and antiepileptic drugs considerably simplified. Video EEG performed after 1 year of PE and immunosuppression showed rare spontaneous jerks, clinically undetectable, appearing as occasional brief EMG bursts, followed by an EEG transient similar to that observed before immunotherapy (fig A₂).

Immunocytochemistry on rat brain slices with patient's IgG and CSF showed staining of cortical neurons (layer V) and apical dendrites with a pattern similar to that of commercial antibody to Kv1.6³ (see supplementary fig 2A–C; supplementary fig 2A–C can be viewed on the *J Neurol Neurosurg Psychiatry* website at <http://www.jnnpjnl.com/supplemental>).

Hyperkplexia or exaggerated startle can be distinguished from the normal startle response by its lower threshold, greater extent and resistance to habituation, criteria that were fulfilled by the features of the reflex movement disorder of our patient. The sequence of muscle activation and delay between EMG bursts recorded on proximal and distal limb muscles indicated a slow conduction time compatible with the activation pattern found in pathological startle reactions.⁴

An exaggerated motor startle reflex is one of the main features of hereditary hyperkplexia, but it has also been described secondary to other disorders involving the brainstem. In genetically transmitted startle disease, hyperexcitability probably results from a dysfunction of glycine mediated inhibition. In our patient, the excessive startle, which improved rapidly after PE, was associated with raised VGKC-Ab in serum and CSF, suggesting that an insufficient hyperpolarising effect might play a pathogenic role. To our knowledge, this is the first report on the association between startle and VGKC-Ab. The lack of neuromyotonia and of MRI changes of LE cannot be explained at present. The faint MRI changes observed in our patient may reflect the different distribution of VGKC within the CNS. The VGKC-Ab in our patients were mainly directed against the Kv1.6 subunit and these antibodies are less frequently observed in patients with LE.⁵

Jerks improved rapidly and dramatically after the first set of four PE. Improvement was then maintained with repeated apheresis and oral cyclophosphamide, with progressive tapering of prednisone up to withdrawal. The rapid response to PE suggests a role for humoral immunity in our patient.

Thyroid autoimmunity has been reported in patients with neuromyotonia or LE with VGKC antibodies.^{1–3} Our patient suffered hypothyroidism, and had positive TPO antibodies. However, the clinical features did not fulfil the diagnostic criteria for Hashimoto encephalopathy as they were not compatible with either the vasculitic or diffuse-progressive type presentation of Hashimoto encephalopathy. Moreover, there is still no evidence for the pathogenic role of thyroid antibodies.

The association of startle, thyroid antibodies, oligoclonal bands and response to plasmapheresis indicates an autoimmune pathogenesis in our patient and suggests that VGKC antibodies should be assayed in patients with CNS hyperexcitability.

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Supplementary data (video 1, 2, 3, avi and fig 2A–C) can be viewed on the *J Neurol Neurosurg Psychiatry* website at <http://www.jnnpjnl.com/supplemental>.

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Repetitive asystole in right insular haemorrhage

The insular cortex is known to be involved in central sympathovagal regulation. Both right and left insular lesions have been associated with cardiac derangements.

Previous stroke studies suggest that right insular lesions may cause reduced inhibition of sympathetic activity resulting in tachyarrhythmias, ECG changes, elevation of troponin T (TnT) and serum catecholamine levels, decreased heart rate variability, higher occurrence of sudden death and overall death rate within 3 months.

In contrast, recent data indicate a significant role of the left insula in mediating the

parasympathetic tone, and therefore lesions in this region may be associated with a shifted balance towards sympathetic activity.¹ In patients surgically treated for epilepsy, direct stimulation of the right insular cortex mainly resulted in sympathetic cardiovascular responses whereas stimulation of the left insula mainly caused parasympathetic reactions (bradycardia).² This is in agreement with the observation that barbiturate infusion into the human left carotid artery produced tachycardia whereas infusion into the right carotid artery generated bradycardia.³

Left insular lesions may be associated with decreased parasympathetic tone, shifting the balance towards enhanced sympathetic outflow and decreased heart rate variability.¹ Left insular strokes have been associated with adverse cardiac outcome, suggesting this mechanism.

Nevertheless, it is possible that both types of responses can be evoked from either insula. In the rat, prolonged left insular stimulation results in both cardiac sympathetic and parasympathetic activation.⁴ Cortical lateralisation of cardiac autonomic regulation has been suggested but the data are contradictory.

