Case report

Protein losing enteropathy due to systemic lupus erythematosus

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SUMMARY We report the case of a 29 year old woman with a protein losing enteropathy caused by systemic lupus erythematosus presenting with periorbital oedema. Only three other cases of protein losing enteropathy due to systemic lupus erythematosus have been described,¹⁻³ two of which were thought to be because of a primary enteropathy,^{1,2} although the exact pathogenesis was unknown. We suggest that both the protein losing enteropathy and periorbital oedema in this patient were because of increased capillary permeability to serum albumin, as a result of products of plasma C₃ conversion which were present in large amounts. It is also of interest that the antigen/antibody system in this patient was RNP/anti-RNP and that DNA antibodies were not detected. This patient falls into a subset of systemic lupus erythematosus in which anti-DNA antibodies are not present, some of which appear to have a more favourable prognosis.⁴

Case report

A 29 year old white woman presented to the dermatology clinic with a history of intermittent periorbital oedema for one year after a holiday in New Zealand, and ankle oedema for three weeks. Further enquiry revealed general malaise and lassitude for several months, Raynaud's phenomenon for two years and secondary infertility of unknown cause for the past eight years. She had been investigated five years previously for polyarthritis at which time the ESR was 28, rheumatoid factor was negative and ANF was positive at a titre of 1 in 60. Since then, she had had mild intermittent episodes of arthralgia in the elbows and the knees and had noticed a mild diffuse alopecia. There was no other relevant personal or family history and she was receiving no medication.

Clinical examination revealed symmetrical periorbital and conjunctival oedema with bilateral pitting ankle oedema and her blood pressure was 95/60. No other abnormalities were found.

INVESTIGATIONS

The following investigations were normal: haemo-

globin, white cell count, serum calcium, phosphate and electrolytes, liver function tests, fasting glucose, creatinine phosphokinase, serum B12, folate, iron and TIBC, radiograph of the chest and hands, and ECG. A 24 hour urine collection showed no protein and no growth was obtained from an MSSU.

The ESR was 114 mm/h (Westergren), blood urea 2.2 mmol/l (normal 3.3-8.3) and serum cholesterol raised at 10.0 mmol/l (normal 3.8-7.0). The serum albumin was grossly depleted at 14 g/l (normal 60-83). The T4 was low at 51 mmol/l (normal 60-170) and T3 at 0.5 mmol/l (normal 1.2-3), with a normal TSH. A barium swallow was normal and a barium meal showed a prominent mucosal pattern because of oedema, with normal rugae and no evidence of Menetrier's disease. A small bowel enema showed wide mucosal folds throughout the proximal small bowel consistent with oedema. A jejunal biopsy showed normal villous architecture although many villi appeared 'bloated' probably because of oedema. There was no evidence of Whipple's disease on light or electron microscopy. An isotopic chromic chloride faecal excretion test was grossly raised at 13.8% (normal <1.8%) indicating heavy protein loss from the bowel. A rectal biopsy and faecal fat excretion were normal.

Immunological investigations revealed that serum antinuclear antibodies detected by indirect immuno-

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fluorescence were repeatedly present in high titre. A speckled pattern of staining was present using rat liver as substrate and a coarsely granular pattern using Hep 2 cells as substrate. Antibody to extractable nuclear antigens detected by counterimmunoelectrophoresis using an extract of rabbit thymus (Pel Freeze Biol., Arkansas) as antigen was present at a titre of 1/256. The specificity of the antibody was to RNP. Antibody to DNA measured by a passive haemagglutination method (Fujizoki, Pharm., Tokyo) was not detected. Plasma C₃ and C₃PA concentrations were repeatedly low with C₃ concentrations between 0.5 g/l and 0.65 g/l (normal 0.6–1.5) and C₃PA concentrations between 0.09 g/l and 0.18 g/l (normal 0.15–0.45). Plasma C₄ concentrations varied between 0.18 g/l and 0.42 g/l (normal 0.25–0.75). Plasma C₃ conversion measured by immunoelectrophoresis in agarose was 30%. Serum immune complexes containing IgG and IgM were detected by a PEG (polyethylene glycol) precipitation method on several occasions. Cryoglobulinaemia was not present. Serum IgM was raised at 3.5 g/l, but IgG and IgA were normal. C reactive protein was not detected. Rheumatoid factor was present at a titre of 1/1280. Examination of a biopsy of normal skin by direct immunofluorescence did not show immunoglobulin, complement or fibrin deposition along the dermo-epidermal junction. A few non-specific IgA and IgM globules were sparsely distributed in the dermal papillae. Examination by light microscopy was normal.

TREATMENT AND PROGRESS

She was started on prednisolone 20 mg daily, increasing to 60 mg daily one week later, as there was no clinical or biochemical improvement. Within a few days her facial oedema was much reduced and by three weeks the serum albumin had risen to 35 g/l, the ESR having fallen to 13 mm per hour. A repeat isotopic chromic chloride faecal excretion test was now normal at 1.78%. After five months the serum albumin has remained stable within the high normal range and the patient remains completely asymptomatic on prednisolone 12.5 mg daily. Interestingly, there remains marked plasma C₃ conversion (50%) despite clinical remission.

Discussion

To our knowledge protein losing enteropathy with systemic lupus erythematosus has previously been described in only three patients. Two of these were thought to have a primary enteropathy, the pathogenesis of which was unknown^{1 2} and the other was secondary to constrictive pericarditis.³ Though

various gastrointestinal manifestations of systemic lupus erythematosus have been described, including mesenteric vasculitis with intestinal infarction, ulceration and perforation, gastric atony, small bowel ileus and ulcerative colitis,⁵ none of these were present in this patient.

It is well known that oedema may occur at presentation or intermittently in patients with connective tissue diseases. Indeed, increased vascular permeability to albumin has been shown in such cases and is thought to be responsible.⁶ Increased vascular permeability resulting in tissue oedema has also been reported after plasma C₃ conversion by some intravenous drugs.⁷ In view of the marked degree of plasma C₃ conversion in this patient, it is interesting to speculate, therefore, that products of C₃ conversion are similarly responsible for increased vascular permeability in the gut and the skin. Unfortunately, however, we did not measure 'capillary permeability' in our patient, and can therefore not exclude the possibility of the oedema being secondary to hypoalbuminaemia, with the primary event being a vasculitis of the gut resulting in protein losing enteropathy.

It is of interest that the nuclear antigen/antibody system in this patient is RNP/anti-RNP and that DNA antibodies were not detected. In the one other report of protein losing enteropathy with systemic lupus erythematosus in which serum DNA antibodies were measured no increase was found.² Such subsets of systemic lupus erythematosus have been described in which anti-DNA antibodies are not present, many of which appear to have a more favourable response to treatment and better long term prognosis.⁴ Certainly our patient has responded well to systemic steroids, as did the other two cases of systemic lupus erythematosus with protein losing enteropathy, in whom treatment was eventually discontinued with no recurrence of signs or symptoms up to one year later.

Finally, this case further emphasises the fact that chronic or periodic oedema should be investigated with a view to an underlying connective tissue disease.

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