## Transient Ischaemic Attacks and Status epilepticus in HTLV-1-Negative Adult T-Cell Leukaemia/Lymphoma

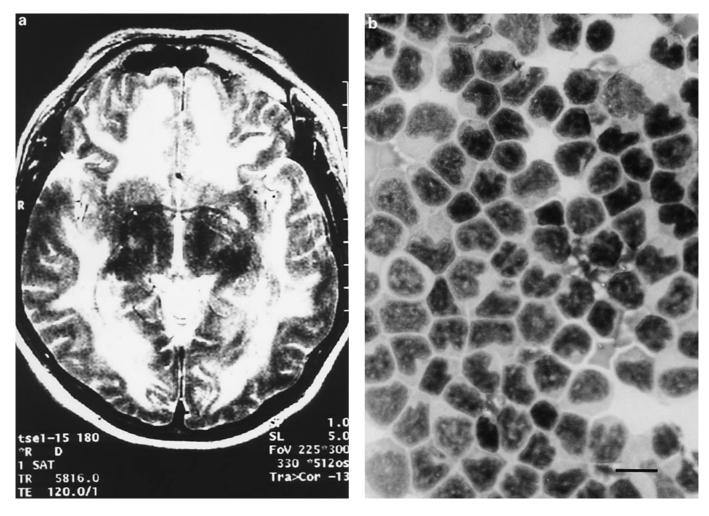
N.J. Gutowski<sup>a</sup>, D.C. Kinsella<sup>b</sup>, C.D. Sheldon<sup>c</sup>, M.A. Pocock<sup>d</sup> Departments of <sup>a</sup> Neurology, <sup>b</sup>Radiology, <sup>c</sup>Respiratory Medicine and <sup>d</sup>Haematology, Royal Devon and Exeter Hospital and School of Postgraduate Medicine and Clinical Sciences, University of Exeter, UK

Adult T-cell leukaemia/lymphomas (ATLL) have an aggressive course and are linked to human T-cell leukaemia/lymphoma virus-1 (HTLV-1). There is a leukaemic phase in >66% often with cutaneous lesions and hypercalcaemia. ATLL has four subtypes: acute (65%), lymphoma (25%), smouldering (5%) and chronic (5%) [1]. A case of HTLV-1-negative ATLL is described. The rare neurological manifes-

tations were transient ischaemic attacks (TIAs) and status epilepticus.

A 37-year-old right-handed man presented with sudden onset numbness affecting the right side of the face, right arm and leg and an expressive dysphasia lasting 10 min. Two days later he had numbness of sudden onset in the same distribution lasting 5 min. There was no weakness or headache. He was a non-smoker who drank alcohol occasionally. After commencing aspirin he had no further events. Examination was normal.

The past history revealed that 20 months before he had had shortness of breath and cough. Diffuse interstitial shadowing was seen on chest X-ray. Transbronchial biopsy showed a patchy, dense interstitial infiltrate of mature T lymphocytes. Lymphocytic interstitial pneumonitis was diagnosed. The following investigations were normal or negative: an infection screen (including HIV-1 and -2), autoantibodies, immunoglobulins and duodenal biopsy. Lymphadenopathy was absent on chest and abdominal computed tomographic (CT) scan. The pneumonitis responded to prednisolone which was



**Fig. 1. a** An axial MRI image ( $T_2$ -weighted; TR 5,816ms/TE 120 ms), pre-chemotherapy. There is marked increased signal involving the white matter of both cerebral hemispheres. **b** Photomicrograph of a centrifuged sample of CSF showing abnormal T lymphocytes with highly convoluted nuclei (flower cells; scale bar = 10 µm).

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maintained at low dosage. After commencing prednisolone a mild peripheral T-lymphocytosis ( $5.6-6.4 \times 10^{9}/l$ ; normal  $1.1-3.5 \times 10^{9}/l$ ) was found. Bone marrow aspirate and trephine were normal.

At neurological presentation, autoantibody, coagulation, thrombophilia, lipid and biochemical screens were normal, except for a small IgG kappa paraprotein band of 3.9 g/l. The peripheral lymphocytosis was  $7.3 \times 10^{9}$ /l. Less mature lymphocytes were seen on blood film. A T  $\gamma$  gene rearrangement was found. Bone marrow aspirate showed 30% lymphocytes and an abnormal lymphoid population. A further infection screen was negative (including HIV-1 and -2 and HTLV-1 and -2 on two occasions).

Eleven weeks after his TIAs the patient was admitted in status epilepticus with generalised tonic-clonic seizures having had a gradual onset headache over the previous 4 days. There were no focal signs. A magnetic resonance (MRI) scan showed diffuse cerebral white matter signal change, sparing the corpus callosum and brainstem (fig. 1a). There was no meningeal enhancement. Cerebrospinal fluid (CSF) revealed 1,200 abnormal convoluted T lymphocytes/µl (fig. 1b), an elevated protein (3.0 g/l) and a normal glucose. An infection screen was negative, intrathecal JC antibody and DNA were not detected. Investigations confirmed ATLL confined to the central nervous system (CNS), bone marrow and blood. The patient responded to phenytoin, phenobarbitone and intrathecal and intravenous methotrexate with folinic acid rescue. He made a complete clinical neurological recovery, but later died of multiple organ failure. A postmortem could not be obtained.

This is an unusual case of HTLV-1-negative lymphoma-type ATLL [1]. The initial pulmonary infiltration was diagnosed as lymphocytic interstitial pneumonitis. The ATLL subsequently infiltrated the cerebral white matter and leptomeninges, causing the rare neurological complications of TIAs and status epilepticus. A minority of seronegative HTLV-1 ATLL cases (7–9.5%) have been reported [2, 3].

The incidence of ATLL CNS involvement varies from 2.5% in Japan (all HTLV-1-positive) [4] to 21% in Brazil [3], leptomeningeal infiltration is commonest [5]. Subclinical involvement may be higher [5]. Most ATLL patients die of systemic disease progression, the median survival time is 6–7 months [3, 4]. Isolated ATLL CNS relapses [5] correlate with a higher lymphocytosis, serum lactate dehydrogenase and calcium levels at diagnosis (not found in the present case).

TIA has only been described in 1 other case of ATLL, but the patient was HTLV-1-positive with a progressive neurological deficit and widespread grey and white matter infiltration [6]. The pathogenesis of TIA may be vascular infiltration as described in intravascular lymphoma. Status epilepticus as a neurological manifestation of ATLL has not been described. This may have occurred because of a sudden onset of leptomeningeal infiltration. Seizure control by anticonvulsants and chemotherapy induced CSF lymphocyte reduction uniquely allowed clinical neurological recovery despite cerebral white matter infiltration.

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