Letters

Treatment of post-traumatic choreo-athetosis with sodium valproate

Sir: We report a study which establishes the efficacy of sodium valproate in the treatment of post-traumatic choreo-athetosis.

A 28-year-old male was admitted to the hospital. At the age of nine years, he fell from a three storey building sustaining severe left sided cerebral damage. He was in coma for about one month, making a gradual recovery over the next four months. During recovery he developed right sided focal seizures, a right spastic hemiparesis and choreo-athetoid movements of the right arm. On examination, the abnormal findings were all on the right side and included a homonymous hemianopia, a spastic hemiparesis, mild limb atrophy, a cortical type of sensory deficit and a Babinski sign. Choreo-athetoid movements of the right arm were present, consisting of flexion-extension of the fingers and wrist supination, pronation and flexion of the elbow, and abduction of the shoulder. These movements were absent in sleep and increased by the stress induced by rapid questioning. The EEG showed sharp waves in the left frontal and temporal areas and a mild degree of slow wave abnormality in the same area. CT of the head showed a large area of decreased density in the left hemisphere with dilatation of the left lateral ventricle.

The patient’s seizures were well controlled with phenytoin, phenobarbital and methsuximide. The patient was started on sodium valproate at a dose of 250 mg by mouth three times a day. Within twelve hours of the first dose, the patient reported improvement in his involuntary movements. After one week, the dose was doubled and then increased to 500 mg four times a day with a dramatic reduction in the frequency of involuntary movements. At this point the patient entered into a controlled trial with placebo to establish the efficacy of sodium valproate in treating his involuntary movements. A single blind study design was used. The patient was not aware whether he was on sodium valproate or placebo, as the two looked identical. Since a mechanical recording device was used to count the frequency of involuntary movements in a thirty minute time period, observer bias was eliminated, thus avoiding the need for a double blind study. Simultaneous EEG and muscle recordings were made. The EEG was recorded to ensure that the involuntary movements were not part of a focal seizure. The muscle activity was recorded from surface electrodes placed on the deltoid, biceps and brachioradialis, the three muscles most involved in this patient’s movement disorder.

The frequency, duration and amplitude of the deflections from the resting state were used to classify the movements into major, moderate and minor. Sodium valproate levels were checked two hours after administering the oral medication. Muscle activity was recorded continuously for 30 minutes each time.

The frequency of major, moderate and minor involuntary movements and the corresponding sodium valproate levels are shown in the table. As serum sodium valproate levels rose, there was a reduction in the frequency of major and moderate involuntary movements. The minor involuntary movements observed at higher levels of sodium valproate were shorter in duration and involved fewer muscle groups compared to moderate and major movements.

The progressive improvement in this patient’s movement disorder as serum sodium valproate levels increased strongly suggests a cause and effect relationship. Furthermore, the “blinded” study design used adds strength to the observation. Recently there have been a growing number of reports of the use of sodium valproate in diverse movement disorders. Two groups reported its use for the treatment of hemiballism. Other movement disorders successfully treated with sodium valproate include Sydenham’s chorea, dysynergia cerebellaris myoclonica, non-epileptic myoclonus and kinesigenic familial paroxysmal choreo-athetosis. In a previous report we emphasised the possible significance of the rapidity of clinical response to sodium valproate. A review of other studies shows that a similar early response is seen in other movement disorders. The patient responded within twelve hours of onset of therapy. However, the biological significance of this observation can only be determined once the exact mechanism of action of sodium valproate is determined.

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References


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Recurrent cerebral abscess in hereditary haemorrhagic telangiectasia

Sir: Cerebral abscess carries a high mortality, with delay in establishing the diagnosis being an important contributing factor. Recognition of any predisposing cause facilitates earlier diagnosis and improves

Table

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<thead>
<tr>
<th>Sodium valproate</th>
<th>Number of movements (in 30 minutes)</th>
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</thead>
<tbody>
<tr>
<td>Serum level (µg/ml)</td>
<td>Oral dose (mgm)</td>
</tr>
<tr>
<td>57.0</td>
<td>500 four times daily</td>
</tr>
<tr>
<td>46.0</td>
<td>500 three daily</td>
</tr>
<tr>
<td>20.0</td>
<td>250 three daily</td>
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<tr>
<td>Below detectable</td>
<td>Placebo</td>
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prognosis. The association of cerebral abscess with pulmonary arteriovenous fistulae is well established, and occurs in approximately 5% of cases. Since pulmonary arteriovenous fistulae are found in over 15% of patients with hereditary haemorrhagic telangiectasia, cerebral abscess may also be a complication of this disease. The following case exemplifies the susceptibility of patients with pulmonary arteriovenous fistulae to cerebral abscess, and emphasises the need for an awareness of this association and of the occurrence of pulmonary fistulae in hereditary haemorrhagic telangiectasia.

