Observations on cardiovascular and neuroendocrine disturbance in the Guillain-Barré syndrome

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SUMMARY Cardiovascular disturbances were found to be a common feature of patients with the Guillain-Barré syndrome who were severely paralysed, requiring assisted ventilation. Glycosuria was noted in association with these disturbances, and in five patients investigated we found impaired glucose tolerance tests at the height of the paralysis. Catecholamine and 17-hydroxycorticosteroid urinary excretions were found to be high in four patients investigated when the neuropathy was most severe, and in one patient plasma cortisol levels were high with loss of diurnal variation. With recovery from paralysis cardiovascular disturbances became less marked, catecholamine and 17-hydroxycorticosteroid urinary excretions reverted to normal, glucose tolerance improved but remained abnormal in three patients during the period of observation. It is suggested that increased levels of catecholamines and cortisol contributed to the development of impaired glucose tolerance and cardiovascular disturbances.

Since the advent of assisted respiration for the treatment of respiratory failure in the Guillain-Barré syndrome the mortality of this disease has been reduced from between 30% and 50% to less than 10% (Miller, 1966). Cardiovascular disturbances are now a significant factor in mortality. We observed an association between cardiovascular disturbance and the presence of glycosuria in the Guillain-Barré syndrome. We report here the results of glucose tolerance tests, catecholamine, and 17-hydroxycorticosteroid urinary excretion in some of our patients.

METHODS

Five patients with the Guillain-Barré syndrome were investigated (see Table). All had an acute symmetrical polyneuritis in which motor involvement predominated over sensory changes; the cerebrospinal fluid protein was high with a normal cell count, except in patient no. 1 whose clinical course was complicated by a subarachnoid haemorrhage. Poliomyelitis and porphyria were excluded by the appropriate tests. All patients developed respiratory failure which necessitated tracheostomy and intermittent positive pressure ventilation (IPPR). They were nursed lying flat and turned two-hourly from side to side. A Complan diet containing 2,500 calories and approximately 400 g of carbohydrate was given by a nasogastric tube.

Blood pressure and pulse rate were recorded half hourly by the nursing staff. Capillary blood glucose

concentrations were measured by a modification of the glucose oxidase method (Clark and Timm, 1968) two hours after a 50 g glucose meal following an overnight fast. Urinary 24-hour 3-methoxyhydroxymandelic acid (VMA) excretions were estimated using the method of Georges and Small (1962). The upper limit for this laboratory is 8 mg/24 hours. Analysis of 24-hour urinary excretion of 17-hydroxycorticosteroids (17-OHCS) was made using the method of Few (1961). Plasma 11-hydroxycorticosteroids (11-OHCS) were estimated according to Mattingley's method (1962).

RESULTS

In all five patients cardiovascular disturbances became apparent as paralysis progressed. All patients developed a pulse rate of over 100 per minute at the height of the neuropathy and blood pressure became extremely labile (see Table). Systolic and diastolic blood pressures were greatly elevated on occasions; readings of 300 mmHg systolic and 140 mmHg diastolic were recorded. A hypertensive crisis was probably responsible for the subarachnoid haemorrhage in patient no. 1. Sudden hypotension with blood pressure readings of 50 mmHg systolic occasionally alternated with hypertensive bouts. Electrocardiographic (ECG) changes occurred in all patients except patient no. 5. These consisted of S-T segment flattening and T-wave inversion

