Porphyria cutanea tarda preceding AIDS

Sir—In porphyria cutanea tarda IgG is deposited in and around blood vessels in the skin and at the dermoepidermal junction, possibly as a result of vascular damage by porphyrin-light reaction. Porphyria cutanea tarda has been reported in patients with known HIV infection or in patients who subsequently developed AIDS. We report a case of porphyria cutanea tarda which preceded AIDS.

A 53-year-old man, not known to be HIV-infected, had blisters on the dorsum of his hands with erosions and milia for four weeks’ duration (figure, top). Erythema of the face and temporal hypertrichosis were noted. The patient did not consume alcohol. Histopathological examination revealed typical features of porphyria cutanea tarda. Direct immunofluorescence study showed intense IgA deposits at the dermoepidermal junction and the dermal vasculature (figure, bottom). Serum protein electrophoresis detected polyclonal gammopathy: IgA 9-6 g/L, IgG 24-7 g/L, IgM 3-72 g/L. Urine uroporphyrin was 543 nmol/day. Liver function tests were normal except for AST of 65 U/L. Hepatitis B surface antigen and anti-HAV and anti-HCV antibodies were not detected. Serum anti-HIV antibody was positive by western blot. CD4 count was 29/μL. Six weeks after the onset of skin blisters and two weeks after the diagnosis of porphyria cutanea tarda, the patient was admitted to hospital with pulmonary insufficiency and neurological abnormalities. He was found to have pneumocystis pneumonia, immunoblastic CNS lymphoma, and AIDS.

The relation between porphyria cutanea tarda and AIDS is unclear. Liver damage by hepatitis or by alcohol consumption cannot account for the development of porphyria in all cases, including ours. HIV infection predisposes patients to photosensitivity, and this may play a pathogenic role. HIV infection may interfere with porphyrin metabolism. Our case and others should alert clinicians to the possibility for HIV infection when encountering patients with porphyria cutanea tarda.

In this patient, the disproportionate increase of serum IgA may account, at least in part, for the IgA deposition in his skin. Interleukin-4 and interleukin-5 are the two T-cell helper subset 2 secreted cytokines responsible for stimulating IgA production by B cells. The massive increase in serum IgA in this patient infers an occurrence of T helper 1 to 2 immune switching, which has been linked to the progression from HIV seroconversion to AIDS as observed in this patient.

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HIV transmission by donor semen

Sir—In September, 1985, in The Lancet, Sydney researchers claimed “convincing evidence for transmission of HTLV-III [HIV]” to four women after in-vitro fertilisation with semen donated by a bisexual man. This report still remains the only evidence for HIV transmission by such means and is also considered one of the most important pieces of evidence proving the infectivity of semen. The evidence for transmission of HIV was based on western blot testing where each individual had the following bands: donor p24/gp41; first woman gp41; second woman p24/gp41; third woman p24/gp41; fourth woman p24. However, the present Australian criteria for a positive western blot are “reactivity to at least one glycoprotein (gp41-5, gp110-120, or gp160) and three other viral proteins of gag (p12, p18, p24, p30, p55) or pol (p34, p53, p68) origin. A negative western blot had to show no reactivity to viral proteins; reactivity to viral proteins that did not fulfil positive or negative criteria was considered indeterminate.” Thus, by the present criteria for a positive western blot in Australia none of the four women or even the donor would be considered HIV positive. Neither would any be positive under the criteria set by the FDA and the American Red Cross. In fact, two of the women would not be positive by any criteria anywhere in the world.

According to Fauci, “the least likely explanation for an indeterminate western blot is that the individual is infected with HIV”, and “The most likely explanation is that the patient being tested has antibodies that crossreact with one of the proteins of HIV. The most common patterns of reactivity are antibodies that react with p24 and/or p55”. The above data pose these questions: have these five individuals been retested and if so, have they all been found positive and by what criteria; if some or all were not found positive have the authors modified or retracted their claims; if not retested, why not and are they still considered to be positive.
infected with HIV; have any of these individuals been treated for HIV/AIDS and if so, with what drugs and on the basis of what tests?

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Fetal antigen 1 and growth hormone in pituitary somatotroph cells

Sir—Fetal antigen 1 (FA1), originally isolated from second trimester human amniotic fluid1 has been characterised as a new circulating member of the epidermal growth factor (EGF) superfamily.2 FA1 is a 32–38 kDa glycoprotein containing six EGF-like motifs, and it has been suggested that FA1 is the enzymatic cleavage product of a larger transmembrane precursor molecule defined by the cDNAs referred to as “human adrenal-specific cDNA, pG2”3,4 and “human delta-like cDNA, dlk”.5 Immunocytochemical analysis of the human embryo and fetus revealed the presence of FA1 in fetal hepatocytes, adrenal cortex, and all glandular cells of the pancreas anlage. In newborn babies and adults, however, FA1 expression seems to be restricted to the insulin producing (β-cells in the islets of Langerhans in the pancreas and to the adenals where the most pronounced staining reaction was seen in zona glomerulosa.5 Moreover, FA1 has been demonstrated in small cell carcinomas and carcinoid tumours of the lung.6 Because of the suggested relation between FA1 expression and neuroendocrine structures we analysed the pituitary gland and found cellular colocalisation of FA1 and human growth hormone (hGH). The figure shows that the FA1 staining was seen as a dot-like pattern corresponding to the Golgi-zone, whereas hGH was more uniformly distributed within the cytoplasm of the somatotroph cells, but with weak staining in the FA1-positive area. The Golgi apparatus is the site of post-translatory modification of proteins before secretion, and these findings suggest that somatotroph cells of the pituitary gland contribute to the circulating pool of FA1. The colocalisation of FA1 and somatotroph cells was observed in all five different apparently normal adenopituitary tissues examined.

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Intermittent maple syrup disease

Sir—The case report by Asola (Nov 18, p 1338)7 emphasises that patients with maple-syrup-urine disease, even mild variants, are at risk of encephalopathy when they are subjected to major metabolic stress. This disorder is widely regarded as very rare but this may not be so. Our experience suggests that the mild variants may be difficult to diagnose and therefore easy to overlook. During the episodes of decompensation, plasma aminoacid profiles are abnormal, but these often rapidly return to normal with treatment. Between attacks, plasma aminoacids are usually normal and the activity of the branched chain o xoacid (BCOA) decarboxylase complex in fibroblasts do not correlate well with the severity of the disease.2 Whole-body leucine oxidation in vivo may provide better insight into the disorder.

We studied two patients. One, a 15-year-old girl, presented at age 4 years with severe encephalopathy requiring intensive care (maximum plasma leucine 1600 μmol/L). Since then, on moderate protein restriction, she has been well with no episodes of decompensation and normal plasma aminoacid concentrations. The second, a boy aged 8 has had two episodes of encephalopathy with raised branched chain aminoacid concentrations but normal BCOA oxidation in cultured skin fibroblasts. Whole-body leucine oxidation was measured with a continuous infusion of 15-C-leucine8 and was 5 μmol/kg per h and 11 μmol/kg per h, 31% and 68% of the reference values of children of similar age.4 We conclude that measurement of the whole-body leucine oxidation establishes the diagnosis more reliably and