A healthy 39-year-old postman was admitted in 1966 with a short history of headache and left focal convulsions. At the age of 32 years he had developed the typical appearances of hereditary haemorrhagic telangiectasia, although there was no family history of this disease. The following year a routine chest radiograph had shown several well-defined opacities subsequently demonstrated by pulmonary arteriography to be multiple arteriovenous fistulae. Successful resection of the largest fistula was performed in 1962. On examination he had clubbed fingers, was centrally cyanosed, with cutaneous telangiectases and a left spastic hemiparesis. No cardiac or extracardiac murmurs were audible. A chest radiograph revealed several coin-lesions consistent with pulmonary arteriovenous fistulae. A carotid arteriogram showed the presence a right-sided avascular space-occupying lesion and at craniotomy a large frontal abscess was drained. Treatment with penicillin and chloramphenicol was commenced with gradual resolution of the hemiparesis. In 1970 he was readmitted with a short history of headache and right focal convulsions. He was febrile with a flaccid weakness of the right arm. Chest radiographs revealed a new pulmonary arteriovenous fistula on the right. An isotope brain scan demonstrated a left frontal abnormality, and at operation a cerebral abscess was evacuated. Culture of the pus grew actinomycoses and he was treated with penicillin with resolution of the weakness.

In 1975 he was admitted with fever and a left hemiparesis. A chest radiograph showed that the previously recorded fistulae had increased in size. A CT scan demonstrated a right cerebral abscess which was aspirated and anaerobic streptococci were cultured from the pus. He was treated with penicillin and eventually made a good recovery. In 1981, after a two day history of fever and vomiting he became drowsy. On admission there was marked neck stiffness but no papilloedema or localising signs. The chest radiograph appearance had not changed, his haemoglobin was 18.2 g/l, and blood gases were compatible with a significant right to left shunt. Lumbar puncture revealed turbid CSF with 1,200 white cells (95% polymorphs) but without organisms demonstrable on Gram stain or culture. CT scan showed the typical appearances of a small abscess in the left temporal lobe, and he was treated with penicillin, chloramphenicol and fluocxacinil. His condition initially improved and serial CT scans showed a reduction in the size of the abscess. However, despite this he had a cardiorespiratory arrest and died.

Neurological symptoms have been reported in 33% of patients with pulmonary arteriovenous fistulae, and are generally more prominent in the presence of a large right to left shunt. In these cases hypoxia and polycythaemia may render patients liable to headaches, TIAs and convulsions, although paradoxical embolism of venous thrombus may also account for many of the transient focal symptoms. An increased incidence of stroke also has been described and may result from a combination of polycythaemia—facilitated thrombus formation, and paradoxical embolism. Rarely, air embolism following haemoptysis, or embolism of thrombus formed in situ in the fistula may be the cause of neurological symptoms. Arterial hypoxia, polycythaemia, and tissue hypoxia secondary to cerebral infarction, all compromise the brain's resistance and render it susceptible to infection. Taken together with a right to left shunt which circumvents the pulmonary capillary filter, a clinically silent bacteraemia or septic microembolism may result in the formation of a cerebral abscess in a patient with a pulmonary arteriovenous fistula. It is of interest to note that several case reports of cerebral abscesses complicating pulmonary arteriovenous fistulae have described the presence of an antecedent or coexistent infection. A cerebral abscess may be the first manifestation in hereditary haemorrhagic telangiectasia of an otherwise asymptomatic pulmonary fistula, and may develop before the skin lesions are apparent. Conversely its presence in a patient with the cutaneous stigmata of the disease invariably means a pulmonary arteriovenous fistula is present, even though its detection may require arteriography because occasionally the chest radiographic appearances are normal.

The abscess is usually single and supratentorial, although multiple, posterior fossa, and recurrent abscess have occasionally been described. However abscesses recurring with such frequency as in the case presented have not previously been reported, and only a few cases of meningitis complicating pulmonary arteriovenous fistulae have ever been documented.

Although pulmonary arteriovenous fistulae are responsible for the majority of neurological complications in hereditary haemorrhagic telangiectasia, cerebral vascular malformations account for over one quarter. Telangiectases are nearly always silent, but occasionally haemorrhage into the brain or subarachnoid space. Cerebral arteriovenous malformations also occur and can produce a constellation of symptoms and signs which are indistinguishable from those secondary to a pulmonary arteriovenous fistula. The rare coexistence of pulmonary and cerebral arteriovenous malformations may necessitate both pulmonary and carotid arteriography when neurological symptoms are present in a patient with hereditary haemorrhagic telangiectasia.

We have reported this case because it is a unique demonstration of the predisposition to cerebral abscess that patients with pulmonary arteriovenous fistulae display. On four separate occasions a cerebral abscess developed, one of which was associated with a meningitis. This complication, together with other hazards of an uncorrected fistula including paradoxical embolism and haemothorax, emphasises the need to resect single fistulae whenever feasible, even if asymptomatic. However operation may be impossible because of advanced age, poor pulmonary reserve, or multiple fistulae. Apart from selected cases who may benefit from therapeutic embolisation of the fistula, these patients will need long term antibiotic prophylaxis. Either penicillin V or oral erythromycin can be used for this purpose, as the majority of organisms isolated from abscesses complicating right to left shunts are susceptible to both antibiotics. However, additional appropriate prophylaxis should be given to cover any potentially bacteraemic procedure, such as dental extraction.

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