Figure 1 A single-photon emission computed tomography scan showing moderate hypoperfusion of the right temporal and parietal lobes during fugue with a follow-up scan 4 days later.

concentration was 0 and a urinary drug screen was unremarkable. A white cell count showed mild neutrophilia, but all other haematological and biochemical indices were normal. Cerebral computed tomography and lumbar puncture were normal. He started receiving empirical intravenous antibiotic and antiviral treatment and was admitted for observation.

The next morning, the patient's headache continued and he remained profoundly amnesic. However, he was able to write down a motorcycle license-plate number which was used by police to identify him. Further history then available from family members and the patient's regular neurologist showed a 20-year history of migraine with aura consisting of blurred vision and scintillation spectra, often followed by unilateral paraesthesias of one hand culminating in frontal headache contralateral to the hand.¹ The patient had experienced numerous prior episodes of amnesia often involving travel within the city and on one occasion several hundred kilometres between cities. Each episode invariably occurred in the context of a migraine, with the fugue state occurring after the onset of headache but not preceding it. The patient had also experienced migraines with shorter periods of amnesia lasting minutes, in which he forgot what he was doing but did not result in travel. On presentation, there were no historical features to indicate a primary psychiatric disorder and nothing to suggest the patient might be malingering. There were no recent psychosocial stressors. Cerebral magnetic resonance imaging (MRI) performed 3 months earlier had shown foci of increased signal in the subcortical white matter, consistent with white matter hyperintensities described in previous imaging studies of migraineurs.² We found no space occupying lesions or other structural abnormalities.

Migrainous fugue was diagnosed, and the patient was given 50 mg of sumatriptan. Within 3 h his headache improved, his autobiographical data returned, and he was suddenly able to give a comprehensive and lucid personal history confirming historical details already sourced from his family and doctors. The role of a single unblinded dose of

sumatriptan in his recovery should be interpreted with caution, as the patient subsequently reported that he had tried numerous drugs for his migraines (including sumatriptan) without success. An electroencephalogram (EEG) performed 3 h after the return of the patient's memory was normal. A SPECT scan also performed at this time showed moderate hypoperfusion of the right temporal and parietal lobes and mild frontal hypoperfusion compared with a follow-up scan at 4 days (fig 1).

Discussion

Fugue states are characterised by a complete loss of memory for all personal details and are often associated with travel from home. Although often witnessed on stage and screen, real-life fugue states are rare. The classical psychogenic dissociative fugue is said to be an unconscious reaction to a traumatic event where the person "forgets" in an effort to cope with the anxiety the event evoked.³ However, a range of organic causes have been reported, including complex partial seizures, drugs and head trauma.³ Changes in cerebral perfusion during migraine have been described in the literature.⁴ We hypothesise that our patient's recurrent fugue states are causally related to migrainous hypoperfusion of the temporal and frontal lobes, and the limbic region, in keeping with the SPECT findings. Markowitsch *et al* investigated a case of autobiographical amnesia and found similar perfusion changes on positron emission tomography scanning.⁵ However, to the best of our knowledge, there have been no previous case reports of fugue in the context of migraine with aura, with changes in cerebral perfusion documented by SPECT scanning.

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Severe chorea with positive anti-basal ganglia antibodies after herpesencephalitis

Chorea has been described as an initial sign of relapse in children with herpes simplex virus encephalitis. We describe the detection of anti-basal ganglia antibodies (ABGA) in plasma and cerebrospinal fluid (CSF) of a 2.3-year-old girl with severe chorea 3 weeks after acute herpes simplex virus (HSV) encephalitis. Although common neuroleptic and antidopaminergic drugs were ineffective, plasmapheresis combined with immunosuppression was followed by rapid and complete neurological recovery. These findings suggest a post-infectious, immune-mediated mechanism in this case of chorea after HSV encephalitis.

