Guillain-Barré Syndrome and Its Variants: A Case of Acute Motor-sensory Axonal Neuropathy in Jamaica

K Fletcher-Peddie[1], R Alfred[2], K Penn-Brown[3], F Gayle[1], DT Gilbert[1], V Elliot[1], TS Ferguson[1, 4]

ABSTRACT

This paper reports a case of a Jamaican young woman who experienced flaccid quadriparesis and bulbar weakness over a three-week period after a gastrointestinal illness. Nerve conduction studies confirmed an axonal type neuropathy consistent with the acute motor-sensory axonal neuropathy variant of the Guillain-Barré syndrome. Recovery, although evident, was slow and was augmented after a course of intravenous immunoglobulin. The patient was discharged from hospital after three months but was re-admitted one week later and eventually succumbed to complications of the illness. This case serves as a reminder that Guillain-Barré syndrome is now the most common cause of acute flaccid paralysis and should be considered early in all patients presenting with flaccid quadriparesis.

Keywords: Acute motor-sensory axonal neuropathy, flaccid paresis, Guillain-Barré syndrome, Jamaica

Síndrome de Guillain-Barré y Sus Variantes: Un Caso de la Neuropatía Axonal Sensorial Motor Aguda en Jamaica

K Fletcher-Peddie[1], R Alfred[2], K Penn-Brown[3], F Gayle[1], DT Gilbert[1], V Elliot[1], TS Ferguson[1, 4]

RESUMEN

El presenta trabajo reporta el caso de una joven jamaicana que experimentó debilidad bulbar y cuadriparesia flácida por un período de tres semanas después de una enfermedad gastrointestinal. Los estudios de conducción nerviosa confirmaron una neuropatía de tipo axonal en correspondencia con la variante de la neuropatía axonal sensorial motora aguda del síndrome de Guillain-Barré. La recuperación, aunque evidente, fue lenta, y aumentó después de que se le aplicara inmunoglobulina intravenosa. La paciente fue dada de alta del hospital después de tres meses, pero fue ingresada de nuevo una semana más tarde, falleciendo finalmente a causa de las complicaciones de la enfermedad. Este caso sirve como recordatorio de que el síndrome de Guillain-Barré es ahora la causa más común de parálisis flácida aguda, y debe tenerse en cuenta temprano en todos los pacientes que acuden con cuadriparesia flácida.

Palabras claves: Neuropatía axonal sensorial y motora aguda, paresia flácida, síndrome de Guillain-Barré, Jamaica

West Indian Med J 2013; 62 (7): 658

INTRODUCTION

Guillain-Barré syndrome (GBS) is characterized pathologically by inflammatory lesions throughout the peripheral nervous system (1). It represents an acute or subacute peripheral polyneuropathy characterized by symmetrical limb weakness occurring in the absence of identifiable causes of genetic, metabolic, or toxic origin. The characteristic presentation of the syndrome involves symmetrical paresis or paresthesia of an ascending nature, with diminished reflexes or areflexia and variable motor, sensory, or autonomic dysfunction (2). Guillain-Barré syndrome is now the most frequent cause of acute flaccid paralysis worldwide and has a 'guarded' prognosis with up to 20% of patients experiencing severe long-term disability and up to 5% of patients dying even after receiving appropriate therapy (3).

From: [1]Department of Medicine, University Hospital of the West Indies, Kingston 7, Jamaica, [2]Scarborough General Hospital, Signal Hill, Tobago, [3]Spanish Town Hospital, St Catherine, Jamaica and [4]Tropical Medicine Research Institute (Epidemiology Research Unit), The University of the West Indies, Kingston 7, Jamaica.

Correspondence: Dr R Alfred, Scarborough General Hospital, Signal Hill, Tobago, West Indies. E-mail: rose24_tt@yahoo.com.

