SEVERE JUVENILE DERMATOMYOSITIS COMPLICATED BY PANCREATITIS

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SUMMARY

We report two boys with juvenile dermatomyositis (JDM) complicated by pancreatitis. One also had hepatitis and probably mild bowel vasculitis, while the other had catastrophic bowel vasculitis with multiple perforations. Both were on corticosteroids, but had features of active vasculitis. The former improved with high-dose i.v. pulsed methylprednisolone, while the latter improved only after immunosuppression with i.v. methylprednisolone, cyclophosphamide and plasmapheresis. Although bowel vasculitis is a known complication of severe JDM, pancreatitis and hepatitis are extremely rare. We have found in a literature search only three other reports of pancreatitis complicating JDM. We wish to alert physicians that pancreatitis may develop in JDM. It should be considered as a differential diagnosis in the child with active disease who develops abdominal pain. Control of vasculitis with adequate immunosuppression, as well as general supportive measures, may be valuable in the treatment of pancreatitis in JDM.

KEY WORDS: Juvenile dermatomyositis, Pancreatitis, Adequate immunosuppression.
Lupus anticoagulant was negative, and the levels of Ig G, A and M showed no immunodeficiency. Anticardiolipin antibody titres were mildly elevated: IgG 14.4 AU (up to 7), IgM 24.9 AU (up to 10) and C3 slightly low at 0.65 (0.75–1.65), C4 was normal at 0.37 (0.2–0.65). The lymphocyte count was initially low at 0.71 x 10^9/l (1.5–4). However, repeat values of these were normal and there were no other markers for lupus.

He was commenced on oral prednisolone at 50 mg daily (~1 mg/kg/day) after his first clinic visit, but continued to deteriorate. He developed severe abdominal pain with radiation to the back and vomiting. On review 3 days later, he looked very ill, had abdominal distension, guarding, rebound tenderness and deepening jaundice. Bowel sounds were absent. Ultrasound of the abdomen showed a bulky pancreas with increased echogenicity and surrounding fluid consistent with pancreatitis and ascites. There was a small pleural effusion. The intrahepatic biliary tree was prominent, but the common bile duct was not dilated. The gall bladder contained some sludge but there were no stones or thickened gall bladder wall. Abdominal X-ray (AXR) showed some loops of distended bowel, but excluded free air under the diaphragm. CT scan confirmed ascites surrounding the pancreas which enhanced uniformly, but did not demonstrate any other underlying cause for the pancreatitis. Blood markers had worsened with rising enzyme levels, especially amylase, ALT and AST (see Table 1).

Our clinical impression then was of severe JDM with worsening hepatitis, pancreatitis and possible gut vasculitis. A white cell scan performed later showed increased uptake in the small bowel consistent with vasculitis. As his clinical deterioration and raised enzymes were present before the onset of steroids, we attributed his deterioration to inadequate control of vasculitis, i.e. it occurred in spite of rather than secondary to steroids. He was pulsed with i.v. methylprednisolone, three doses of 1 g given on consecutive days. In addition, ileus and pancreatitis were managed conservatively with a nil-by-mouth regime, nasogastric suction, careful fluid and electrolyte balance, and colloid support. The patient also received i.v. octreotide (somatostatin analogue) to decrease pancreatic secretions, omeprazole to decrease gastric acid secretion, antibiotic cover and self-controlled analgesia via morphine infusion.

With this immunosuppression and supportive treatment, he showed dramatic improvement within days, both clinically and in laboratory markers. Within weeks, amylase, muscle and liver enzymes approached normal.

He needed total parenteral nutrition for a short period, but was eating heartily and participating in physiotherapy within 2 weeks. He was subsequently maintained on prednisolone and cyclosporin A.

### CASE 2

An Irish boy first developed proximal muscle weakness at the age of 9 yr in December 1992 when he noticed difficulty getting up from a squatting position and was slow in football. He got progressively weaker, his gait deteriorated and he developed redness over the lateral malleoli, malar prominences, eyelids and metacarpal-phalangeal joints. Muscle biopsy confirmed the diagnosis of JDM and he initially responded to oral steroid treatment at 29 mg (0.5 mg/kg/day). ANA, RF and antibodies to DNA and ENA were negative. Complement and immunoglobulin levels were normal. His dose of steroids was gradually decreased after the first 2 months.

However, he had intermittent episodes of severe abdominal pain over the next 2 yr. Investigations performed locally resulted in a diagnosis of left-sided pelvi-ureteric junction obstruction (PUJO) with hydropnephrosis and pyelonephritis which necessitated nephrostomy and subsequent nephrectomy in 1994. The kidney specimen showed chronic inflammation and segmental scarring, but no evidence of vasculitis nor autoimmune aetiology.

Over the next year, he developed progressive deterioration with increasing weakness, rash and dysphagia. This was unresponsive to increased oral...
Some causes of acute pancreatitis in children

<table>
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<th>Causes</th>
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<tbody>
<tr>
<td>1. Drugs and toxins [15, 21, 22] corticosteroids, azathioprine, cimetidine, non-steroidal, tetracycline, erythromycin, sulphamethizole, frusemide, thiazides, valproate</td>
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<td>4. Obstructive [15, 24] SLE, HSP, PAN, Kawasaki, Crohn’s, hyperlipidaemia, hypercalcaemia, uraemia, refeeding after starvation, carnitine palmitoyl transferase II deficiency</td>
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<td>6. Traumatic [15, 25]</td>
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secondary to a systemic disease process. While available data may not be consistent to support a definite disease association with pancreatitis, drugs may be a co-factor in inducing pancreatitis [21].