HSV encephalitis accounts for 10-20% of all viral encephalitis in the US.¹ Occasionally, chorea has been described as an initial sign of relapse with often poor prognosis. At least three pathogenic mechanisms are possible: occurrence of late-onset symptoms of the initial viral infection, recurrence of viral replication (owing to incomplete treatment of the initial HSV encephalitis or by selection of clones of aciclovir-resistant virus), or induction of a deleterious immunoinflammatory reaction.² Autoimmune-mediated brain disorders are well known after group A β haemolytic streptococcal infections: for example, Sydenham's chorea or paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS). Here, we

Figure 1 Timetable shows the course of disease and treatment over a 5-month period. Graduation of the bottom line reflects biweekly intervals. Common neuroleptics and antidopaminergic drugs were ineffective in altering severe chorea and ballism, leading to tube feeding and artificial ventilation. Full triangles, plasma and CSF samples with positive anti-basal ganglia antibodies (ABGA), empty triangles, negative ABGA on western immunoblots. Plasmapheresis was conducted five times, every other day, each exchanging a plasma volume of 60 ml/kg.

report on a case of severe chorea with positive ABGA 3 weeks after acute HSV encephalitis.

At 2.3 years, a previously healthy girl experienced acute HSV encephalitis with positive type 1 HSV polymerase chain reaction (PCR) in CSF and was treated with aciclovir, 30 mg/kg/day, for 15 days with rapid recovery. Follow-up HSV PCR in CSF was negative. Cranial magnetic resonance imaging (cMRI) showed bilateral temporal oedema and cortical necroses. Owing to several symptomatic focal seizures, she was discharged on oxcarbamazepine.

Three weeks after the initial onset, she developed a compulsive behaviour, restlessness, disturbed circadian sleep–wake rhythm and, within days, developed severe chorea. Streptococcal serology and antinuclear factors (ANF) as well as HSV 1 PCR and HSV 1 immunoglobulin (Ig) M in CSF were found to be negative, whereas HSV 1 IgG was found to be positive. cMRI showed bilateral cystic temporal lesions and mild, diffuse signal changes in supratentorial white matter; the basal ganglia appeared normal. An electroencephalogram (EEG) showed moderate generalised slowing and focal bitemporal spike wave discharges. Aciclovir (60 mg/kg/day for 21 days) and intravenous immunoglobulins (0.4 g/kg/day for 5 days) were of no benefit. Common drugs were ineffective (fig 1), and progressive swallowing difficulties necessitated nasogastric tube feeding. Five weeks after onset of chorea, nasotracheal intubation became necessary owing to severe laryngeal and pharyngeal dystonia.

ABGA, determined by immunoblotting in three pairs of samples, showed the presence of a specific, 60-kDa protein in plasma and in CSF. The antigen used was derived from human

caudate and putamen, flash frozen within hours of death. According to these findings, high-dose intravenous methylprednisolone (20 mg/kg/day for 3 days) was given, but remained clinically ineffective. Intermittent plasmapheresis and systemic immunosuppression resulted in rapid improvement and extubation after 2 weeks. Prednisolone was slowly tapered off over the next 6 weeks and prophylactic oral application of aciclovir (30 mg/kg/day) was stopped. cMRI at that time showed bilateral temporal cysts with surrounding gliosis and moderate global brain atrophy.

Extubation was followed by rapid and full neurological recovery over the following weeks. EEG showed persistent mild slowing over both temporal lobes without epileptic discharges. ABGA could not be detected immediately after the last plasmapheresis and in further plasma samples taken at different time intervals thereafter. Eighteen months after plasmapheresis, the patient experienced no further relapse.

Discussion

Our patient developed severe compulsive behaviour and chorea 3 weeks after an episode of HSV encephalitis. A relapse was excluded by negative HSV 1 PCR in CSF. Chorea and ballistic movements were resistant to common neuroleptics and antidopaminergic drugs. Nasogastric tube feeding and mechanical ventilation were necessary owing to swallowing difficulties and laryngeal stridor.

