

A. R. Gande  
I. R. Taylor  
K. M. Nolan

## Autonomic instability and hypertension resulting in subarachnoid haemorrhage in the Guillain-Barré syndrome

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A. R. Gande (✉) · I. R. Taylor ·  
K. M. Nolan  
Southampton General Hospital,  
Tremona Road, Southampton SO16 6YD,  
UK  
e-mail: RGande@aol.com  
Tel.: + 44(1425)47 03 80  
Fax: + 44(1202)44 26 72

Anaesthetic department,  
Southampton General Hospital,  
Tremona Road, Southampton SO16 6YD,  
UK

**Abstract** We report the case of a 47-year-old woman with Guillain-Barré syndrome who developed autonomic instability and hypertension and subsequently developed a subarachnoid haemorrhage. This was manifested clinically by a seizure which began focally and became generalised. Computer tomography demonstrated a localised haemorrhage in the left central sulcus. Control of the hypertension was achieved with intravenous labetalol. Autonomic instability and hypertension are frequently reported in Guillain-Barré syndrome. Sub-

arachnoid haemorrhage is an uncommon but serious complication.

**Key words** Subarachnoid haemorrhage · Polyradiculoneuritis · Sympathetic nervous system

### Introduction

Guillain-Barré syndrome (GBS) is an acute demyelinating polyneuropathy with an annual incidence of 0.75 to 2 cases per 100,000 population [1]. Its presentation and clinical course are highly variable. Typically, the disease follows a trivial infection and begins with painful paraesthesia and muscular weakness, initially distal but progressing proximally. Facial muscles, eye movements and the muscles of respiration and swallowing may all be affected. Autonomic instability is a frequent accompaniment, especially in patients with more severe disease [2]. There may be under- or overactivity of the sympathetic or parasympathetic nervous system [3]. Typical findings are abnormal sweating, hypertension, postural hypotension, electrocardiographic changes, arrhythmias and sphincter disturbance.

We report a case in which a prolonged period of hypertension in a previously normotensive patient with clinical and laboratory findings of GBS culminated in a period of profound cardiac rhythm disturbance and a fo-

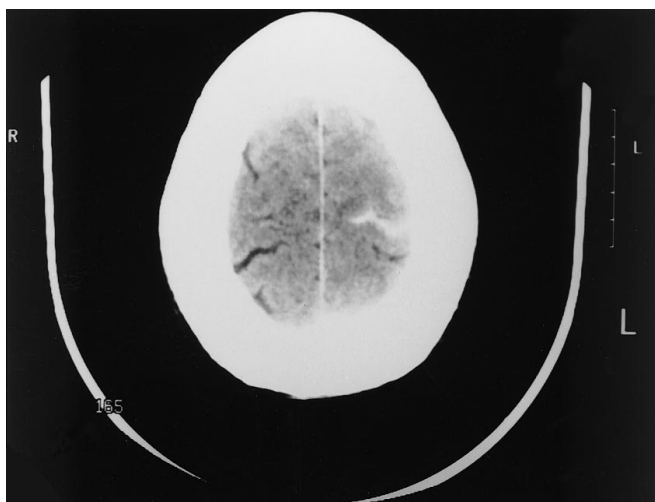
cal onset seizure. Computer tomography demonstrated a localised subarachnoid haemorrhage.

### Case report

A 47-year-old woman was admitted with a 5-day history of progressive paraesthesia, limb weakness and breathlessness. The preceding week the patient reported an episode of diarrhoea, which settled spontaneously. On the day prior to admission she developed a frontal headache and leg weakness to the extent that she was unable to walk. Bladder and bowel function were normal. Her past medical history was unremarkable and she was on no regular medication.

Initial examination revealed bilateral lower motor neurone weakness affecting all limbs. The weakness was maximal proximally and associated with absence of knee and ankle reflexes. There was no objective sensory deficit. Fundoscopy was normal.