TABLE
CLINICAL FEATURES AND INVESTIGATIONS

	Patient no. 1 (age 56, female)					Patient no. 2 (age 16, male)				
	1	2	3	4	5	1	2	3	4	5
Age of illness										
Blood pressure										
Stability (mmHg)										
Systolic variation	—	88 ± 27	74 ± 38	30 ± 14	31 ± 16	40 ± 14	40 ± 13	27 ± 11	24 ± 10	18 ± 8
Diastolic variation	—	42 ± 16	42 ± 20	23 ± 10	17 ± 8	30 ± 0	31 ± 9	22 ± 8	18 ± 9	13 ± 7
Range of BP (mmHg)										
Systolic	—	110 to 250	50 to 300	120 to 180	100 to 160	100 to 160	100 to 190	110 to 170	100 to 150	110 to 140
Diastolic	—	60 to 140	0 to 150	50 to 110	60 to 110	50 to 100	50 to 110	60 to 110	60 to 100	60 to 90
Heart rate (/min)	—	70 to 160	80 to 120	60 to 100	60 to 100	80 to 130	75 to 135	80 to 130	70 to 100	75 to 100
ECG changes	—	+	—	+	—	—	+	—	—	○
Urinary excretion of VMA (mg/24 hr)	—	17.5	—	2.3	—	—	12.3	3.2	—	—
Urinary excretion of 17-OHCS (mg/24 hr)	—	14.1	—	—	—	—	—	—	—	—
Normal range	—	—	21.9	—	8.3	—	54.9	—	—	8.3
Urinary variation of plasma 17-OHCS (μg/100 ml.)	—	—	2.5 to 11	—	—	—	—	3 to 14	—	—
Urinary blood glucose (mg/100 ml.)	—	264	—	198	131	—	118	120	—	83
	Patient no. 3 (age 63, female)					Patient no. 4 (age 72, male)				
	1	2	3	4	5	1	2	3	4	5
Age of illness										
Blood pressure										
Stability (mmHg)										
Systolic variation	40 ± 26	83 ± 33	52 ± 10	27 ± 11	13 ± 6	31 ± 12	60 ± 16	70 ± 18	62 ± 21	27 ± 21
Diastolic variation	30 ± 17	51 ± 14	32 ± 8	25 ± 7	13 ± 6	24 ± 14	31 ± 9	44 ± 12	45 ± 15	19 ± 13
Range of BP (mmHg)										
Systolic	140 to 200	70 to 220	80 to 170	90 to 160	110 to 130	130 to 190	70 to 170	70 to 180	70 to 180	90 to 170
Diastolic	80 to 120	80 to 130	50 to 100	40 to 100	60 to 80	70 to 130	50 to 110	30 to 110	30 to 115	30 to 115
Heart rate (/min)	85 to 120	80 to 130	75 to 125	75 to 120	75 to 95	80 to 105	70 to 120	55 to 130	75 to 125	75 to 110
ECG changes	+	+	+	—	○	+	+	+	—	○
Urinary excretion of VMA (mg/24 hr)	6.4	10	—	—	4	6.6	17.3	10.2	—	4
Urinary excretion of 17-OHCS (mg/24 hr)	16.3	—	—	2.7	—	—	15.3	—	—	4.1
Normal range	—	—	2 to 10.3	—	—	—	—	4 to 14.5	—	—
Urinary variation of plasma 17-OHCS (μg/100 ml.)	9 a.m. 36.4 11 p.m. 28.2	—	—	9 a.m. 22.8 11 p.m. 9.5	—	—	—	—	—	—
Urinary blood glucose (mg/100 ml.)	—	208	—	—	127	107	—	138	158	124
	Patient no. 5 (age 55, male)									
	1	2	3	4	5					
Age of illness										
Blood pressure										
Stability (mmHg)										
Systolic variation	—	26 ± 9	27 ± 12	25 ± 6	11 ± 5					
Diastolic variation	—	24 ± 5	33 ± 6	23 ± 13	13 ± 6					
Range of BP (mmHg)										
Systolic	—	110 to 150	110 to 150	100 to 140	100 to 130					
Diastolic	—	60 to 90	60 to 100	50 to 90	60 to 80					
Heart rate (/min)	—	75 to 115	70 to 115	65 to 105	60 to 85					
ECG changes	—	○	○	○	○					
Urinary excretion of VMA (mg/24 hr)	—	—	—	—	—					
Urinary excretion of 17-OHCS (mg/24 hr)	—	—	—	—	—					
Normal range	—	—	—	—	—					
Urinary variation of plasma 17-OHCS (μg/100 ml.)	—	—	—	—	—					
Urinary blood glucose (mg/100 ml.)	—	240	—	—	68					

KEY

Stages of illness

1. Onset of illness to tracheostomy and I.P.P.R.
2. Tracheostomy and I.P.P.R. to height of paralysis.
3. Height of paralysis to commencement of weaning off ventilator.
4. Weaning period.
5. Off ventilator.

* Blood pressure lability is represented by the mean (±SD) daily range of systolic and diastolic blood pressures of each stage of illness.

† Normal range corrected for age and sex.

+ Present.

○ Absent.

