LETTERS TO THE EDITOR

Laryngeal involvement as a presenting symptom of systemic lupus erythematosus

Sir: The actual prevalence of laryngeal involvement in systemic lupus erythematosus (SLE) is unclear, but it seems to be very uncommon.¹ Furthermore, laryngeal vasculitis in SLE is even more rare and has been scarcely reported.² In fact, in the lupus erythematosus textbook of Wallace and Dubois no mention is made of the actual prevalence and type of damage of the larynx.³ We have recently seen a young man with SLE, who developed hoarseness as the first symptom.

A 33 year old white man was admitted in December 1988 with a five week history of hoarseness. Three weeks later he noticed anorexia, weight loss, oral ulcers, arthritis, palpable purpura, and paraesthesia in the legs. Before admission the patient had only received non-steroidal anti-inflammatory drugs, without improvement. His medical history was uneventful.

Initial examination showed a normal blood pressure, a temperature of 37°C, and a pulse of 90 beats a minute. Polyarthritis, oral ulcers, and palpable purpura in the legs were noticed. An indirect laryngoscopy showed complete paralysis of the right vocal cord without masses and with no evidence of external compression.

Laboratory investigations showed a haemoglobin of 132 g/l and a white blood cell count of $9.7 \times 10^9/l$ with $1.261 \times 10^9/l$ lymphocytes. The erythrocyte sedimentation rate was 49 mm/hour (Wintrobe). The blood chemistry was normal, but the blood urea was 6.5 mmol/l and the serum creatinine was 159 $\mu\text{mol/l}$ with a normal glomerular filtration rate. A chest x ray was normal. Four weeks after admission the creatinine rose to 451 $\mu\text{mol/l}$ while the glomerular filtration rate dropped to 42 ml/min. Urine analysis showed innumerable red blood cells and 14 white blood cells per high power field, and granular and hyalin casts. Albuminuria of 2.49 g in 24 hours was also noted. Immunological studies showed antinuclear antibodies and anti-double-stranded DNA antibody.

A kidney biopsy was done and showed a diffuse proliferative glomerulonephritis with an activity index of 20 and chronicity index of 6. A skin biopsy showed a leucocytoclastic vasculitis, and a nerve conduction study was compatible with a peripheral neuropathic pattern.

The patient was treated initially with three 'bolus' of intravenous methylprednisolone (1 g/day). One month later, because of further evidence of kidney damage, treatment was started with intravenous cyclophosphamide, while treatment was continued with 60 mg prednisone in one dose. Six months later the serum creatinine was 186 $\mu\text{mol/l}$. The hoarseness and the paraesthesia improved rapidly after the initial methylprednisolone bolus.

Systemic lupus erythematosus was diagnosed in our patient according to the 1982 revised criteria—that is, he had non-erosive arthritis, oral ulcers, lymphopenia, kidney damage, and positive antinuclear antibodies.⁴ As no evidence of masses or extrinsic compression was found at laryngoscopy and the chest x ray was

normal, excluding pulmonary hypertension, we concluded that vasculitis was the underlying mechanism of this patient's hoarseness. We were unable to exclude the possibility that neuropathy involving the recurrent laryngeal nerve was the underlying mechanism of damage. We feel, however, that the concomitant appearance of vasculitis in the skin shown by skin biopsy and the prompt resolution of dysphonia following the administration of the methylprednisolone suggests that vasculitis was the mechanism of damage.

Laryngeal nerve palsy as a manifestation of SLE is an uncommon phenomenon and to the best of our knowledge it has not been reported as the initial manifestation. In the report of Asherson *et al* of pulmonary hypertension in SLE one patient had vocal cord palsy which might have been vasculitic in origin. The same authors in 1985 described two patients with vocal cord paralysis in SLE secondary to pulmonary hypertension,⁵ excluding vasculitis as the cause of the dysphonia. Other authors have reported recurrent laryngeal nerve palsy secondary to direct compression of the nerve by a dilated pulmonary artery.⁶ We feel that the hoarseness in our patient was not secondary to pulmonary hypertension because of the normal chest x ray and because of the rapid disappearance of the hoarseness following the methylprednisolone.