Case report

We report the case of a 51-year-old man with right insular haemorrhage who suffered from repetitive asystoles during his stay in our neurological intensive care unit (NICU). The patient had a history of treated arterial hypertension and presented with sudden onset left sided hemiplegia and somnolence. Cranial CT showed a right insular haemorrhage with intraventricular blood (approximate volume 22 ml). CT angiography did not show any arteriovenous malformation or aneurysm. The patient was treated within the 4 h window with activated recombinant factor VIIa (rFVIIa) and phenytoin because of left sided partial seizures. Because of the developing obstructive hydrocephalus, the patient was intubated, mechanically ventilated and an external ventricular drainage was inserted. The ventilator associated pneumonia was treated with ciprofloxacin and piperacillin with tazobactam, which were later changed to meropenem. Within the first 9 days, phenytoin, a beta blocker and propofol were administered without any complications for 8, 6 and 4 days, respectively.

After reduction of analgesedation on day 9, the patient suddenly developed asystole requiring cardiopulmonary resuscitation. Episodes of sudden asystoles without preceding bradycardia recurred up to five times with a duration of 10–50 s. At the time of the first asystole, the patient was on a low dose of beta blocker, phenytoin and propofol. These drugs were discontinued and phenytoin was substituted for levetiracetam. All asystole events were managed successfully with 0.5–1 mg atropine. A transthoracic cardiac pacemaker was placed temporarily. The observation was made that the asystoles were triggered by vagal stimulation (eg, the patient breathing against the ventilator, manipulation of the endotracheal tube or suctioning). The next day, the bradycardiac episodes ceased by minimal handling, deep analgesedation and after placement of a tracheotomy. No temporal relation of asystoles with any newly started medication was observed. Subsequent cardiological workup, including repeat ECGs, serum TnT and creatine kinase-MB levels and transthoracic echocar-

diography, revealed no cardiac disease. On day 12, transient depression of the ST segment as well as elevation of cardiac TnT to 0.04 µl/l was noted. By day 13, the ST segment and cardiac TnT level had normalised.

Discussion

To our knowledge a case of asystole in a patient with right insular haemorrhage has not yet been reported. We have found one case reporting asystole in acute right middle cerebral artery (MCA) stroke involving the territory of the right insular cortex.⁵ We hypothesise that the asystole resulted from the right insular haemorrhage which induced a shift in autonomic balance with disinhibition of the left insular parasympathetic influence. Triggered by vagal stimulation, the parasympathetic outflow imbalance may have been responsible for the cardioinhibitory effects and asystole.

Another phenomenon observed in this patient was ST depression and TnT elevation. Observations made in physiological animal models suggest that stimulation of the left insula may result in ST depression, QT prolongation, pronounced bradycardia and rhythms ending in asystole.⁴ Interestingly, these changes were associated with elevated noradrenaline levels suggesting that left insular activation may result in both parasympathetic and sympathetic responses.⁴ Similarly, we assume that our patient had a complex autonomic imbalance favouring left insular effects, which may be interpreted as both parasympathetic and sympathetic dysregulation. Interestingly, an important delay between stroke onset and the development of asystole and/or ST depression and TnT elevation was observed. This agrees with the observations of Pasquini⁶ that autonomic changes associated with insular damage in acute stroke may have a delayed appearance.

It could be argued that we cannot completely exclude the possible prothrombotic effect of rFVIIa. However, the dynamics of ST segment changes and TnT levels were not characteristic of a possible cardiac origin. Furthermore, the drug is unlikely to have been the cause of the ST and TnT changes because of the short half life of rFVIIa. Phenytoin, beta-blockers and propofol have the potential to cause bradyarrhythmias and in combination may have contributed to generating the asystoles. However, there was no temporal association between the introduction of medications and the asystole events. Moreover, these drugs were administered continuously for several days without any complications. There was no electrolyte imbalance or any other condition favouring cardiac rhythm disturbances. Intracranial pressure remained stable (<10 mm Hg) for the whole observation period.

In the context of previous data, the coexistence of the insular cortex lesion and the cardiac derangements is highly suggestive of a causal association.

Our case and the results of previous studies demonstrate the ambiguity of central autonomic disturbances mediated by lesions affecting the central autonomic network, in particular the insular cortex and connections between the left and right insula. However, the close association of insular lesions with cardiac derangements is strong, and intensive monitoring of patients with this type of lesion is necessary.

