

hyperreflexia would not exclude a diagnosis of botulism.

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Herpes simplex encephalitis following a skull fracture

Herpes simplex encephalitis is an uncommon and severe infection, in which early detection and treatment significantly improve the outlook.¹ We report a case following a depressed skull fracture.

A nine year old boy with diabetes since the age of two was admitted with a head injury following a fall from his bicycle. Examination revealed a right frontal laceration. Skull radiographs showed an extensive bifrontal fracture, depressed on the left. At operation brain and cerebrospinal fluid was seen oozing from the laceration. A bicoronal scalp flap was turned. The depressed area was elevated and cleaned, and a burr hole was made to aid exposure and repair of a dural tear on the right. Ampicillin and flucloxacillin were given intravenously for three days and subsequently orally for four more days. He was

discharged on day 5 with no neurological deficit, and was given sodium valproate prophylactically.

On day 20 he was readmitted with a two day history of moodiness and staring episodes culminating in a generalised convulsion. Neurological examination was normal and he was afebrile. Blood sugar was 8 mmol/l. Diazepam was given rectally when a generalised convulsion was observed on the ward. A diagnosis of post traumatic epilepsy was made. An electroencephalogram showed moderate amplitude irregular waves in the frontal leads compatible with the recent injury. By day 23 he had had further episodes preceded by sensations of odd tastes and manifesting as altered consciousness with jaw clenching, drooling and post-ictal left sided weakness. Carbamazepine was added, and the frequency of these episodes decreased. On day 25 a cranial CT scan was normal.

On day 27 he developed a pyrexia and right sided earache. Examination of the ear was normal. The fever recurred the following day, and intermittent seizures progressed to focal status epilepticus which was controlled with an infusion of chlormethiazole. Lumbar puncture revealed 38 white cells, predominantly lymphocytes, and one red cell per high power field. CT scan showed an area of mixed density with enhancement in the right temporal region (figure). This raised the possibility of either an evolving bacterial abscess (although the CT scan lesion was contralateral from the site of the depressed part of the fracture), or a focal encephalitis. He was accordingly treated with chloramphenicol 100 mg/kg/day, benzylpenicillin 200 mg/kg/day, metronidazole 22 mg/kg/day, and acyclovir 10 mg/kg/day. On day 29 he deteriorated with diabetic ketoacidosis. A small ulcer was seen on his lip. A further electroencephalogram showed diffuse severe abnormality, with very high amplitude irregular delta waves occurring in all leads. Despite his increasingly critical condition, a right craniotomy was performed on day 31 to exclude the possibility of an abscess, and this revealed soft inflamed brain with no abscess. Histology of the biopsy specimen showed cerebral cortex containing foci of necrosis with oedema. Perivascular cuffing with lymphocytes was observed; occasional polymorphs and eosinophilic cells were seen. Gram stain for microorganisms was negative.

Herpes simplex virus was identified on electron microscopy, and was also subsequently cultured from the biopsy specimen. He was given ventilation for four days post-operatively. Acyclovir was continued for 10 days. Recovery was complicated by a dense left hemiparesis and a pseudobulbar palsy. Subsequently, he made an impressive recovery, and is currently able to run, but has dysarthria, and has little use in his left hand.

Intracerebral bacterial infection is a well recognised but, with appropriate management, a relatively uncommon complication of compound skull fractures, occurring at a rate of 4% in one large series.² There are no previous reports of herpes simplex encephalitis (HSE) following a skull fracture. Contamination of the wound is the route of spread of bacterial infection, but our case presumably represents a reactivated latent infection (from viral deoxyribonucleic acid present in the brain) in response to the considerable stress of the injury, rather than inoculation during the original injury.

Absence of a fever and an initially normal CT scan delayed the identification of infection as the cause until 10 days after the onset of symptoms, during which time the diagnosis was of post traumatic epilepsy. Craniotomy and brain biopsy are not felt to be mandatory to reach a diagnosis of HSE in children in whom there is little to suggest an alternative diagnosis,³ but in this case it was felt important to exclude the possibility of a cerebral abscess.

Focal seizures with altered consciousness should always alert the clinician to the possibility of HSE, even in the absence of a fever or CT scan changes.

