Letter

Subacute peripheral neuropathy of unknown cause complicating active borderline (dimorphous) leprosy

Sir: Leprosy is uncommon in the United Kingdom and this is perhaps one reason why patients are referred to special departments, sometimes for months or years, before a diagnosis is established.¹ Particularly in the case of those forms of the disease called borderline or dimorphous, which lie between the tuberculoid and lepromatous poles of the spectrum of leprosy, various factors, including infection, trauma, psychological upset, drugs and pregnancy may produce immunological disturbances which are damaging to the patient's tissues and which may contribute to difficulties in diagnosis. Furthermore, patients with leprosy may also suffer from other conditions causing neuropathy. We recently encountered a patient with leprosy in the UK whose clinical course was complicated by the development of a sub-acute peripheral neuropathy of unknown cause.

A 38-year-old female Iraqi school-teacher first presented in 1965 with numbness in the right hand. Over the next 5 years she developed progressive weakness of both hands and feet and in 1968 a nerve biopsy and myelogram were performed in Baghdad, but no diagnosis was made. From 1970 to 1976 her hands and feet became increasingly deformed. At this stage a visiting neurologist made the diagnosis of leprosy and she was started on dapsone 200 mg daily which was reduced to 100 mg and stopped when she became pregnant in 1977. In 1979, she re-started dapsone at 100 mg/day but stopped after one year and took no further medication of any kind thereafter except vitamin B complex tablets.

Three months before arrival in the UK in 1981, she developed an acute illness with sore throat, fever, mild aches and pains all over the body, marked swelling of the hands and feet and the rapid development of bilateral wrist and foot drop. Her voice became weak and she had choking dysphagia with nasal regurgitation. She was taking no drugs apart from vitamin B complex and drank no alcohol. These symptoms had improved but she still remained weak. Examination after arrival in the UK revealed a thin apprehensive woman of above average intelligence with widespread wasting of the limb muscles. Under her right breast there was a 2 by 3 cm raised,

red lesion with indefinite outer borders, but a definite "punched out" inner border. There were two hypopigmented macules on the back of the neck, of vague outline and each about 2 cm in diameter. In the cranial nerves she had decreased touch and pain perception on the left side of her face. There was bilateral facial nerve weakness of lower motor neuron type, much worse on the left side and inability to close the lower lids of her eyes (lagophthalmos). Corneal reflexes were intact. There was asymmetrical thickening of many peripheral nerves, including the great auricular, supra-clavicular, lateral popliteal and superficial peroneal. She had gross wrist and foot drop with a marked flexion deformity of her hands; there was resorption of the distal phalanges shown on radiographs but no other trophic lesions. Limbs showed severe distal weakness with normal tone. She had symmetrical glove-and-stocking sensory loss to above her knees and elbows, whilst vibration sense was retained in her feet but not in her hands. There were ill-defined patches of sensory loss over the abdomen and between the scapulae. All peripheral reflexes were absent and she was unable to walk. Investigations revealed Hb 13.4 g/dl, WBC $8.9 \times 10^9/l$, platelets $447 \times 10^9/l$, ESR 33 mm in the first hour. Urea and electrolytes, liver function tests and glucose were normal. Serum B12, folate, glucose-6-phosphate dehydrogenase, faecal and urinary porphyrins, serum lead and mercury levels were all normal. Serology for syphilis (RPR and TPHA) was negative. The reciprocal viral titres (complement fixation) were as follows: Herpes simplex 16, varicella zoster 8, enterovirus 8 and CMV 64. Although the CMV IgM was positive, the latex test for rheumatoid factor was positive but the Rose Waaler test was negative indicating a possible false-positive test: for CMV infection. IgM to EBV was negative; the T3 was 2.3 nmol/l. The immunoglobulins were all raised, IgG 25.7 g/l (normal 7.2-19); IgA 5.3 g/l (0.8-5); IgM 2.1 g/l (0.5-2). Auto-antibodies including anti-nuclear factor, gastric parietal cell antibody, smooth muscle antibody and anti-mitochondrial antibody were all negative. The throat swab grew a light growth of beta haemolytic streptococci group A but no corynebacteria. The Schick test was negative. An initial diphtheria anti-toxin level was 0.2-1 u/ml and one month later it was 1-2 u/ml. (This indicated previous exposure as she had not been immunised). A lumbar puncture on first admission was traumatic; it showed no white cells, red

cells $1,600 \times 10^9/l$, normal glucose, protein 1.7 g/l and no organisms. Repeat lumbar puncture 18 days later confirmed a raised protein of 2.0 g/l, with 8 white cells (all lymphocytes) red cells $106 \times 10^9/l$; the albumin was 1.1 g/l and IgG 0.38 g/l (ratio 0.39). There were no oligoclonal bands. *Electromyographic studies* (Dr Geoffrey Rushworth, Oxford): using coaxial needle electrodes, the following muscles were examined on the left side of the body—brachio-radialis, biceps, deltoid, abductor pollicis brevis, first dorsal interosseus, abductor digiti minimi, frontalis, levator labii superioris and mentalis. The conclusions were as follows "The small muscles of the left hand are completely denervated, and it would appear that maximum degeneration of their motor fibres has taken place. The left brachial radialis is severely denervated and surviving motor nerve fibres conduct at a reduced velocity (estimated at 25 m/s). The left biceps is also moderately severely denervated, and again there is some reduction in the motor fibres innervating this muscle. The deltoid is much less affected. The left facial muscles are partly denervated and again the surviving motor nerve fibres show a marked reduction in their maximum motor velocities. Mentalis is the least affected of the facial muscles. These findings indicate that segmental demyelination of motor nerve fibres plays some part in the pathological process and that it affects principally the proximal muscles." The complete denervation of the distal muscles was considered to be due to leprosy. Although the involvement of the proximal muscles in a recent episode could have been due to a Guillain-Barré syndrome, it was pointed out that the onset had been sub-acute and that there has been some axonal degeneration as well as segmental demyelination. ECG was normal. Radiographs of the skull revealed evidence of her myelogram 13 years earlier with opacities at the base of the skull due to contrast medium. Slit-skin smears of her skin lesions were negative for acid-fast bacilli, but bacilli were found in granular or fragmented form in biopsies of the left great auricular nerve and of the skin lesion below the right breast. These biopsies also showed a picture of mid-borderline (dimorphous) leprosy (BB on the Ridley-Jopling scale²), with features of reversal (upgrading) reaction.³ She was treated with rifampicin, dapsone and prednisolone and improved markedly over 2 months. On discharge, she was able to walk. A cerebrospinal fluid protein discharge was 0.7 g/l.

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The main diagnosis of borderline leprosy in reversal (upgrading) reaction in this woman was undisputed. There was no evidence to suggest an excessive intake of dapsone, or the ingestion (in normal or excessive doses) of any drug which could have caused a neuropathy, and the clinical findings were not in keeping with heavy metal poisoning. Rapid deterioration of nerve function due to cell-mediated immune processes in a reversal (upgrading) reaction in leprosy was a possibility, but this could not have accounted for the raised CSF protein, regurgitation of fluid through the nose and the total loss of limb jerks. None of the other conditions considered and investigated offered any explanation for such extensive and severe neuropathy of sudden onset. The crucial question of her clinical progress between the acute illness in February and her presentation in this country in early May cannot be fully answered, partly because of language difficulties. However, the available evidence obtained through interpreters suggested that her paralysis progressed over a period of at least 2 months. Thus, although a Guillain-Barré syndrome was considered, it is perhaps more likely that the complicating illness was a sub-acute peripheral neuropathy of unknown cause.

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