LETTERS

Fatal vascular occlusion in juvenile dermatomyositis

Juvenile dermatomyositis (JDMS) is a relatively rare disease characterised by vasculopathy.[1–4] Involvement of the gastrointestinal tract may occur in some subjects and is often life threatening. We describe here a case of fatal JDMS with gastrointestinal perforation. Immunohistochemical examination by antibody against factor VIII seems to be useful for evaluating the pathological basis of vasculopathy in JDMS.

A 13 year old Japanese girl was admitted in April 1994 with high fever, muscle pain, and muscle weakness. She noticed a facial rash for two months before admission. Physical examinations were; blood pressure 135/90 mm Hg, temperature 38°C, and weight 50 kg. She presented with an erythematous rash on her face, neck and arms, heliotropic eruption, Gottron's sign, and nail fold telangiectasia. Proximal muscular weakness and pain were prominent. Laboratory findings were as follows; stool occult blood negative, leucocyte count 5800/mm^3, erythrocyte count 4800 × 10^3/mm^3, thrombocyte count 109 × 10^3/mm^3, and serum C reactive protein value normal. Muscle enzyme examination showed; glutamic oxaloacetic transaminase 294 IU/l, creatinine phosphokinase 5960 IU/l, and lactate dehydrogenase 1469 IU/l. Rheumatoid factor, antinuclear antibody and other autoantibodies were all negative. Electromyogram findings showed short and small motor units. Muscle biopsy specimen showed variation in fibre size and perivascular inflammatory cell infiltration in the connective tissue. JDMS was diagnosed according to the criteria of Bohan and Peter.[2] No features of other connective tissue diseases or malignant neoplasms were present.

Intravenous prednisolone (60 mg/day) was started. However, dysphagia occurred and thrombocytopenia (41 × 10^3/mm^3) with increase in platelet associated IgG (268 ng/10^7 platelet) was apparent. Three courses of methylprednisolone pulse therapy (1000 mg/day for three days) and two courses of high dose intravenous immunoglobulin (20 g/day for five days) were prescribed followed by intravenous methotrexate (100 mg/day every two weeks). Although thrombocytopenia and the increase in serum muscle enzyme had improved, abdominal pain, haematemesis, and melaena resulting from multiple gastrointestinal ulcers were noted. Cyclophosphamide pulse therapy (750 mg/day, every two weeks) and plasma exchange were not effective and oesophageal and bowel perforation occurred. After the resection of perforated lesions, peritonitis occurred and she died of massive abdominal haemorrhage seven months after admission (fig 1).

Surgical findings showed three perforated areas (lower oesophagus, ileocaecal region, and gastric antrum). Pathological examination of these lesions showed occlusion of both arteries and veins. The internal elastic lamina of arteries were intact (fig 2A). Intimal hyperplasia was seen in some vessels and some other vessels were occluded by fibrin thrombi with proliferation of the endothelial cells, characterised by positive staining for factor VIII (fig 2B and C). Some vessels showed infiltration of lymphocytes and foamy macrophages to the adventitia and media.

In JDMS, an autoimmune connective tissue disease, the microvasculature is thought to be the fundamental site of pathology. Banker and Victor reported that the earliest pathological changes of vessels were perivascular collections of inflammatory cells, followed by intimal hyperplasia of arteries and veins.[1] Vessel lumen may be occluded by thrombi, fibrin or swollen endothelial cells.[1–4]

In our case the occluded vessels consisted of intimal hyperplasia and fibrin thrombi with proliferated cells, which were stained with anti-factorVIII antibody, an endothelial cell marker.[5] Although the level of factor VIII related antigen was not measured in this case, a high level of factor VIII related antigen in JDMS has been previously reported by some authors.[3 6–8] Our immunohistochemical findings suggest the endothelial cell dysfunction in the vasculopathy of JDMS and also suggest that anti-factor VIII antibody is useful for evaluating the pathological basis of vasculopathy in JDMS.

Thrombocytopenia seen in our case was accompanied by an increase in platelet associated IgG, and improved after treatment with prednisolone and intravenous immunoglobulin. This suggested that her thrombocytopenia resulted from autoimmune thrombocytopenia associated with dermatomyositis, which has been reported in only two adult cases.[9 10] This is the first report of autoimmune thrombocytopenia in JDMS.

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T TAKEDA
A FUJISAKU
S JODO
T KOIKE
Department of Medicine II

A ISHIZU
Department of Pathology, Hokkaido University School of Medicine, Sapporo, Japan

Correspondence to: Dr T Takeda, Department of Medicine II, Hokkaido University School of Medicine, Kita 15-jo, Nishi 7-chome, Kita-ku, Sapporo 060, Japan.