Steroids have been implicated as a possible cause of pancreatitis from animal experiments and clinical studies [7, 12, 26–29]. Pancreatitis associated with corticosteroid therapy has been described in children by Baar and Wolff [18], as well as Marczynska [30]. Possible mechanisms include increased volume/viscosity of pancreatic secretions [31], hyperlipidaemia [29], fluid and electrolyte imbalance [32], hypersensitivity [18] and intravascular coagulation [33].

In the numerous reports of pancreatitis complicating SLE in adults as well as children [3–15], some patients were on treatment (e.g. steroids, azathioprine, antimetabolites, antibiotics, thiazides) or had other conditions (e.g. infection) which may have caused pancreatitis, but in some no other cause was present but active SLE. Reynolds et al. [11] reported 20 cases of SLE, of whom 19 recovered with minimum complications despite increased or continued steroids. The pancreatitis occurred in the absence of other precipitants including corticosteroids in four of their patients (who presented with pancreatitis) and in three previously reported cases [8, 10, 34]. Pancreatic inflammation was typically associated with multiple organ involvement. Autopsy and experimental studies [9, 34] suggest that the vasculitis of SLE with subsequent obliterator arterial and venous thrombosis is the likely pathophysiological basis for pancreatitis.

Pancreatitis associated with JDM is very rare. Baar and Wolff [18] reported a 2-year-old boy with JDM and congestive heart failure who developed abdominal pain and an upper abdominal mass, and who subsequently died. The post mortem showed necrosis of the pancreas and peripancreatic fatty tissue. In this child, pancreatitis could have been due to inadequately controlled systemic disease. Petrou et al. [19] reported an 11-year-old girl with JDM who developed recurrent pancreatitis. She had been treated with methylprednisolone, cyclophosphamide, azathioprine, cyclosporin, plasmapheresis and thiazides. The pancreatitis may have been due to active JDM or its therapy prior to the development of pancreatitis. Finally, in 1989 Heckmatt et al. [20] reported two out of 14 children with JDM entering a trial of cyclosporin A who had developed pancreatitis previously, although it is not clear whether this was related to drugs, disease activity or some other reason. All 14 children had been on steroids at some time, 10 had received azathioprine.

In this report, we have described two boys with chronically active JDM who developed pancreatitis. One child had overt bowel vasculitis with multiple perforations. The other had widespread cutaneous ulceration and hepatitis as well as probable low-grade bowel vasculitis as noted on white cell scan. Pancreatitis was manifested by severe abdominal pain, nausea, prostration, guarding and rebound tenderness. Pancreatitis was confirmed by raised amylase as well as ultrasound and CT scan in one boy, and at laparotomy in the other. Both were treated with corticosteroids, but one had a raised amylase even before starting steroids. They were not at the time on other drugs known to cause pancreatitis and did not have evidence of the infections associated with pancreatitis. They both responded to aggressive measures to suppress vasculitis as well as general supportive measures. One responded dramatically to i.v. pulsed methylprednisolone even though it is a drug that could cause pancreatitis, while the other improved after aggressive immunosuppression. Therefore, we suggest that the pancreatitis in these two boys was part of widespread vasculitic activity due to JDM similar in pathogenesis to SLE patients with pancreatitis. Of some interest are the moderately raised anticardiolipin antibodies in Case 1. A report by Font et al. in 1989 [35] suggests that these antibodies are present in many multistystem autoimmune diseases: 6% in adult dermatomyositis patients.

It is important to take abdominal pain seriously in children with JDM. Causes include life-threatening bowel vasculitis with ulceration, haemorrhage, necrosis and perforation, as well as pancreatitis, hepatitis, ascites and renal vessel occlusion. Although pancreatitis is extremely rare, it can be fatal from cardiovascular collapse, respiratory distress or renal failure. It should be considered early in the child with abdominal pain and differentiated from other causes. The diagnosis of pancreatitis is largely clinical. Ultrasound and CT scan help in identifying an enlarged hyperechoic pancreas with surrounding fluid. Amylase values are often raised, but may not be [36]. There are also other causes of a raised amylase in a child with abdominal pain besides pancreatitis, including penetrating or perforated peptic ulcer, mesenteric thrombosis, intestinal obstruction, appendicitis and osteomyelitis [25]. However, it was only at laparotomy that pancreatitis was diagnosed in one of our patients as the pancreas was not visualized on ultrasound at the time because of a distended fluid-filled gut.

Treatment of pancreatitis should include general supportive measures which include colloid, fluid and electrolyte support, adequate analgesia, and prevention of secondary infection. The use of somatostatin or its analogue octreotide should be considered. Complications such as hypocalcaemia and hyperglycaemia should also be sought and managed where possible. Drugs known to precipitate pancreatitis should be discontinued. If underlying widespread vasculitis is considered the likely cause of pancreatitis, then adequate immunosuppression is necessary to bring this under control.

REFERENCES
3. Goldberg BH, Bergstein JM. Acute respiratory distress in