Hypertension and papilloedema in the Guillain-Barré syndrome

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SUMMARY Three patients with the Guillain-Barré Syndrome are described, one of whom was relapsing. Hypertension persisted for three to four months in two patients, associated with increased urinary excretion of catecholamines. Baroreceptor sensitivity, although depressed, did not explain the hypertension. It may be due to lesions affecting either central vasomotor control or peripheral sympathetic nerve activity. Two patients had papilloedema. This has been attributed in the literature to defective reabsorption of CSF due to high protein concentration. Normal reabsorption of isotope labelled albumin from the subarachnoid space argues against this explanation in our cases.

Although somatic nerves are predominantly affected in the Guillain-Barré syndrome, vasomotor disturbances, including hypertension may occur (Eiben and Gersony, 1963; Marshall, 1963; Davies and Dingle, 1972). This might stem from depression of baroreceptor activity, defective central control of blood pressure, abnormal sympathetic nerve function, or catecholamine release. Three cases are described; hypertension was prolonged in two, and of short duration in the third. Urinary catecholamines were estimated. Two patients with papilloedema had isotope encephalography to test for defective reabsorption of cerebrospinal fluid.

Case 1

A 40 year old woman had an influenzal illness with tingling in the hands in January 1971. Ten days later numbness of the feet and weakness of the arms developed, progressing to complete paralysis of the legs during the next three days. There was a past history of thyrotoxicosis. She had been normotensive in three pregnancies, and her blood pressure was recorded as 110/70 mmHg in 1969.

On admission to a general hospital she had slight left ptosis, right facial weakness, moderate weakness of the upper limbs, profound weakness of the lower limbs, impairment of pin prick and light touch

sensation below the knees, depression of all tendon jerks, and flexor plantar responses. Ocular fundi were normal. The blood pressure was 180/120 mmHg. The pulse rate was 120/minute and slowed with carotid sinus pressure. There was no cardiac abnormality.

At the end of the first week in hospital she developed a chest infection with impaired ventilation (FEV_1 1 litre; alveolar pCO_2 = 46.7 mmHg), was transferred to the Northern General Hospital and improved 24 hours after starting treatment with ampicillin and receiving physiotherapy (FEV_1 = 1.4 litre, pCO_2 = 38 mmHg).

The rise in blood pressure is illustrated in Fig. 1, with gradual decrease in blood pressure to 120/70 mmHg after 15 weeks in hospital. The resting pulse rate was 100-120/minute for two weeks, about 90/minute for four weeks, then fell to 80/minute.

Six weeks after admission, she complained of headache and anorexia. On examination she now had papilloedema with haemorrhages and exudates, but normal visual acuity. The optic discs gradually returned to normal in the next four weeks. There was progressive recovery of normal power over eight months.

Full blood count, blood urea and electrolytes, ECG, ANF, VDRL, Paul-Bunnell titre, intravenous pyelogram, renogram, chest and abdominal radiographs were normal. Findings at lumbar puncture, and urinary hydromethoxymandelic acid (HMMA) excretion are shown in the Table. Intra-arterial brachial artery pressure recordings showed normal responses to the Valsalva manoeuvre; baroreceptor sensitivities, measured by estimating the cardiac

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Fig. 1 Case 1. Supine blood pressure recordings at weekly intervals after admission. Times of HMMA collections and of presence of papilloedema are shown.

slowing induced by injection of phenylephrine (Gribbin *et al.*, 1971) were 3.74, 4.4, and 3.95 increase in pulse interval (ms) increase in systolic pressure (mm) on 4 March, 27 April, and 17 August, respectively. Applying a regression equation for predicting baroreceptor sensitivity from age and mean arterial pressure (Gribbin *et al.*, 1971), the log sensitivities were 0.573, 0.648, and 0.597, while the predicted sensitivities were 0.851, 0.928, and 0.904, on these dates.

Isotope encephalography by injection into the

lumbar subarachnoid space of ¹³¹I-labelled albumin (RISA) on 5 April, with rectilinear scanning at two, four, eight and 24 hours, showed normal distribution and rate of decrease of the isotope in the cranial subarachnoid space.

Case 2

A 19 year old man developed a mild upper respiratory tract infection in January 1972, followed by tingling in the hands and feet and weakness of the limbs two weeks later.