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Could lamotrigine be useful in status epilepticus? A case report

Lamotrigine, a new putative antiepileptic drug¹ may have been effective in a case of status epilepticus. The patient was a 17 year old, mentally handicapped, right handed girl who had experienced epilepsy of unknown aetiology from the age of nine months and had been attending our clinic since 1981. At the time of her latest admission to hospital, the patient had been taking a combination of carbamazepine and phenobarbitone at daily doses of 1200 and 200 mg, respectively for about a year, with partial control of seizures (nocturnal tonic fits: 10-30 per month; atypical absences: 3-5/month; atonic seizures: 3-5/month). Interictal EEG recording was characterised by diffuse slow waves, occasionally accompanied by spikes or polyspikes isolated or grouped in symmetrical, generalised bursts. She was admitted to hospital for an unexplained sudden increase in tonic seizures (up to 4-6/hour without recovery of consciousness between fits). A

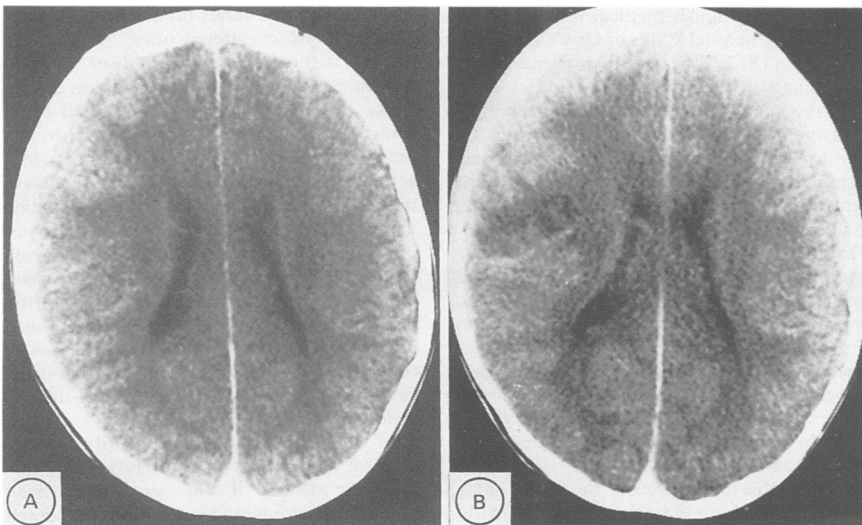


Figure Evolution of the right temporal lesion shown in CT scans; normal scan on day 25, lesion apparent on day 28.

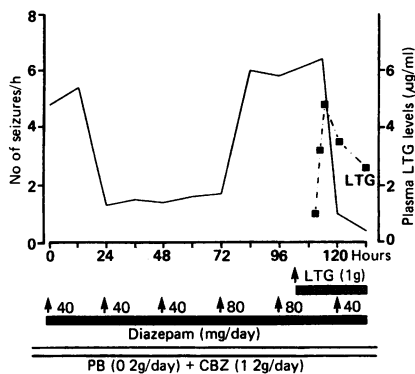


Figure Seizure frequency, drug doses and plasma concentrations of lamotrigine in the patient studied.
LTG = lamotrigine; PB = phenobarbitone; CBZ = carbamazepine.

nasogastric tube was inserted and intravenous fluids (0.9% NaCl) were started. An iv bolus injection of 10 mg of diazepam given over five minutes did not affect seizure activity (fig). Further 10 and 20 mg iv boluses of diazepam were injected after one and four hours respectively with a decrease in the number of seizures (up to 1/hour).

On the second day, an iv infusion of diazepam was started at a dose of 40 mg/24 hours and the same infusion rate was maintained for the third day. As seizures were continuing (1–2/hour) and with increasing frequency, on the fourth day the diazepam infusion rate was doubled (that is, 80 mg/24 hours). No effect was observed and the rate of infusion of diazepam was kept at 80 mg/24 hours for the fifth day.