Undoubtedly, SLE is a disease with many protean and occasionally unpredictable symptoms and signs, which may form part of the disease spectrum. We suggest that persistent hoarseness should be added to these.

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Childhood adrenal insufficiency, chorea, and antiphospholipid antibodies

Sir: Carette and Jobin in a recent issue of the *Annals* reported a patient with adrenal insufficiency, deep vein thrombosis, and antiphospholipid antibodies.¹ Simultaneously, Asherson and Hughes in a different journal reported another adult with a very similar picture except for the absence of antinuclear antibodies.² Our attention was drawn to these two cases because we have recently encountered a similar case.

A 15 year old white girl was admitted to the Children's Hospital of Philadelphia in March 1989 with a recent diagnosis of Addison's disease. She subsequently developed chorea without other clinical features of systemic lupus erythematosus. A high positive antinuclear antibody titre (1/1280) prompted consultation with the rheumatology service. Further investigations showed the absence of antibodies to dsDNA, extractable nuclear antigen, and adrenal tissue, a prolonged partial thromboplastin time, and highly increased levels of IgM anticardiolipin antibody (enzyme linked immunosorbent assay (ELISA)); the IgG anticardiolipin antibody was also slightly raised. She was treated with haloperidol and corticosteroids (1 mg/kg daily). She improved neurologically and tolerated a slow tapering of corticosteroid treatment in the following weeks. This patient, except for her age, is similar to those already reported.^{1 2}

Primary adrenal failure is very rarely seen in systemic lupus erythematosus,³ and chorea is a well recognised, but also a rare manifestation. We feel that this young girl represents a paediatric example of the 'primary antiphospholipid syndrome'.⁴ In a recent series of 12 patients with chorea Asherson *et al* noted a strong association with anticardiolipin antibodies.⁵ Six (50%) of these patients were defined as having 'lupus like' syndromes owing to a lack of defined criteria for systemic lupus erythematosus.⁵ Our patient would seem to belong to that subset.

The main cause of adrenal insufficiency is autoimmune destruction of the adrenal glands. Two thirds of patients with Addison's disease have antiadrenal autoantibodies in their sera.⁶ The cause of the disease in the remaining one third is less well defined but includes chronic infections and granulomata. It is of great interest that possibly a new 'subset' may be emerging within the group of patients with primary antiphospholipid syndrome, and it is clearly of interest to search for these antibodies in patients with primary adrenal failure, even if their pathophysiological significance is still unclear.

Patients with and without systemic lupus erythematosus with positive anticardiolipin antibodies often have thrombotic complications, but a pathogenetic role for those antibodies has not been established as yet. In some patients with adrenal failure a 'vascular' cause has been suggested.^{1 2 7} An antibody mediated block in steroidal synthesis should possibly also be considered. In vitro studies might be helpful in answering this question.

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Leucopenia after gold and sulphasalazine treatment

Sir: I read the interesting report by Bliddal and colleagues of three patients who developed leucopenia after both gold and sulphasalazine treatment.¹ HLA-DR3 as a marker for toxic reactions after treatment with gold or D-penicillamine could not be shown. Patient 1, however, was apparently a carrier of HLA-B27. It is well known that female patients with rheumatoid arthritis, who are HLA-B27 positive, have a significantly higher risk for drug induced agranulocytosis, not only after treatment with levamisole^{2,3} but also with other antirheumatic drugs.⁴ Thus under these conditions the possibility should be considered that in this patient, in the absence of HLA-D3, HLA-B27 may be the risk indicator for her relapsing leucopenia.

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Sir: Thank you for your interesting comments on our article about HLA types of patients with leucopenia.

Our patients all had classical rheumatoid arthritis and none was positive for antinuclear antibodies. The observation in a small group of patients of HLA-B27 in just one case does not justify further conclusions.

Like many others we no longer use levamisole treatment for patients with rheumatoid arthritis.