On examination he had weakness of the upper limbs, and moderate weakness of the lower limbs, normal sensation, absent tendon jerks, and flexor plantar responses. The blood pressure was 180/120 mmHg and pulse rate 115/minute.

Between the eighth and 10th days after admission, he developed dysarthria, dysphagia, facial weakness, ptosis, diplopia, and impaired ventilatory function. After tracheostomy, artificial ventilation was required for four weeks. ACTH, 80 international units, was administered for 11 days. The hypertension persisted during, and for six weeks after, this period of ventilatory failure (Fig. 2). There was gradual recovery of power in 18 months.

Blood count, blood urea, and electrolytes, ECG, and viral antibody titres were normal. Lumbar puncture and catecholamine excretion results are shown in the Table.

Case 3

A 24 year old woman developed, in September 1974 when six months pregnant, diplopia for three weeks, and weakness of the right leg which persisted until after delivery of a normal baby, when she recovered except for a slight residual limp. In February 1975

Table Data in three cases

		Lumbar puncture results									
		Normal	Case 1			Case 2			Case 3		
Days after admission:			1	8	55	1	9		13	31	56
CSF protein	0.600 g/l	0.95	1.56	2.36		0.94	1.92		1.91	1.32	1.13
CSF pressure	150 mmH ₂ O	125	140	220		130	180		220	190	180
		Urinary catecholamine excretion (μmol/24 h)									
		Case 1			Case 2					Case 3	
Days after admission:		31	40	135	6	9	62	63	97	20	
HMMA	61.0	75	43	18							
Conjugated metanephrines	0.7-3.0				3.1	3.3	1.3	—	—	1.2	
Noradrenaline*	133 ± 33		—		—	369	—	260	178		
Adrenaline*	38 ± 15		—		—	91	—	28	28		
Total catecholamine*	171		—		—	460	—	288	206		

*Method adapted from Anton and Sayer (1962).

Fig. 2 Case 2. Supine blood pressure recordings at weekly intervals after admission. Fluctuating blood pressure for the first five weeks represented by continuous lines for the highest BP and broken lines for the lowest BP on the day of the recordings. Times of total catecholamine and conjugated metanephrine collections, IPPV, and ACTH treatment are shown.

weakness of the right leg increased, diplopia recurred and, in May 1975, she developed paraesthesiae in the feet and the fingers. On admission to a general hospital she had, on examination, partial bilateral sixth nerve palsies, loss of all tendon jerks, flexor plantar responses, intact abdominal reflexes, and moderate global weakness of the right leg.

At lumbar puncture the CSF protein was 2.0 g/l, with fewer than five cells per ml. Skull and chest radiographs, lumbar pneumoencephalogram, and cerebral isotope scan were normal. There was no improvement with dexamethasone 1 mg four times daily, or prednisolone 60 mg, daily, but two months later, without treatment, her symptoms improved markedly.

In mid-August 1975 she deteriorated again, and, despite oral prednisolone 60 mg daily, became tetraplegic, and was transferred to the Neurological Unit.

On examination, there were bilateral sixth nerve palsies, normal ocular fundi, flaccid tetraplegia, absent tendon jerks and plantar responses, 'stocking' sensory loss to the mid-calf. The blood pressure was 190/80 mmHg. There was no abnormality of heart, chest or abdomen.

On the third day after admission her blood pressure rose to 140/110 mmHg, and continued at this level for three days, then decreased to 120/90 mmHg with varying diastolic pressures between 90 and 70 mmHg in the next four weeks, gradually settling to diastolic pressures between 60 and 70 mmHg.

Two weeks after admission she was noted to have bilateral papilloedema but no visual impairment. The papilloedema varied considerably, in that it was most marked after recumbency, and less after sitting up. There was gradual improvement in motor power between one and four months after admission when she was discharged. In January 1976, she was normal except for slight weakness of the right leg and absent tendon jerks; the blood pressure was 100/70 mmHg.

CSF and urinary conjugated metanephrine results are shown in the Table. The CSF pressure and the protein concentration were raised. Full blood count, glucose tolerance test, urea and electrolytes, serum calcium and phosphate, liver function tests, protein-bound iodine, VDRL, ANF, Epstein-Barr virus titre, urinary porphyrins, plasma and urinary cortisol, and chest radiographs were normal. Motor nerve conduction velocities in the right median and ulnar nerves were very slow at 24 and 16 m/s. Intra-arterial blood pressure recordings with Valsalva manoeuvre, angiotensin, and stress were normal. The lowest recorded FEV₁ was 2 l when the results of blood gases were within normal limits. Fluorescein angiography showed changes consistent with papilloedema. An isotope encephalogram showed normal reabsorption of ¹³¹I-labelled albumin.