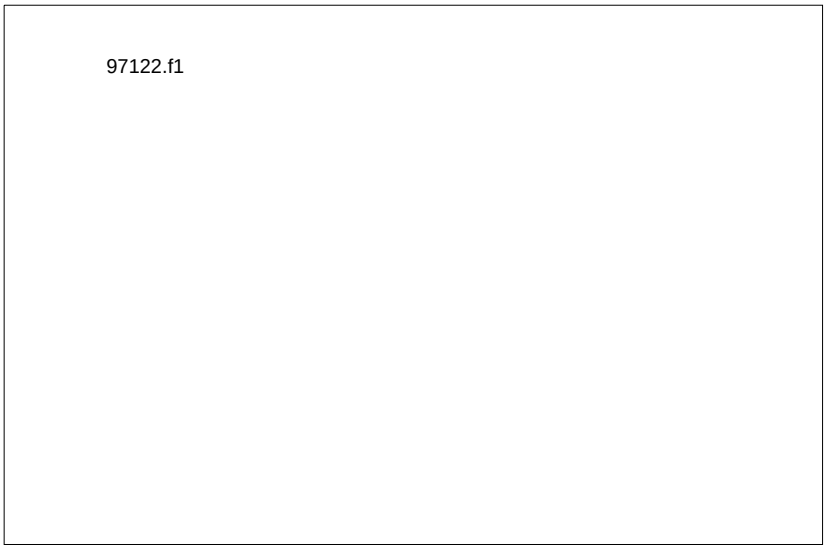

Figure 1 Clinical course. PSL=prednisolone; m-PSL=methylprednisolone; MTX= methotrexate; IVIG=intravenous immunogloburin, CY=cyclophosphamide pulse therapy; PE=plasma exchange; Plt=platelet.

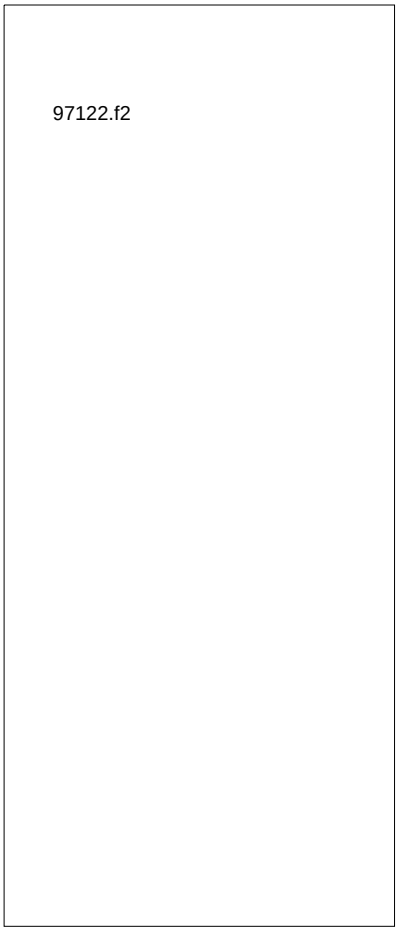

Figure 2 (A) Vascular lesion at the oesophageal perforation. Both the artery (left) and vein (right) were occluded. The internal elastic lamina of the artery was intact, elastica Van Gieson stain. (B). The serial section of figure 2A. Deep blue fibrin obliterated the lumen of the vein, PTAH stain. (C) The serial section of figure 2A and 2B. Endothelial cells were stained with anti-factorVIII antibody (F8/86, mouse IgG1, DAKO), immunohistochemical stain for factor VIII. Bar=0.5 mm.

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Polyarteritis nodosa associated with precore mutant hepatitis B virus infection

Currently there is a trend to support the use of antiviral therapy as the first line treatment of polyarteritis nodosa (PAN) associated to hepatitis B virus (HBV) infection.[1 2] A combination of a short course of corticosteroids, plasma exchange, and interferon α (INFα) has been proposed. However, we have doubts about this approach in all cases and circumstances of PAN related to HBV infection. One of these circumstances would be precore mutant HBV infection.