— Not done.

affecting mainly leads II and III, AVF, and V_1 to V_3 but occasionally seen in AVL and V_4 to V_6 . Patient no. 4 developed ventricular extra systoles. Blood gas estimations in all patients ruled out anoxia, hypercapnia, and hypocapnia ($pCO_2 < 30$ mmHg) as possible factors for these disturbances except in patient no. 4. Difficulty was experienced in weaning him off the ventilator because he suffered from chronic bronchitis and ankylosing spondylitis and occasionally became hypercapnic ($pCO_2 < 59$ mmHg). This possibly contributed to the vasomotor instability seen in this stage of his illness. Patients nos. 1, 2, and 3 had retention of urine which was quickly recognized and required catheterization. This event did not appear to contribute to the cardiovascular disturbances. As the paralysis diminished the cardiovascular disturbances became less marked and the ECG reverted to normal in all except patient no. 1 (see Table).

Glycosuria was noted in patients nos. 1, 3, and 5 at the height of the illness. Impaired glucose tolerance developed in association with this as indicated by a high two hour blood glucose concentration (see Table). As the neuropathy abated, glucose tolerance improved and reverted to normal except in patients nos. 1, 3, and 4. There was no family history of diabetes mellitus in any of these patients. VMA estimations in four patients revealed a higher than normal urinary excretion at the height of the illness when cardiovascular disturbance was severe. With recovery from paralysis VMA excretion returned to within normal limits (see Table). The urinary excretion of 17-OHCS followed a similar pattern (see Table). Plasma 11-OHCS concentrations were measured in patient no. 3 and were high, with loss of diurnal variation during deterioration of the neuropathy. Plasma concentrations returned to normal and diurnal variation was re-established when the neuropathy improved.

DISCUSSION

Hypertension and tachycardia contributed to the death of 11 of 50 fatal cases of Guillain-Barré syndrome examined by Haymaker and Kernohan (1949). An abnormally labile blood pressure was also noted by Marshall (1963) and Eiben and Gersony (1963); the latter regarded this as a poor prognostic sign. One of our patients, not included in the present series, died after a hypotensive episode and patient no. 1 developed a sub-

arachnoid haemorrhage, probably as a result of a hypertensive crisis. Cardiovascular disturbances characteristically occur only in severely paralysed cases at the height of the illness. Apart from patient no. 4, these disturbances could not be attributed to poor ventilation. Marshall (1963) also noted that these disturbances occurred in well ventilated patients.

It has been suggested that these disturbances are due to autonomic nervous system involvement. Appenzeller and Marshall (1963) suggested a central lesion but Spalding and Smith (1963) postulated an interruption of the autonomic reflex in both the efferent and afferent pathways. The pathological findings of Matsuyama and Haymaker (1967) revealed lesions of the intermediolateral horns of the spinal cord, sympathetic trunk, ganglia, and the IXth and Xth cranial nerves.

Although stress may have played a part in the increased urinary VMA excretions in our patients, this could also be due to irritative lesions of the sympathetic nervous system and failure of uptake of catecholamines in damaged parts of this system. It is known that a denervated organ has heightened sensitivity to catecholamines and the cardiovascular disturbance seen in our patients may be due to the combined effect of increased concentrations of catecholamines and impairment of the carotid sinus reflex. The subarachnoid haemorrhage could have contributed to the high VMA urinary excretion in patient no. 1, though Hallpike, Claveria, Cohen, and Lascelles (1971) report normal values of catecholamine excretion in this condition. Our finding of increased catecholamine excretion in the Guillain-Barré syndrome confirms Mitchell and Meilman's (1967) original observation. Transient non-specific ECG changes were noted in their case and myocarditis was seen in seven cases examined by Haymaker and Kernohan (1949). Van Vliet, Burchell, and Titus (1966) found similar myocardial lesions in patients with pheochromocytoma and it is possible that the ECG changes in the Guillain-Barré syndrome are due to the increased catecholamine levels.

Stress associated with the illness was probably responsible for the increased urinary excretions of 17-OHCS and high plasma cortisol levels with loss of diurnal variation (Jacobs and Nabarro, 1961).

We have been able to find only one previous report, by Kocen (1957), of the association of

impaired glucose tolerance and the Guillain-Barré syndrome. Increased blood levels of catecholamines and cortisol found in our patients probably contributed to this.

The mechanisms responsible for the increased catecholamine excretion in patients with the Guillain-Barré syndrome need further elucidation. Increased concentrations of noradrenaline relative to adrenaline would support the hypothesis that it is due to a sympathetic nervous system disturbance rather than to adrenal medullary stimulation secondary to stress. The administration of α -adrenergic and β -adrenergic blocking drugs to patients with life-threatening cardiovascular disturbance should certainly be considered.

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