Discussion

Hypotension (Birchfield and Shaw, 1964), fluctuating hypertension (Marshall, 1963; Davies and Dingle, 1972), and persistent hypertension (Eiben and Gersony, 1963) have been previously noted in the Guillain-Barré syndrome. The frequency of hypertension has varied from none in a review of 97 cases (Weiderholt *et al.*, 1964), to 29 out of 48 cases (Eiben and Gersony, 1963). Hypertension has been noted most frequently in patients with ventilatory failure, but in our first case ventilatory impairment was transient, while, in case 2, hypertension preceded and outlasted ventilatory failure. Case 3 had no respiratory difficulties.

There are several possible mechanisms for the hypertension. Experimental denervation of baroreceptors (Dickinson, 1966), and lesions of vagal and glossopharyngeal afferent nerve fibres in man produced experimentally (Guz *et al.*, 1966) or by kanamycin toxicity (Corcoran *et al.*, 1960), cause hypertension. In case 1, cardiac slowing with carotid sinus pressure, and the normal response to the Valsalva

manoeuvre, indicated preservation of some baroreceptor function. The baroreceptor sensitivities, taking into account the patient's age and mean arterial blood pressure, were low, but are of the order found by Gribbin *et al.* (1971) in patients with idiopathic hypertension, and could be interpreted as adaptive changes to hypertension, a mechanism which has been described experimentally (McCubbin *et al.*, 1956; Aars, 1968). The baroreceptor sensitivity remained low even when the blood pressure had returned to normal, suggesting that hypertension was not secondary to depressed baroreceptor sensitivity, or *vice versa*.

Appenzeller and Marshall (1963) suggested a disturbance of central control of blood pressure. Pathological studies suggest that central involvement is usually minimal (Haymaker and Kernohan, 1949; Asbury *et al.*, 1969), but lesions may occur in the brain stem (Roseman and Aring, 1941; Lowenberg and Foster, 1945). There is also pathological (Matsuyama and Haymaker, 1967; Asbury *et al.*, 1969), and clinical (Spalding and Smith, 1963) evidence of peripheral sympathetic nerve lesions.

The high urinary catecholamine excretion in cases 1 and 2 corroborates Mitchell and Meilman's (1967) study in one patient, and the report of increased hydroxymethoxymandelic acid excretion during the acute phase in patients requiring ventilation (Davies and Dingle, 1972). Hypertension may occur after acute stress in man (Brod *et al.*, 1959), and chronic stress in animals (Forsyth and Harris, 1970). While the stress of the severe illness in our patients could have caused the hypertension and high catecholamine excretion during the acute phase, its persistence into the recovery phase suggests a structural lesion affecting catecholamine release. The adrenaline is derived from the adrenal medulla, whereas the noradrenaline may arise, at least in part, from sympathetic nerves. This increased release of noradrenaline, adrenaline, and their metabolites could arise either from a peripheral sympathetic nerve lesion, including the innervation of the adrenal medulla, or from a central disorder of vasomotor control.

Papilloedema was noted when the CSF pressure was 220 mmH₂O in both cases. The protein concentrations were 2.76 and 1.91 g/l. Blood pressure recordings were about 140/90 and 120/90 mmHg. The absence of visual impairment in either case is against 'papillitis'. The occurrence of papilloedema, with raised intracranial pressure in the Guillain-Barré syndrome has been described previously and reviewed by Morley and Reynolds (1966). The two hypotheses for explaining the increase in intracranial pressure are defective reabsorption of CSF (Denny-Brown, 1952; Gardner *et al.*, 1954) and cerebral oedema (Joynt, 1958). Isotope encephalography has

been used to study defective CSF reabsorption, but has not previously been reported in this condition. The normal distribution and rate of reabsorption of ¹³¹I-albumin in the subarachnoid space in both cases argues against a major defect of reabsorption of CSF. Although there is no direct evidence for cerebral oedema apart from Joynt's (1958) report of intracellular oedema in one case, or clinical features of a central disturbance, the increased intracranial pressure may, like the similarly obscure disorder of benign intracranial hypertension, arise from oedema rather than impaired CSF reabsorption.

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