to normal. She remained relatively well for eight weeks but then needed re-admission with a leucopenia (0.9 × 10^9/l), recurrent herpes zoster and a chest infection. She was again confused with paranoid ideas. Her EEG showed diffuse changes, less pronounced than before. Prednisone only was resumed and she slowly improved. She remains in clinical remission (18 months later) on prednisone 20 mg on alternate days. Her family report her personality as changed; she is socially inconsiderate, apathetic and lacking in spontaneity. Despite global improvement in cognitive function, she has slight residual dysphasia and short-term memory difficulties.

Despite the lack of direct histological evidence, there are strong grounds for suggesting that the neuropsychiatric disorder observed was the result of central nervous system involvement in the Wegener's granulomatous process. The polydipsia and visual difficulties, noted early on may have been consequent upon contiguous invasion by granulomatous tissue from the nose or paranasal areas. The generalised disturbance, with evidence of cortical deficits appears more probably related either to remote cerebral granuloma or vasculitis than to further local extension. The fact that the neuropsychiatric disturbance arose following cessation of immunosuppressants and resolved following their reintroduction, makes their role as causative confusional agents improbable, nor could an infective or metabolic cause be detected.

Reviewing the few existing reports of pathological change in the brains of patients with Wegener's granulomatosis, it seems that diffuse cerebral involvement may occur with necrotic foci in optic nerves, thalamus, cerebellum and cortex.18 Recently Oimomi et al18 partially resected a lesion from the right parietal lobe of a patient with Wegener's granulomatosis in which granulomatous foci and necrotising angiitis coexisted. In that case, as in this, there was no evidence of renal involvement, an observation also made by Sahni19 in his patient with a reversible dysphasia. These patients conform to the concept of limited Wegener's granulomatosis, in which it appears effective to treat the neurological complications with glucocorticoids.

In the present case, the persistence of memory difficulties, language problems and personality change, suggests that structural damage has occurred. The patient's depressed and withdrawn presentation was initially attributed to her recent bereavement partially obscuring the eventual diagnosis of a cerebral granulomatosis responsive to treatment. Neuropsychiatric symptoms appearing in a patient with Wegener's granulomatosis should alert the clinician to this possibility.

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References

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Chronic meningitis in Fabry's disease

Sir: The usual neurological manifestations of Fabry's disease are two-fold: bouts of pain in the extremities due to peripheral nerve damage and cerebro-vascular accidents due to the thickening of vessel walls in the brain.1 Both are a consequence of the intracellular deposition of trihexosylceramide.2 The cerebro-spinal fluid (CSF) is normal or shows transient abnormalities. We report a case of Fabry's disease presenting as a chronic meningitis.

A 54-year-old male was first admitted to hospital because of an unexplained fever. For ten years, he had had painful paraesthesiae of hands and feet, oedema of the lower limbs, cardiomegaly and deafness. Six months before admission, he had developed fever, diarrhoea, back pain and lymph node enlargement. A lymph node biopsy specimen showed numerous macrophages with foamy cytoplasm. The diagnosis of Whipple's disease was proposed, although a biopsy of the jejunum was not conclusive. Oxytetracycline was given for nine months but proved ineffective. Upon readmission, the findings were similar with the exception of anaemia, leucopenia and thrombocytopenia. A bone marrow aspiration was normal. After a few days, the patient complained of headache. The neurological signs and symptoms were unchanged. The ESR was 120 mm/hour. CSF analysis showed 26 white cells and low glucose level. Repeated lumbar punctures confirmed the diagnosis of chronic meningitis (table.) No infectious disease was found (tuberculosis, brucellosis, listeriosis, mycosis, syphilis). A liver biopsy specimen was normal. There was no evidence of sarcoidosis or malignancy. The patient received isoniazid, rifampin and ethambutol for four months without effect. Steroids (10 mg/kg daily) were then added. They produced some improvement in clinical and laboratory abnormalities, but relapses occurred whenever the dose of steroid was reduced. Eighteen months later, a rise in the blood creatinine level (198 nmol/l) disclosed renal failure. The urinalysis was normal. A kidney biopsy specimen showed intracellular deposits of lipid in the glomeruli and tubules. The diagnosis of Fabry's disease was further substantiated by a decrease alpha-galactosidase activity in the plasma: 0-23 nmol/ml/hr (control: 7-9), in the white blood cells: 6-2 nmol/h/mg protein (control: 39) and in the urine: 1-1 nmol/ml/h (control: 13-8). Thin layer chromatography showed a massive excretion of trihexoside and digalactosyl ceramide in the urine. A history of deafness and death in early adulthood of several male relatives had been recorded in the family. The patient died of peritonitis, after a perforation of the small bowel while still on steroids.