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Destructive spine lesions in ankylosing spondylitis

Sir: We read with interest the article by Aufdermaur entitled 'Pathogenesis of square bodies in ankylosing spondylitis'.¹ In this case report of a patient with ankylosing spondylitis the author provided histopathological evidence to suggest a primary acute and chronic inflammatory lesion, resulting in destruction

Severe destructive lesions of C6 and anterosuperior spondylitis of C5.

of the vertebral bodies, followed by new bone formation.

It might be interesting to recall our case of destructive cervical vertebral lesions showing ankylosing spondylitis in a 19 year old woman.² During her disease of 18 months' duration she had inflammatory pain of the lumbar spine, sacroiliac joints, knees, and heels; radiographs showed bilateral sacroiliitis; HLA typing was A3, 9, B7, 12 and erythrocyte sedimentation rate 60 mm/1st h. From the start of her disease she had had inflammatory pain of the cervical spine. Radiographs showed severe destructive lesions of the 6th cervical vertebra without discal lesions or cervical ankylosis, and a milder anterosuperior spondylitis of the 5th cervical vertebra (figure). There was no history of trauma. Surgical biopsy excluded a tumorous or infectious process. Spinal fusion (C4-7) was performed, and cervical pain disappeared with non-steroidal anti-inflammatory drugs. Histopathological examination of the 6th cervical vertebra biopsy specimen showed the absence of any inflammatory cells and the presence of spongiosa surrounded by fibrous tissue.

These findings are consistent with those of Aufdermaur; the inflammatory cervical pain, which was noted as an early symptom of the disease in our patient, might have been due to the inflammatory lesion of the vertebral body, and the present histopathological findings might represent the reparative stage with scar and new bone formation. It is noteworthy that this severe destructive cervical lesion was the first manifestation of ankylosing spondylitis in this patient.

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Low incidence of antinuclear antibodies in dermatomyositis with malignancy

Sir: In 1958 Walton and Adams first classified 'polymyositis/dermatomyositis with malignancy' as a distinct subset of polymyositis.¹ Recent prospective controlled studies, however, cast doubt upon the increased incidence of malignancy in polymyositis/dermatomyositis.^{2,3} If the association of polymyositis/dermatomyositis with malignancy happens by mere coincidence, serological features in these diseases with and without malignancy should not be different. The purpose of our preliminary study was to clarify this point in 36 patients with dermatomyositis.

Dermatomyositis was diagnosed according to the diagnostic criteria of Bohan and Peter.⁴ Thirty six patients were diagnosed as having pure adult dermatomyositis. These patients were further divided into two groups: 12 patients with dermatomyositis with malignancy (nine definite and three probable dermatomyositis) and 24 patients with dermatomyositis without malignancy (16 definite and eight probable dermatomyositis). Patients with dermatomyositis which overlapped with other connective tissue diseases were excluded from this analysis. Existence of malignancies was proved histologically by biopsy or necropsy, or both. Antinuclear antibodies were tested by indirect immunofluorescence with HEp2 cells (Kallstad, Chaska, Mn, USA) as substrates. Serum samples giving apparent fluorescence at a dilution of 1:40 were considered positive. The χ^2 test was used for the statistical analysis.

Positive antinuclear antibodies were found in 13/24 (54%) patients with dermatomyositis without malignancy, but they were found in only 2/12 (17%) of those with malignancy ($p < 0.03$). The low incidence of antinuclear antibodies in dermatomyositis with malignancy suggests the presence of a different serological background from that in the dermatomyositis without malignancy. This conclusion supports the view that a distinct subset of dermatomyositis exists—dermatomyositis with malignancy.

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Inhibition of xanthine oxidase by allopurinol: its lack of effect on models of inflammation

Sir: In response to an article published in the *Annals*, entitled 'Inhibition of xanthine oxidase by allopurinol: A therapeutic option for ischaemia induced pathological processes?',¹ we wish to report our findings on the effect of xanthine oxidase inhibition in models of joint