A 37 year old man was diagnosed with PAN. The initial clinical manifestations were mononeuritis multiplex, orchitis, mild renal failure (creatinine: 168 µmol/l, proteinuria of 0.6 g/dl), abdominal pain, and prolonged fever. Leucocytosis (30 000 WBC, 80% neutrophils), serum asparate aminotransferase: 94 U/L, serum alanine aminotransferase: 244U/l, increased erythrocyte sedimentation rate (90 mm/h) and complement consumption were also observed. Histological diagnosis was performed by testicular biopsy. Infection with HBV precore mutant was present (HBsAg +, HBeAg −, Anti HBe Ag +, Anti HBc Ab IgG/M +, HBV DNA 1180 pg/ml). Retrospective sequence analysis of the serum HBV DNA showed the presence of the precore mutant (substitution of G to A at nucleotide 1896). A therapeutic regimen of prednisone 1 mg/kg per day (twice a week) with rapid discontinuation (one week), plasma exchange, and INFα was started. Significant improvement in clinical symptoms and laboratory data, including renal function, with regression of sediment anomalities and normalisation of the creatinine occurred with this treatment. HBV DNA load (measured two weeks after INFα) and transaminases values were similar to previous range. Four weeks later, while receiving this treatment, abdominal pain, prominent leucocytosis, increased erythrocyte sedimentation rate, and decreased complement component 3 were observed again. The patient developed acute pulmonary oedema secondary to myocarditis associated with vasculitis (left ventricular ejection fraction: % EF: 38%; previous EF: 72%); electrocardiography was non-specific and serial creatine kinase measurement was in the normal range. A diagnosis of relapse of PAN with probably secondary myocarditis was made. This situation was controlled with furosemide, digoxin, and intravenous pulses of methylprednisolone 1 g/day, for three days; a pulse of cyclophosphamide 1200 mg intravenously was also administered. INFα and plasma exchange were stopped. Two weeks later the % EF was 45%, and the patient was discharged with oral prednisone and monthly cyclophosphamide pulses. Six months later the patient achieved clinical remission.

We are cautious to recommend antiviral treatment as first line treatment in polyarteritis associated with HBV. The experience with INF in the treatment of polyarteritis is still limited. To our knowledge, this is the first case report of PAN associated with a precore mutant strain of HBV incapable of synthesising HBe antigen; therefore, there is no previous experience with INF. The precore defective HBV is present in one third of patients in the Mediterranean with chronic HBV infection.[3] It has been speculated that the absence of HBe Ag in the hepatocyte membrane prevents the elimination of infected cells by immune system stimulated by INF. It is considered a viral infection with few trends to spontaneous remission and more progressive in comparison with the infection caused by the wild type virus. In general, the treatment with INF in the chronic hepatitis produced by this variate is unfavourable. The rates of relapses are very high in patients who have precore mutant compared with wild type HBV infection (40–90% compared with 13%)[4–6]; and it is recommended to include these patients in multicentric and controlled trials.[7] On the other hand, HBV mutant infection has been associated with fatal liver failure after immunosuppressive therapy.[8] Precore mutant HBV associated PAN should be considered as an individual entity whose therapeutic approach is complex and not defined at present. It is necessary to perform prospective studies to evaluate the exact role of immunosuppressive and antiviral therapy, including new antiviral agents.

M MIGUELEZ
J BUENO
P LAYNEZ
Hospital Nuestra Señora de La Candelaria, Internal Medicine Department, Santa Cruz de Tenerife, Canary Islands, Spain

Correspondence to: Dr M Morales, C/ Cra General del Norte, Km 15, no 304, 38330 La Laguna, Tenerife, Canary Islands, Spain.

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Polymyalgic presentation of Sjögren's syndrome: a report of three patients

We report on three patients who presented with polymyalgia but on subsequent clinical and laboratory assessment showed findings consistent with primary Sjögren's syndrome.

Clinical, immunological, and genetic differences exist now to classify Sjögren's syndrome (SS) more clearly into primary and secondary SS than in the past.[1 2] Primary SS patients can present with a plethora of symptoms although most patients present with sicca complaints, lethargy or arthralgia. Polymyalgia, as presenting complaints of primary SS, has not been reported previously.

Our patients presented during a two year period with proximal aching and stiffness associated with a raised erythrocyte sedimentation rate (ESR) and all three responded characteristically as in polymyalgia rheumatica (PMR) patients to oral prednisolone therapy.[3] Subsequent investigations and clinical evaluations (table 1) however raised the possibility of primary SS as the underlying condition, confirmed by the usual immunological parameters and all three patients showed some features of the sicca syndrome, although none had a history of swelling of the salivary gland.[1 2]

Follow up over at least a two year period showed that patients were relieved of their PMR symptoms but other clinical and laboratory features persisted, except for normalisation of the ESR. None, however, has yet been able to stop taking prednisolone altogether.

Table 1 Demographic and clinical details of patients

	Age	*Sex*	*Dry eyes**	*Xerostomia†*	*PMR Duration*	*ESR on presentation*	*RF*	*ANF*	*Ro*	*La*	*Protein electrophoresis*
Patient 1	54	F	+	+	2 years	65	+	+	+	+	polyclonal increase in γ globulins
Patient 2	62	F	+	−	1 year	70	+	+	+	+	polyclonal increase in γ globulins
Patient 3	52	F	−	+	6 months	58	−	+	+	+	NK

*Both subjective and objective with impaired tear production (Schirmer's test reading <5 mm in 5 minutes). †Both subjective and objective (lack of saliva pool under tongue). NK, not known.