In the present case, the discovery of a chronic meningitis was misleading since Fabry's disease is not listed among the many causes of chronic meningitis.3 The hypothesis that the meningitis was due to an intercurrent disease is unlikely as no other cause was found during the two year follow-up. CNS involvement in Fabry's disease seldom produces permanent changes in the CSF. Although intracellular deposits of lipid in the brain are common,4 sometimes extending to the arachnoid,4 the CSF remains normal or shows a mild increase in protein.5 Cellular changes have been occasionally noticed in the wake of cerebral attacks.6 Low glucose level was never mentioned. We believe that this is the first documented case of chronic meningitis in Fabry's disease. Fabry's disease should be added to the ever-growing
Letters

Table

CSF abnormalities (Steroids were started in February 1982)

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<td>Cell/mm³</td>
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<tr>
<td>P.N.: Polymorphs</td>
<td>26</td>
<td>25</td>
<td>31 (M: 54%)</td>
<td>2</td>
<td>14 (M: 63%)</td>
<td>5</td>
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<tr>
<td>M: Monocytes</td>
<td></td>
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<tr>
<td>LY: Lymphocytes (Ly: 71%)</td>
<td>4-8%</td>
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<tr>
<td>Protein g/l (% Gammaglobulin)</td>
<td>1-23</td>
<td>1-43</td>
<td>1-71</td>
<td>1-02</td>
<td>1-18 (10)</td>
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<td>Glucose g/l (Blood Glucose level: g/l)</td>
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<td>0-30 (1-18)</td>
<td>0-50</td>
<td>0-40 (0-90)</td>
<td>0-63</td>
<td>0-58</td>
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List of possible causes of chronic meningitis.

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References


Accepted 24 December 1984

Acute acquired toxoplasmosis causing neuropito-meningoencephalitis in an immunocompetent boy

Sir: Neurological involvement occurs in only 4-8% of cases of symptomatic acquired toxoplasmosis.1 The disorders include2 encephalopathies, meningoencephalitis, and enlarging cerebral mass lesions but, to date, optic neuritis has been reported only incidentally.3-5 Immunocompromised hosts usually are affected.6

A 13-year-old Caucasian boy, with unrecognised rare psychomotor seizures since the age of ten, developed, in mid-December 1981, progressive bilateral amaurosis with slight obtundation, moderate occipital headache and transient macular rash on the left inferior eyelid. On 8 Jan, 1982, inability to count fingers at 30 cm, normal peripheral visual fields on confrontations, bilateral reactive mydriasis, full oculomotor movements and normal ocular fundi were noted by a consultant ophthalmologist. Methylprednisolone 20 mg per day resulted in minimal improvement in vision, but fever and a generalised tonic-clonic seizure occurred.

On admission, on 19 Jan, 1982, central temperature was 38-3°C, and there was minimal obtundation. The bilateral central scotoma persisted, but oculomotor movements, pupils and ocular fundi were normal. Clinical examination was otherwise normal. CT scan showed bilateral areas of decreased density in the medial prefrontal regions with slight enhancement after contrast injection and no mass effect. EEG and right carotid angiography were normal. Lumbar puncture (table) showed 70/mm³ mononuclear cells with rare plasmocytes and normal protein, immunoglobulin G and glucose levels. Bacterial cultures were negative. Erythrocyte sedimentation rate was 3 mm/h. Routine blood and urine analysis and chest radiographs were normal. Tuberculin skin test was one plus. Daily infusions with 200 mg hydrocortisone hemisuccinate were given, with an immediate correction of the temperature and a moderate improvement in vision.

Two weeks after admission, the results of serodiagnosis were received. They were positive for Toxoplasma gondii (table) but negative for Rickettsia, Leptospira, Treponema pallidum, Brucella, Salmonella, Mycoplasma pneumoniae, Chlamydia, Myxovirus, Enterovirus, Herpes simplex virus, Cytophalagovirus, Adenovirus. The Paul-Bunel-Davidson reaction was negative. From 5 Feb, spiramycine 3 g and sulfadiazine 3 g per day were given orally for 45 days, with prednisone 30 mg per day for the 1st month, 15 mg per day for the 2nd month and 15 mg any other day for the 3rd month. Vision dramatically improved and the patient was discharged.

Three months later there was no complaint. Visual acuity, visual fields, ocular fundi and CSF analysis were normal. CSF inoculation into mice was negative. In August 1982, results were normal for serum and urinary electrophoresis and immunoelectrophoresis, serum circulating immune complexes, complement components, auto-antibodies to nuclear and organ antigens. Peripheral blood count, T and B cells percentages, T-cell subsets as determined by OKT monoclonal antibodies gave, as the only abnormal result, a slight increase of phenotype T 8 + (F Touraine, Hôpital Neurologique, Lyon). The HLA-typing was positive for the A₂, B₁, BW₃₄, and CW₅₇ antigens.

The patient was periodically re-examined up to Jan 1984. Fever and optic neuritis never occurred. After Jan 1983, the Sabin-Feldman test positivity decreased to 1:800 in serum. In Jan 1984, the electroretinogram was normal and pattern-reversal visual evoked responses were normal for the right eye (102 ms) but delayed for the left eye (116 ms). The cryo-preserved original sera were retested in May 1984 (J Andre, Institut Pasteur, Lyon), using the IgM-ELISA kit for T gondii (Labsystems, Helsinki). There was a slightly positive result for the first sample only.

This immunocompetent boy suffered from an acute meningoecephalitis with bilateral optic neuritis. The diagnosis of T gondii infection was considered from the results of initial serodiagnostic tests performed twice at a two-week interval. The Sabin-Feldman test was highly positive in the serum when first performed and a single high titre of 1:32 000 or more is considered as diagnostic.7 The possibility of missing the ascending phase of the antibody production is well-known,8 and, in our case, the overt disease had been progressing for at least 5 weeks. The IgM-IFA test was negative, but antitoxoplasmic IgM production can disappear after the first weeks of the infection, especially in

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