In parallel to Sydenham's chorea and PANDAS, we hypothesised that chorea after HSV encephalitis could also be an immune-mediated process. By means of western immunoblotting, we detected ABGA in three pairs of plasma and CSF. Compared with ELISA and

indirect immunofluorescence methods, ABGA western immunoblotting shows the highest sensitivity and specificity.³ In patients with PANDAS, the pathogenicity of ABGA was shown by positive and negative predictive values of 97% and 91%, respectively. This suggests that ABGA may be pathogenic.³

Molecular mimicry may play a major part in Sydenham's chorea as well as in PANDAS. Owing to antigen similarity, antibodies to streptococcal epitopes may cross react with specific basal ganglia antigens and lead to basal ganglia dysfunction or destruction.³ Another hypothesis raised in acute disseminated encephalomyelitis speculates that a disturbed blood–brain barrier may lead to systemic antigen presentation of proteins of the central nervous system and thus induce antibody formation.⁴ We found similar concentrations of ABGA in plasma and CSF of our patient and thus cannot distinguish between primarily systemic or autochthonous IgG production.

Plasmapheresis eliminates circulating systemic antibodies and was successfully applied in children with obsessive–compulsive disorders and tic disorders. On the contrary, systemic immunosuppression inhibits ongoing systemic as well as autochthonous ABGA production. Thus, a combination of these two approaches is reasonable. In our patient, ABGA were negative in plasma and CSF taken 10 days after initiation of this protocol.

Chorea after or associated with HSV encephalitis was primarily believed to be caused by late-onset symptoms or relapse of HSV encephalitis.^{2–5} As HSV 1 PCR was negative in some of the presented cases, it may be speculated that at least some of these patients may have

had immune-mediated chorea after herpes encephalitis. Our patient showed rapid and full neurological recovery within 6 weeks after plasmapheresis, accompanied by systemic immunosuppression.

Arguing against the risk of plasmapheresis in a potentially self-limiting process, disease duration may play an important part in the outcome. Some patients with HSV 1 PCR-negative relapse reach complete remission, but in most, relapse leads to additional neurological damage and poor outcome or death.²⁻⁵ In our patient, the diffuse signal change in the supratentorial white matter indicated a subtle but widespread inflammatory process accompanying the onset of chorea. cMRI 3 months after the onset of chorea showed moderate brain atrophy. Limitation of the disease process may have led to an improved neurological outcome in our patient.

This, to our knowledge, is the first report on ABGA-positive chorea after HSV 1 encephalitis. An underlying autoimmune mechanism was suggested by the finding of positive ABGA in plasma and CSF, as well as by rapid clinical improvement after plasmapheresis and systemic immunosuppression. Over an 18-month observational period, the girl did not show any relapse of compulsive behaviour or chorea.

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Brain stem encephalitis with central neurogenic hyperventilation

Central neurogenic hyperventilation (CNH) was defined by Plum and Swanson in 1959 as a syndrome of decreased PaCO₂, raised PaO₂ and respiratory alkalosis, in the absence of radiographic evidence of pulmonary congestion or inflammation.¹ A 72-year-old man was increasingly dyspnoeic for the past 6 months before local hospitalisation. In this period he lost weight, and his gait became ataxic. He needed more sleep, started to shake and fainted twice. He was fully awake as he walked into the hospital. Arterial blood gas analyses showed pH 7.59, pCO₂ 1.9 kPa (14.3 mm Hg), bicarbonate 18 mmol/l, base excess -12 mmol/l and pO₂ 15.2 kPa (114 mm Hg). Arterial blood gas analysis using an arterial catheter during sleep gave the same results. He was breathing at a frequency of 30/min.

The patient was transferred to a central hospital. On arrival, he was fully awake, but had slurred speech. Eye movements were saccadic and dysconjugate when he looked upwards, and there was a slight proximal tetraparesis. Deep tendon reflexes were hyperactive and Babinski sign was positive on the left foot. Spirometry, thoracic x ray, computed tomography of the brain and thorax were normal. Examination of the cerebrospinal fluid (CSF) was carried out on three occasions: 2 weeks after hospitalisation, and 2 and 12 weeks later. On the first occasion, there were 5 leucocytes/ml and a protein concentration of 0.78 g/l (upper normal limit 0.7 g/l). On the third occasion, examination disclosed 11000 leucocytes/ml (of normal appearance) and a protein concentration of 1.24 g/l. Oligoclonal bands were not present on agarose gel electrophoresis, and a test for antibodies against Borrelia was negative. CSF lactate was not analysed. A test for antinuclear antibodies including subgroups was entirely negative, suggesting no autoimmune disease. Electrolyte status in serum including sodium was normal.

