Letters

Tetrahydrobiopterin metabolism in senile dementia of Alzheimer type

Sir: The rate controlling co-factor in the synthesis of the neurotransmitters dopamine and noradrenaline is 5, 6, 7, 8-tetrahydrobiopterin (BH4). Disturbances in BH4 metabolism have been detected in various disease states showing neurological dysfunction. Recently, significantly reduced serum biopterin levels were reported for subjects diagnosed in life as senile dementia of Alzheimer type using a microbiological assay technique. We now report the use of HPLC to investigate the BH4 metabolism in subjects diagnosed post-mortem as suffering from dementia.

At post-mortem examination, samples of cerebro-spinal fluid (CSF) were obtained from demented subjects characterised as suffering from Alzheimer's disease or cerebrovascular disease, as well as from a group of age-matched controls. All subjects had been prospectively assessed for the presence or absence of dementia. Analysis of these samples was carried out using HPLC with a fluorescence detector, and the total biopterin estimated by acid/iodine oxidation prior to HPLC separation.

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Meningitis and disseminated cutaneous zoster complicating herpes zoster infection

Sir: Herpes zoster or shingles is commonly seen as a painful and unpleasant condition affecting a single dermatome. Rarely, however, more serious neurological complications may develop including meningo-encephalitis, encephalomyelitis, cranial nerve palsies and peripheral neuropathy. It is less well known that herpetic zoster infection can present as aseptic meningitis.

A 24-year-old computer operator from Guyana presented with a two day history of bifrontal headache aggravated by coughing and straining at stool, neck stiffness, photophobia and left-sided sharp chest pain which was worse with inspiration. On the day of admission he developed nausea and proasse. He had lived in Britain since the age of eight years and had not contracted chickenpox when aged ten. One year previously he had been vaccinated against smallpox. On examination he was unwell but not obtunded. His temperature was 38-5°C. He had marked neck stiffness with positive Kernig’s and Brudzinski’s signs and mild photophobia. The rest of the examination was completely normal. Initial investigations revealed Hb 13-5 g/dl, WBC 7-2 x 109/l (neutrophils 49%, lymphocytes 40%, monocytes 10%) and his blood film showed “reactive lymphocytes”. A biochemical profile including liver function tests, chest radiograph and ECG were normal. A lumbar puncture yielded clear CSF under normal pressure. Microscopic examination showed 410 WBC/mm3 (95% lymphocytes). Gram and acid-fast stains were negative. The CSF protein was 1-08 g/l and CSF glucose 4-0 mmol/l (blood glucose 5-3 mmol/l). Subsequent culture for viruses and bacteria was sterile. He improved considerably within 24 hours, but two days after admission a vesicular eruption suddenly appeared over the left posterolateral chest wall in the region of T5 dermatome at the site of his original chest pain. Over the next three days additional disseminated vesicles developed on the arms, legs and trunk. Characteristic herpes viruses were not seen when the vesicular fluid was examined by electron microscopy. An additional series of investigations was performed on EEG was normal; no viruses were isolated from CSF, throat or stool culture; serum varicella-zoster complement fixation test titre (VZ CFT) were <1/8 on admission, 1/64 after one week, 1/512 after two months and although cross-reacting herpes simplex antibody was detected there was no significant rise in titre; CSF VZ CFT titre was 1/8 after one week when the

Table: Concentrations of neopterin and biopterin in cerebrospinal fluid

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>Total neopterin in µg/l (mean ± SD)</th>
<th>Total biopterin in µg/l (mean ± SD)</th>
<th>Neopterin/biopterin ratio (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Senile dementia of Alzheimer type (8)</td>
<td>51-89</td>
<td>20-4±13-0</td>
<td>19-6±11-0</td>
</tr>
<tr>
<td>Cerebrovascular disease (3)</td>
<td>81-89</td>
<td>14-7±4-2</td>
<td>5-5±2-2</td>
</tr>
<tr>
<td>Control (7)</td>
<td>78-91</td>
<td>42-2±34-5</td>
<td>49-9±22-3</td>
</tr>
</tbody>
</table>

Using the Wilcoxon sum of ranks test, the values for total biopterin (biopterin + BH2 + BH4) were significantly lower (p < 0.05) in patients with senile dementia of Alzheimer type and cerebrovascular disease than in controls, although the neopterin levels were not significantly different. Other subjects suffering from neurological disorders also were investigated. Pick's disease patients showed reduced biopterin concentrations (13-5 and 22.0 µg/l) with neopterin concentrations of 37-0 and 60 µg/l respectively. One Huntington's chorea patient showed reduced levels of biopterin (16-0 µg/l) and neopterin (19 µg/l). A single cerebrovascular disease subject with no symptoms of dementia showed a reduced concentration of biopterin (15-0 µg/l) and a neopterin concentration of 44 µg/l.