Investigations showed an elevated white cell count of  $10.4 \times 10^9/l$  (with a normal differential count), forced vital capacity (FVC) of 2.5 l, cerebral spinal fluid (CSF) protein of 1718 mg/l (normal range 0–500 mg/l) with a white cell count of  $2/mm^3$ , red blood cell count of  $5/mm^3$ , glucose 4.3 mmol/l and no organisms



**Fig. 1** Computer tomography of the brain showing subarachnoid blood in the left central sulcus

seen on microscopy. Chest radiograph was unremarkable. Stool culture was negative for *Campylobacter*. A diagnosis of GBS was made and a 5-day course of immunoglobulin (0.4 g/kg per day) commenced. Four-hourly monitoring of FVC was continued on the ward.

During the next 24 h, the limb weakness progressed. Her FVC fell to 1.5 l and she developed a lower motor neurone left facial nerve palsy. She became subjectively short of breath.

Three days following admission to hospital the patient was transferred to the intensive care unit (ICU) for close monitoring of respiratory function. She remained stable over the next 12 h with no further deterioration in FVC. Arterial blood gases on air showed arterial oxygen tension ( $\text{PaO}_2$ ) 12.3 kPa, arterial carbon dioxide tension ( $\text{PaCO}_2$ ) 4.9 kPa, pH 7.44, peripheral oxygen saturation 96%. The following morning she was noted to be hypertensive with a blood pressure of 210/105 mmHg, for which she was commenced on oral nifedipine 10 mg twice a day. This subsequently reduced her blood pressure to 180/85 mmHg. Central venous pressure readings during this time were 12–14 mmHg.

That evening the patient had a seizure which was focal in onset, beginning on the right side of the face, and then became generalised. While 100% oxygen was being administered she had runs of self-terminating ventricular tachycardia lasting for up to 10 successive beats and then developed a supraventricular tachycardia of 170 beats/min. A rapid sequence induction was performed and she was intubated and ventilated. The patient was cardioverted to sinus rhythm with a single synchronised DC shock of 100 J.

CT (Fig. 1) showed a concentration of subarachnoid blood in the left central sulcus. Anteriorly in the frontal lobe was a region of apparently thickened cortex with increased attenuation. No abnormal vessels were seen.

The arrhythmias were now presumed to be secondary to the subarachnoid haemorrhage, in the absence of any other obvious precipitants. Serum potassium was 4.2 mmol/l, she was not hypoxic, hypercarbic or acidotic ( $\text{PaO}_2$  12.1 kPa,  $\text{PaCO}_2$  4.6 kPa, pH 7.45), and there were no preceding electrocardiographic changes. Neurosurgical opinion was sought, and in view of the unusual location of the haemorrhage it was thought not to be due to aneurysmal disease and therefore cerebral angiography was considered to be unnecessary.

She was commenced on nimodipine 60 mg 4-hourly and phenytoin. She remained intubated for 9 days as her ICU stay was complicated by pneumonia and a failed extubation due to laryngeal oedema. During this period she required a labetalol infusion at 20 mg/h to control hypertension.

Further investigations revealed a normal autoimmune profile. Nerve conduction studies showed severe demyelinating polyneuropathy with denervation indicating secondary axonal loss. Magnetic resonance imaging could not detect any evidence of signal alteration or structural abnormality in the left frontal lobe in the region of the CT documented lesion. Normal flow void enhancement was seen in the superior sagittal sinus. The report stated that an aneurysm could not be totally excluded but this would be an unusual pattern of aneurysmal subarachnoid haemorrhage and the differential of cortical vein thrombosis was raised.

She was discharged to the general ward 11 days after admission to the ICU and transferred to the rehabilitation unit 2 weeks later. Two months later she continued to improve slowly with almost normal function of the upper and lower limbs and can mobilise with a frame. There are no abnormalities indicating cerebral dysfunction and her facial palsy has recovered completely. Atenolol 25 mg/day is still required to control hypertension; however, nimodipine and phenytoin were withdrawn after 3 weeks with no adverse sequelae.