Magnetic resonance imaging (MRI) of the brain carried out on four occasions, ranging from 1 week after hospitalisation to 13 weeks later (5 weeks before death), showed high-signal intensity lesions on T2-weighted and fluid-attenuated inversion recovery sequences in the ventral parts of the medulla oblongata, pons, mesencephalon, and in the medial parts of both temporal lobes (fig 1). There was a recent infarction in the left thalamus, which was shown on diffusion-weighted imaging. From the first to the second series, 3 weeks apart, there was a slight progression of pathology, whereas findings were principally unchanged on the next two occasions. DWI showed high-intensity lesion in the left thalamus on the first series, decreasing at the next, whereas lesions in the anterior part of the medulla oblongata showed high-signal intensity at the second series and repeatedly thereafter. Infusion of intravenous morphine 1-2 mg/h for 2 days reduced the hyperventilation without reducing the level of consciousness.

However, brain stem dysfunction progressed. Swallowing was impaired and led to four consecutive aspiration pneumonias, which could not be prevented by a tracheostomy. His condition gradually worsened; he was bedridden and was not able to hyperventilate, and was in need of continuous ventilator support. After 3 months of intensive care the family was counselled, the treatment was withdrawn and the patient died.

Histological examination of the brain showed a widespread non-expansive inflammatory process

Figure 1 Magnetic resonance imaging: fluid-attenuated inversion recovery series, sagittal view, showing widespread high-signal lesions from the upper part of the medulla oblongata all the way to the diencephalon.

throughout the brain stem, thalamus, corpus striatum and large areas of central white matter in the cerebrum and in the cerebellum. There was proliferation of microglia cells and seemingly activated lymphocytes. Lymphocytes were also seen infiltrating the meninges and surrounding vessels, although there was no vasculitis. Microglia cells expressed CD68, whereas most lymphocytes were T cells expressing CD8 and CD45RO. No T cells were CD4 or CD5 positive. A striking atrophy of neurones was seen in the affected areas of the brain. No microbial agents were identified.

CNH may be seen in comatose patients with head injury, stroke or infection. However, there are few reports on CNH in conscious patients. Our patient had normal consciousness during the 6 months before hospitalisation, making an infectious process in the CNS less probable at this stage. During the hospital stay, however, his mental status varied, paralleling critical illness episodes, in concert with the increasing magnetic resonance and CSF pathology. Thus, during the last 3-4 months before death, there were increasing signs of CNS pathology compatible with the post mortem findings of diffuse widespread inflammation.

The arterial blood gas analyses were compatible with a longstanding respiratory alkalosis. A base excess of -12 mmol/l was mostly due to retained acid to partially compensate for the loss of CO₂ via the lungs. The presence of hyperventilation during sleep distinguishes CNH from the traditional hyperventilation syndrome. Along with normal lung and cardiac examinations, the patient fulfilled the criteria of CNH.¹

In this case, lesions in the pons and medulla, visualised by MRI and confirmed by histopathological studies, may disrupt inhibitory afferent pathways to the respiratory centre. This is in accordance with most of the other reports on CNH.² One patient with CNH, however, had only a lesion in the thalamus.³ Our patient also had an infarction in the same area. However, according to the MRI characteristics, the infarction was too recent to explain symptoms of CNH for more than 6 months.

Neoplasms, primary CNS lymphoma in particular, are by far the most common cause of CNH, even though lymphomas constitute <1% of brain tumours.⁴ We have also previously described CNH in a patient with a pontine tumour.⁵ Others have reported astrocytoma, medulloblastoma, invasive laryngeal carcinoma,