The lower neopterin levels in patients with cerebrovascular disease and senile dementia of Alzheimer type suggest a dilution effect, possibly due to loss of brain tissue, which could account for the lower total biopterin concentrations. Alternatively, the low biopterin concentrations could be due, at least in part, to an impairment of tetrahydrobiopterin metabolism. This is in agreement with other results which show a reduced BH4 level in the CSF of a group of pre-senile dementia subjects.

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serum VZ CFT titre was 1/64; serological screening for other viruses was negative; syphilitic serology, Paul-Bunnell and sickle tests were negative; a second lumbar puncture performed one week after admission revealed 432 WBC/mm³ (95% lymphocytes), CSF protein 0-38 g/l, CSF glucose 2-7 mmol/l (blood glucose 5-9 mmol/l). The immunoglobulin and complement levels were normal and skin tests for cell-mediated immunity showed normal responses. He was well at follow-up six months later.

During chickenpox infection, virus in the skin vesicles probably ascends intraxonally along nerves to the sensory ganglia where it may reside latently for many years. Reactivation of zoster causes inflammatory necrosis of the ganglion with degeneration of related nerve roots accompanied by severe neuritis, a unilateral segmental inflammatory myelitis and localised leptomeningitis. As many as 40% of patients with uncomplicated zoster have a mild pleocytosis or a slightly elevated CSF protein or both. Nevertheless, despite this “localised meningitis”, clinical menigitis is extremely rare. Where it occurs it is usually in association with encephalitis. The most common presentation is meningitis with a disturbed sensorium but ataxia, convulsions and coma may supervene and in addition myelitis and cranial nerve palsies may further complicate the clinical picture. Hypoglycorrhachia is a recognised feature of infection with herpes zoster where meningitis, meningoencephalitis and encephalomyelitis occur. The CSF glucose of 2.7 mmol/l (blood glucose 5.6 mmol/l) in our patient is consistent with, but less marked than in the previous reports cited. The diagnosis of herpes zoster meningitis may be rapidly established by immunofluorescent staining of varicella-zoster antigen on CSF cells or measurement of varicella-zoster antibody in CSF by indirect immunofluorescence. Varicella-zoster antibody measured by complement fixation tests must be interpreted in relation to the serum antibody level. Dissemination of herpes zoster occurs in less than 2% of the general population and usually among older age groups. In immunosuppressed patients particularly those with lymphoproliferative disease or taking corticosteroids, this rises to 15% of cases of zoster. Although the prognosis is good complications are both unpleasant and serious; effective therapy may now be available in the form of acyclovir and possibly vidarabine.

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References


Neurological lupus erythematosus with tonic seizures simulating multiple sclerosis

Sir: Neurological manifestations occur in 20-60% of all patients with systemic lupus erythematosus (SLE). Included among previous clinical reports of neurological lupus are references to features resembling multiple sclerosis. Although well recognised in multiple sclerosis, tonic seizures have not been previously described in patients with SLE. A patient with serologically proven SLE is described who presented with clinical features consistent with multiple sclerosis including tonic seizures.

A 51-year-old single woman presented in February 1980 with a seven week history of pain, numbness and weakness of the right arm. Numbness gradually progressed to the right leg, left leg and then left arm associated with a band of numbness over the epigastrium. There was a transient Lhermitte's phenomenon and for three weeks horizontal diplopia. Over seven weeks she had become increasingly unsteady with leg weakness and was confined to bed. Apart from pneumonia one year previously there was no significant past history. On examination she was alert but bed bound with a moderately severe spastic quadriparesis. There was pseudooptochiasm and moderate ataxia of the arms. The deep reflexes were normal with bilaterally extensor plantar responses. Superficial sensation was intact but there was marked loss of proprioception and vibration sense in hands and feet. Apart from a first degree horizontal nystagmus on right and left lateral gaze, cranial nerve examination was normal. The general examination was normal. It was felt that the patient had evidence of two lesions, one in the brain stem and the other, major, lesion in the posterolateral columns of the high cervical cord. Investigation revealed an ESR of 94 mm in the first hour with a white cell count of 3,800/mm³ and normal differential white cell count. Anti-nuclear anti-

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