Bohan and Peter criteria[8]. Muscle biopsy was performed in each patient to confirm diagnosis. Electromyography detected myopathic abnormalities consistent with myositis. All patients were tested for anti-Jo-1 antibody; other myositis specific antibodies were not evaluated. All patients were receiving prednisone and 4 of 5 patients were also taking cytotoxic drugs (Table 1). Therapy was kept stable for more than 3 months before cytotoxic drugs were withdrawn for inefficacy or side effects. After one week wash-out and written informed consent and approval by the Ethics Committee, therapy with 25 mg etanercept subcutaneously (sc) twice a week was given. Muscle enzyme tests were repeated. Proximal muscle strength was assessed by a functional multiple-point scale, scoring from 1-6 for upper limbs and 1-7 for lower limbs, with 0 representing no weakness and 7 representing worst weakness ever[9].

Patient 1. A woman was diagnosed with DM one year before. Treatment with prednisone (1 mg/kg/day) and MTX (15 mg/wk) was ineffective, and therapy with high dose methylprednisolone (1 g/day for 3 days) and cyclophosphamide (1 g at day 4) was initiated. Nevertheless, myositis remained active with proximal muscle weakness and high creatine kinase (CK) levels. Etanercept 25 mg sc twice a week was started and prednisone dose was slowly decreased to 25 mg/day. After 1 month, her disease flared, requiring hospital admission. Etanercept was stopped and the patient began receiving intravenous immunoglobulin (IVIG) infusions (1 g/kg/day for 3 days) every 3 months, azathioprine (100 mg/day), and MTX (15 mg/wk). The patient's condition improved and CK returned to normal levels after 6 months. Prednisone dosage was tapered and ceased after 3 months.

Patient 2. A woman was diagnosed with DM 3 years before. Anti-Jo-1 antibodies were present. She also had hepatitis C virus (HCV) infection and was treated only with prednisone (ranging between 25 and 15 mg/day) without achieving complete remission of her disease. Etanercept 25 mg sc twice a week was started but her disease slowly worsened with increased muscle weakness and CK after 3 months. Etanercept was discontinued and prednisone was increased to 25 mg/day with partial recovery of myositis. Etanercept did not change liver function tests or HCV replication (reverse transcription polymerase chain reaction, RT-PCR, quantitative assay).

Patient 3. A man was diagnosed with DM with Jo-1 antibodies 5 years before. Despite therapy with prednisone (10 mg/day) and MTX (10 mg/wk), DM flared with worsening of muscle strength and rash. Prednisone was increased to 30 mg/day with slight amelioration. Etanercept 25 mg twice a week was added but no improvement of DM was achieved. Etanercept was discontinued and treatment with MTX (15 mg/wk) and azathioprine (100 mg/day) induced gradual recovery from the disease.

Patient 4. A woman was diagnosed with DM 2 years before. Since therapy with prednisone (15 mg/day) and azathioprine (2 mg/kg/day) was ineffective,

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Table 1. Clinical characteristics of patients with DM at study entry. All patients had a rash.

Patient	Age, yr	Sex	Disease Duration, yr	Prednisone, mg/day	Cytotoxic Drug
1	39	F	1	25	MTX (15 mg/wk)
2	59	F	3	15	—
3	72	M	5	30	AZA (100 mg/day)
4	63	F	2	15	AZA (100 mg/day)
5	52	F	4	10	CYS (250 mg/day)

MTX: methotrexate; AZA: azathioprine; CYS: cyclosporine.

etanercept 25 mg twice a week was given. Despite a reduction of CK, lactate dehydrogenase (LDH) increased and the patient complained of more weakness following attempts to reduce prednisone dosage. After 3 months, etanercept was stopped and a combination of MTX (15 mg/wk) and azathioprine (100 mg/day) was effective.

Patient 5. A woman was diagnosed with DM with Jo-1 antibodies 4 years before. Therapy with prednisone (1 mg/kg/day) and MTX (15 mg/wk) induced complete remission of the disease. Prednisone was tapered to 10 mg/day and after 1 year, her disease progressively relapsed and therapy with etanercept 25 mg twice a week was initiated. After further worsening of DM, etanercept was stopped, and treatment with prednisone (15 mg/day), MTX (10 mg/wk), and azathioprine (100 mg/day) was given, with rapid improvement of the disease.

RESULTS

Clinical data for each patient during etanercept therapy are shown in Table 2. CK levels slightly declined only in Patient 4, but in the same patient, LDH levels increased at 3 months. In Patients 1, 2, and 5 CK levels rose, while in Patient 3 they remained stable. Prednisone was not tapered in any patients because attempts to do so led to a flare of myositis. Electromyography did not show any changes with respect to baseline observations.

DISCUSSION

Efficacy of TNF-α blockade, mainly infliximab, has recently been reported in a few cases of PM/DM[5-7].

We assessed the efficacy of etanercept in 5 patients with active DM. Patients could not be defined as steroid resistant because prednisone was not increased to the highest dosage in each case. Therapy with etanercept failed to improve muscle strength, decrease muscle enzymes, ameliorate rash, or spare prednisone intake. Withdrawal of previous cytotoxic drugs might have been unfavorable, but despite that, etanercept therapy cannot be considered effective in our series of patients with DM.

A weakness of our study might be the short treatment duration with etanercept. However, in other reported cases, clinical and biologic responses were observed within a few weeks, and we believe that etanercept therapy should have given some benefit to our patients within 3 months. The discrepancy between our study and previous reports is not entirely clear, but might stimulate a debate on both the treatment and pathophysiology of DM.

Of note, our patients with DM improved after therapy with MTX in combination with azathioprine, and in one case with IVIG, suggesting that TNF-α inhibition by etanercept is not critical in treatment of DM, as reported in juvenile DM[10], and that broad immunosuppressive therapy is required to treat this disease. However, a placebo-controlled randomized trial may resolve the disparate data reported.

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Table 2. Clinical data for patients with DM receiving etanercept therapy. All variables were measured at baseline and at 3 months after etanercept treatment. Muscle weakness was assessed by a functional score (1–6 for upper limbs and 1–7 for lower limbs; 0 = no weakness; 7 = worst weakness ever).

Patient	CK		LDH		Prednisone, mg/day		Muscle Weakness Lower Limbs		Muscle Weakness Upper Limbs	
	Baseline	3 mos	Baseline	3 mos	Baseline	3 mos	Baseline	3 mos	Baseline	3 mos
1	1960	3173	660	775	25	25	3	5	2	4
2	352	655	260	255	15	15	2	3	1	2
3	420	438	220	198	30	30	2	2	2	2
4	385	280	245	440	15	15	2	2	2	2
5	434	1349	190	286	10	15	2	3	2	3

CK: creatine kinase (normal: < 190 U/l); LDH: lactate dehydrogenase (normal: < 220 U/l)

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