During the first hours of the fifth day fits were occurring at a frequency of 6–7/hour. Since an intravenous preparation of phenytoin (a very effective drug in status epilepticus) is not available in Italy, lamotrigine was started at 7 am on the fifth day (30 hours after doubling the infusion rate of diazepam). Consent was obtained from the Protocol Review Committee and from the patient's parents. A 600 mg loading dose of lamotrigine (100 mg capsules, Wellcome Research Laboratories, Beckenham, UK) was given over four hours (200 mg × three administrations at two-hour intervals), followed by two additional 200 mg doses over the next 20 hours. Five hours after starting lamotrigine the fits became less frequent (five fits during the subsequent six hours and three during the following 13 hours). As the seizures remained well controlled (two to three per day), after three days the patient was discharged on phenobarbitone (100 mg twice a day), carbamazepine (400 mg three times a day) and lamotrigine (200 mg twice a day). The range of plasma drug concentrations (µg/ml) over the observation period were: phenobarbitone 30.7–35.6, carbamazepine 6.9–10.3, diazepam 0.5–1.8 and lamotrigine 0.4–4.9.

Our patient had a generalised convulsive status epilepticus, a condition which is known to be particularly resistant to treatment and to present frequent spontaneous remissions. However, both the inefficacy of diazepam at the increased rate infusion (that is, 80 mg) and the marked fall in frequency of fits five hours after lamotrigine administration suggest that the termination of status epilepticus in our patient may reasonably be attributed to lamotrigine. Single oral doses of drug (120–240 mg) had been found to be rapidly effective

within one to two hours in reducing interictal spike activity and the photosensitive range in epileptic patients.^{2,3} In addition, lamotrigine has been recently reported to dramatically reduce very frequent generalised tonic-clonic seizures⁴ and atypical absences⁵ and to stop the occurrence of non-convulsive status episodes.⁵

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First description of myasthenia gravis in Spain

Non medical classical literature occasionally yields detailed observations on some neurological disease which was unrecognised at the time. In the eighteenth century old literary traditions such as idealistic descriptions of protagonists, were replaced by a more realistic approach; heroes were portrayed as normal human beings, and this resulted in the description of real people complete with their medical conditions.

Sir Thomas Willis is usually credited with the first description of myasthenia gravis in western medical literature.¹ His report in 1672 of a woman who was able to "speak freely" on occasions but at other times became "mute as a fish" has been ascribed by some authors to hysteria rather than myasthenia. Masteller² recently suggested the existence of a still earlier historical description of myasthenia in an American Indian, in 1644. The first well documented case of myasthenia published in English medical literature was reported by Samuel Wilks of Guy's Hospital, London in 1877.³ The term myasthenia gravis was coined in 1895 by Jolly.⁴

In the Spanish literature, the first report of myasthenia appeared in a book written by Benito Pérez Galdós, a famous Spanish writer living in the second half of the nineteenth century. In *Tristana*,⁵ published in 1892, Galdós wrote:

"From her life full of work she was left with a nervous weakness and weakness of the eyelid muscles. She opened her eyes only halfway, and this with difficulty on certain days, or at times when certain winds ruled, sometimes reaching the point where she had to lift up her upper eyelid with her fingers when she wanted to see well any person. In addition, she was ill from her chest, and when the winter came along she was very ill."

Myasthenia gravis seems the most likely explanation for this clear description of an old woman with intermittent ptosis.

Galdós was an excellent observer of Span-

ish society during his lifetime. In addition to his well-recognised literary merits, he deserves the credit for the first description of myasthenia in the Spanish literature.

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MATTERS ARISING

Neuropsychological deficits in patients with minor head injury after concussion and mild concussion

I read with interest the report by Drs Leininger, et al,¹ further documenting "organic" mental deficits in patients with "minor head injury." Unfortunately, Dr Leininger and colleagues have failed to describe the basis for characterising their patients as having sustained "minor head injuries," other than implying that these patients suffered only brief periods of loss of consciousness. The emphasis on "organic" neurological deficits in patients with "minor head injury" is extremely appropriate and long overdue.

In my view, however, the major problem in this area is in the definition of "minor head injury." In most series the patients are considered to have suffered only "minor head injury" if they have suffered short duration loss of consciousness and no major disturbance of language or motor or visual functions. Most neurologists would affirm that only a relatively limited portion of the brain is actually involved in these specific four areas of brain function, and patients can easily sustain damage to large areas of brain tissue focally or diffusely without disruption of these particular and relatively limited areas of brain. Thus patients classified in this simplistic fashion as having suffered "minor head injury" may in reality have suffered loss of considerable portions of their brain and the discovery of "organic" neurological deficits should come as no surprise.

It would be much more helpful to the medical community and to those with this epidemic disease if the term "mild head injury" were confined to patients documented not to have lost brain tissue either focally or diffusely. However, diffuse loss of brain tissue