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Transient cauda equina compression syndrome and headache caused by internal vertebral venous plexus engorgement in a teenage female with vena cava inferior agenesis and iliac vein thrombosis

The internal vertebral venous plexus (IVVP) is part of the vertebral venous system (VVS). This system is the main alternative venous pathway, which joins, parallels but at the same time bypasses the caval venous system. The clinical relevance of the VVS is underestimated. We report on a patient who presented with cauda equina compression syndrome that was caused by engorgement of the IVVP. IVVP engorgement resulted from bilateral iliac vein thrombosis for which congenital agenesis of the inferior vena cava (IVC) was diagnosed as the predisposing factor.

Case report

A 17-year-old female, with an unremarkable medical history, was referred to our hospital. She had suffered progressive lower back pain for 14 days and a cramp-like burning sensation in her left leg for 11 days. In addition, she had paroxysmal paresthesias in both feet. On the day of referral she was unable to walk because of diffuse non-radicular pain and weakness in both legs which developed within seconds after standing up. In this position, she also suffered from severe headache and vomiting. Physical examination revealed a body temperature of 37.6°C. Both inguinal fossae were tender to palpation. Neurological examination, including

fundoscopy, was unremarkable. Laboratory tests revealed elevated C reactive protein (233 mg/ml (normal <4 mg/ml)), leucocytes ($8.9 \times 10^9/l$ (normal $4.0\text{--}10.0 \times 10^9/l$)) and thrombocytes ($611 \times 10^9/l$ (normal $150\text{--}350 \times 10^9/l$)). Echography confirmed the clinical suspicion of bilateral iliac vein thrombosis. CT of the abdomen (fig 1A) showed: (i) aplasia of the infrarenal IVC segment, (ii) bilateral thrombosis of the iliac veins and (iii) extensive dilatation/distension of the ovarian and renal veins as well as the external vertebral venous plexus (EVVP) and the azygos vein. MRI of the lumbar spine (fig 1B, C) showed cauda equina compression due to engorgement of the lumbar IVVP. Brain CT was normal.

It was concluded that the cauda equina compression was caused by engorgement of the lumbar IVVP in the presence of a congenitally compromised venous drainage of the lower limbs and small intestine due to IVC agenesis (IVCA). She was given warfarin which was replaced later by coumarine. Recovery was complete within 1 week. Oral contraceptives were discontinued. At follow-up after 1 year, she had no complaints.

Discussion

IVCA was regarded as a major precondition for the lumbar IVVP engorgement that developed in our patient after iliac vein thrombosis. The latter caused an increased caudal inflow into the IVVP, while this venous pathway was already challenged by IVCA. In acute thrombosis of a normally developed IVC, congestion is the dominant cause of enlarged epidural veins. This may similarly provoke radicular pain. IVCA, which we demonstrated in our patient, is one of the developmental variations that may occur during the embryogenetic formation of the IVC in the sixth to eighth gestational weeks (incidence rates vary between 0.6 and 3.0%). IVCA is most frequently detected in the evaluation of deep venous thrombosis or as an incidental finding.

Alternative routes for venous return in the absence of IVC are, respectively, the (hemi-) azygos system, the vertebro-lumbar route, the anterior abdominal wall veins and the transumbilical portocaval route (fig 2). The vertebral route is involved in 95% of patients and is the sole route in 70% of such cases. Anterior abdominal wall veins are used in 15% of cases, almost always in addition to the vertebro-lumbar route. The anterior abdominal wall venous pathway requires higher pressure to overcome venous valves and is only used if common iliac veins are thrombosed. Transumbilical portocaval shunting is found in 15% of patients and is the sole route in one-third of those cases.¹

In our patient, the infrahepatic segment of the IVC continued as the hemiazygos vein to the superior vena cava. Cauda equina compression and headache were logically explained by the functional anatomy of the VVS. The VVS is a valveless extradural plexiform venous network with a longitudinal pattern. It can be divided into three intercommunicating divisions: (1) the IVVP consists of veins surrounding the dura mater within the spinal canal (2), the basivertebral veins comprise the vessels within the vertebral bodies and (3) the EVVP surrounds the vertebral column.² The IVVP extends the entire length of the vertebral column and finds a cranial terminus in the dural sinuses. The system communicates with the segmental (intercostal) veins of the thoracic-abdominal wall and with the azygos system and thus forms a “bypass” of the