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EFFICACY OF INTRAVENOUS IMMUNOGLOBULIN THERAPY IN A CASE OF JUVENILE DERMATOMYOSITIS

To the Editor:

Intravenous immunoglobulin (IVIg) has recently been shown to be an effective treatment for refractary dermatomyositis in children (1-3) and adults. Here we describe another case of Juvenile Dermatomyositis (JD) which improved dramatically after treatment with IVIg that was refractary to corticosteroids and cytotoxic therapy.

A. C. aged 14, a Caucasian female, was first referred to our hospital in January 1993 because of erythema and telangiectasia of the face, upper limbs and trunk associated with a history of asthenia, fever and weight loss for 2 months. Gottron's papules were present on the skin of all fingers. She also presented arthritis of the knee joints and a vasculitis lesion of the chest. The diagnosis of dermatomyositis was confirmed by the demonstration of high levels of serum creatine phosphokine, aldolase and lactate dehydrogenase, hepatic enzymes (GOT 50 U/L, GPT 73 U/L (n.v. up to 39), LDH 648 U/L (n.v. 230-460), CPK 758 U/l (n.v. 24-195), electromyography and muscle biopsy. All the immunological tests carried out (ANA, nDNA, anticardiolipin, ENA, AECA, ANCA) were negative.

The patient was initially treated with prednisone in doses of 1 mg/kg/day for two months, without improvement. Moreover, after one month, the patient developed intolerance to the high doses of corticosteroids (i.e., cutaneous striae on the thighs, disappearance of the menstrual cycle). The laboratory tests showed a progressive rise of hepatic and muscle enzymes (GOT 356 U/L, GPT 490 U/L, LDH 715 U/L) and ESR and PCR. The therapy was supplemented with cyclophosphamide as pulse treatment of 500 mg of cyclophosphamide every 4 weeks for a total of 4 pulses. At this point we started therapy with intravenous immunoglobulins (400 mg/kg/day) on 5 consecutive days every month continuing prednisone in doses of 1 mg/kg/day.

The patient was examined from clinical and immunochemical points of view before starting the infusional therapy with intravenous immunoglobulins and subsequently each month before the infusion.

Clinical improvement was observed during the first 3 cycles. After the 3rd cycle, fever and asthenia disappeared and the cutaneous lesions showed significant improvement. The levels of serum hepatic and muscle enzymes gradually returned within the normal range (GOT 18 U/L, GPT 10 U/L, LDH 302 U/L, CPK 176 U/L) (Table I). At this point the dose of corticosteroids was reduced to 0.5 mg/kg/day.

While we are writing the present report, the patient is still continuing therapy with intravenous immunoglobulins (IVIG) at a dosage of 100 mg/kg once a month and prednisone at the dose of 5 mg/day.

The initial symptoms and the cutaneous lesions have completely disappeared. All the immunochemical tests carried out up to now remained within normal limits.

Intravenous immunoglobulin therapy has emerged over the last decade as a potentially useful immunomodulator in a number of autoimmune or immunomediated diseases (4-6).

How IVIg works is not completely understood. Several mechanisms have been identified and implicated in explaining IVIg's immunomodulatory effects. Interactions between Fc fragments of infused IgG and Fc receptors on immunocompetent cells have been described (7-8). Anti-inflammatory effects of IVIg include an ability to down-regulate cytokine production and dismission by actived marcophages (9). A number of immunomodulatory effects are thought to result from the vast number of anti-idiotypes contained in IVIg preparations.

TABLE I: *Modification of laboratory tests before and after IVIg therapy*

	BEFORE	AFTER
ESR	68 mm	23 mm
GGT	490 U/L	36 U/L
GOT	356 U/L	18 U/L
GPT	490 U/L	10 U/L
LDH	715 U/L	302 U/L
CPK	968 U/L	176 U/L
ALDOLASE	4.08 U/L	3.5 U/L
ANA	NEGATIVE	NEGATIVE
nDNA	NEGATIVE	NEGATIVE
ENA	NEGATIVE	NEGATIVE
JO1	NEGATIVE	NEGATIVE
PM1	NEGATIVE	NEGATIVE
PM2	NEGATIVE	NEGATIVE
ACA	NEGATIVE	NEGATIVE
aCL	NEGATIVE	NEGATIVE

Anti-idiotypes may be directed against the recipient autoantibodies (10-11) involved in the pathogenesis of many autoimmune diseases including antiplatelet, antineutrophil cytoplasm (12) and anticardiolipin. Anti-idiotypic antibodies may also bind and down regulate the B-cell receptor for antigen thus decreasing autoantibody production. Anti-idiotypes may also influence the function of T-cells resulting in an activation or suppression of their activity (13). There is also evidence that the effects of IVIg are not solely related to the passive transfer of blocking IgG but reflect active and long-standing immunomodulation (14).

At present the primary antibody immunodeficiencies, immune thrombocytopenic purpura and Kawasaki's syndrome are the conditions for which there is a proven role for IVIg use. In other autoimmune disorders the therapy also appears to be effective but the studies reported to date contain small numbers of patients and most have been uncontrolled. Although we are aware of the fact that the clinical improvement could be ascribed to a delayed effect of steroids and cyclophosphamide as well as to the natural fluctuation of the disease, we do believe that the case presented is a further demonstration of the efficacy of IVIg also in JD with severe systemic vasculitis. As a matter of fact the Ig therapy was started 1 month after the last subministration of cyclophosphamide and the patient still remains in remission after 24 months of Ig treatment, now reduced to 100 mg/kg once a month. Despite the high cost of the treatment, we suggest that IVIg should be used more frequently in autoimmune disorders of young patients because this treatment is safer than the conventional immunosuppressive therapy. It is clear, however, that there is a need for well-designed controlled trials also focused on establishing the optimal dosage in order to reduce the costs of the therapy.

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ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES IN FAMILIAL MEDITERRANEAN FEVER

To the Editor:

Familial Mediterranean Fever (FMF) is a genetic disease of unknown aetiology characterized by recurrent episodes of fever, polyserositis, arthritis and erythematous skin lesions (1,2). An inflammatory reaction occurs during an acute attack, and the serum levels of acute phase reactants including ESR, C-reactive protein and fibrinogen increase. Despite extensive studies, the aetiology and pathogenesis of FMF remained obscure. Because of clinical resemblance between FMF and some autoimmune diseases such as systemic lupus erythematosus (SLE), many clinicians investigated and suggested an autoimmune mechanism in this disease (3,4). In addition, serum autoantibodies have been found in FMF patients (4).

The clinical relevance of anti-neutrophil cytoplasmic autoantibodies (ANCA) is well established in the diagnosis and management of patients with necrotizing vasculitis and glomerulonephritis (5). Perinuclear staining ANCA (pANCA) has been recognized in patients with inflammatory bowel disease (6). The most important target antigen of pANCA is myeloperoxidase(MPO) and it reacts with antigens within the cytoplasm of neutrophils (5). In addition, polymorphonuclear leukocyto-