## Discussion

This case shows many of the typical features of GBS. The preceding diarrhoeal illness, and the distribution of sensory and motor symptoms with facial and respiratory weakness, are characteristic as are the hypertension, arrhythmias, CSF and electrophysiological findings. Central nervous system involvement is uncommon [1] though delirium has been reported in association with autonomic dysfunction in GBS [3], as has seizure activity [4]. In this case, the focal onset of the seizure, beginning with the right side of the face, correlates well with the site of the subarachnoid haemorrhage and, in the absence of any history of epilepsy, is most likely explained by the intracranial lesion.

It is now thought that autonomic neuropathy affects most patients with GBS. The manifestations may be mild, such as tachycardia or postural hypotension, but there may be life-threatening arrhythmias including sinus arrest. Indeed, paroxysms of severe autonomic dysfunction may be followed by sudden death [3]. In a recent review, Zochodne [5] states that autonomic dysfunction is an important cause of death in GBS, in addition to respiratory failure and thromboembolism. In one series of 100 patients [2] there were 13 fatalities, 7 of whom developed serious arrhythmias and 4 of whom died directly as a result of the rhythm disturbance.

Hypertension, a known predisposing factor for subarachnoid haemorrhage, occurs in between 28 and 61% of cases of GBS [2, 3] and may persist after resolution of the neurological symptoms. The mechanism has not been fully elucidated, but there is evidence for excessive sympathetic activity as a cause. An early

study [6] showed that limb blood flow in affected patients failed to increase in response to a rise in blood temperature; the authors suggest a disturbance of central vasomotor control may be responsible. Studies of haemodynamic variables in patients with GBS [7] have demonstrated elevated cardiac index and systemic vascular resistance, providing further evidence of sympathetic overactivity. Several authors have demonstrated high levels of urinary catecholamine excretion in hypertensive patients with GBS [8], which could be explained by either a central or a peripheral lesion leading to increased sympathetic tone. Although there is little information available from post-mortem studies, one report of findings in three patients showed degenerative changes in the paravertebral sympathetic ganglia, and in a later report of a detailed post-mortem examination of one patient there was significant involvement of the sympathetic chain, with ganglionic infiltration and demyelination, accompanied by changes in the intermediolateral horns of the spinal cord [9].

Reports of the consequences of hypertension in GBS have included chest pain, encephalopathy and, to our knowledge, one case of subarachnoid haemorrhage [8]. In the latter report, the haemorrhage was attributed to a hypertensive crisis (presumably causing an intracranial aneurysm to rupture, although cerebral angiography findings are not reported). We postulate that a period of hypertension was also responsible for the haemorrhage in our patient. Neurosurgical consultation was obtained; it was thought that an aneurysm at the site of the haemorrhage was extremely unlikely and that angiography and its attendant risks were not warranted. A cerebral vasculitis was considered, although a negative autoimmune profile militates against this.

In view of the potential for serious complications arising from hypertension, as exemplified by this case, it would seem prudent actively to seek evidence of autonomic dysfunction in all cases of GBS and to monitor elevations in blood pressure closely. Vasodilating agents are perhaps best avoided because of their potential for producing reflex tachycardia. The potential for excessive response to antihypertensives and vasopressors would suggest use of agents with shorter half-lives, and the ability carefully to titrate dose to response favours intravenous agents. Esmolol has been used in GBS to control sinus tachycardia, in a dose of 50 µg/kg, then infused at 250 µg/min [10].

Management of subarachnoid haemorrhage in the context of GBS should focus on avoidance of rebleeding and vasospasm. Meticulous attention to airway control and ability to clear secretions is also essential, particularly in those with already compromised respiratory function. Additional sympathetic drive resulting from inadequate sedation and airway manipulation may further predispose to hypertension and arrhythmias increasing the risk of rebleeding; appropriate use of sedatives is essential. The calcium channel blocker nimodipine has been shown to improve neurological outcome following subarachnoid haemorrhage, possibly through amelioration of vasospasm.

In summary, we describe a patient who experienced autonomic neuropathy in association with severe GBS, resulting in hypertension, subarachnoid haemorrhage and a seizure. Autonomic neuropathy is extremely common in GBS and accounts for a large proportion of the fatalities. Hypertension often results and can have serious consequences. It therefore warrants careful assessment and management, in a setting where the response to treatment can be monitored appropriately.

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