Diagnostic approach to GBS is based on clinical, laboratory, and electrophysiological criteria. The history is of paramount importance and is characterized by symmetric flaccid paresis associated with varying combinations of pain, paresthesia and numbness. The National Institute of Neurological Disorders and Stroke (NINDS) has defined the weakness as progressive (over a four-week period) in their diagnostic criteria developed to guide physicians in making the diagnosis (4). The Brighton Collaboration GBS Working Group (5) has defined key clinical and epidemiologic features required for case definitions for GBS. The Working Group has stated in their case definition that limb weakness in GBS should be "bilateral and relatively symmetric" (generally with progression from legs to arms and bulbar muscles), associated with decreased or absent deep tendon reflexes in weak limbs, a monophasic illness pattern, an interval between onset and nadir of weakness between 12 hours and 28 days, subsequent clinical plateau, electrophysiologic findings consistent with GBS, cytoalbuminologic dissociation (*ie* elevation of cerebrospinal fluid (CSF) protein level above laboratory normal value, CSF total white cell count < 50 cells/mm^3 and absence of an identified alternative diagnosis for weakness). There are three levels of diagnostic certainty (5). Level 1 includes all of the above, while levels 2 and 3 do not meet CSF or electrophysiological studies criteria, respectively.

Guillain-Barré syndrome more commonly has a demyelinating type on histology, but variants exist. Histologically, GBS may be classified as having demyelinating and axonal subtypes, namely, acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN) and acute motor-sensory axonal neuropathy (AMSAN). Acute motor-conduction-block neuropathy, another GBS variant, is believed to be a mild form of AMAN (2, 3). In Europe and North America, demyelinating GBS accounts for up to 90% of cases, but in other countries such as China and Japan, the axonal type GBS account for 30−65% of cases (3).

In this paper, we present a case of axonal type GBS and discuss issues related to the presentation and diagnosis of GBS and its variants.

CASE REPORT

The case is that of a 27-year old Jamaican woman, of African descent, with no prior history of chronic illnesses. She was well up until one week prior to her initial admission to hospital, when after having a meal of chicken and rice at a local restaurant, she experienced gastrointestinal symptoms with diarrhoea and vomiting approximately six hours post consumption. Over the ensuing days, the diarrhoea stopped, but the vomiting continued and she was unable to tolerate oral rehydration fluid. She presented to a peripheral hospital one week later with confusion and new onset generalized tonic clonic seizures. She was afebrile, appeared dehydrated and had lethargy, but normal limb strength on examination. Laboratory investigations were significant for severe hyponatraemia and an elevated creatine kinase. She was treated with phenytoin and received amoxicillin/clavulanic acid for aspiration pneumonia. The hyponatraemia worsened despite hydration and she was then transferred to the University Hospital of the West Indies (UHWI) for further management.

On presentation to UHWI (two weeks after her initial illness), she was found to be euvolaemic. Her urine was also noted to be dark. She was fully oriented, but had impaired short term memory and mild proximal weakness at the hips bilaterally. Her neck was supple. Over the following week her hyponatraemia was corrected with fluid restriction and hypertonic saline. An endocrinology consultation was requested and the endocrinology team felt that her electrolyte disturbance was a case of idiopathic syndrome of inappropriate antidiuretic hormone (SIADH) secretion.

While in hospital, approximately three weeks after the diarrhoeal illness, she developed quadriparesis which progressed to complete paralysis over approximately two weeks. She also developed bulbar muscle involvement with dysarthria and dysphagia and required a nasogastric tube for feeding.

Stool for campylobacter was negative but was done two weeks after initial illness so this might have been too late to make the diagnosis. Lumbar puncture revealed no albuminocytologic dissociation. Serum creatine kinase was initially elevated but normalized during hospitalization (Table 1). Thyroid function tests were normal. Serology for leptospirosis, HIV, HTLV-1, Hepatitis B and C were negative. An extensive collagen vascular screen, urine protein electrophoresis, urine aminolevulinic acid (ALA) and serum heavy metal screen (arsenic, mercury, bismuth, and antimony) were negative. Computed tomography and magnetic resonance imaging of the brain (Figs. 1A–C) and cervical spine, including diffusion weighted image one month after she became quadriparetic, were negative for compressive lesions of the spinal cord or features of osmotic demyelination. Muscle biopsy of her thigh displayed severe atrophy with no perifasicular infil-trates or vacuoles or regeneration. Table 1 presents a sum-mary of laboratory results during hospitalization.

Electromyography revealed moderate to abundant positive sharp waves and fibrillation potentials with absent fasciculation potentials and no voluntary motor unit action potentials (MUAP) in all muscles sampled. Nerve conduction studies revealed unelicitable F responses, compound muscle action potentials (CMAPs) and sensory nerve action potentials (SNAPs) at all peripheral (radial, median, ulnar, peroneal, tibial and sural) nerve stimulation sites tested. Findings on nerve conduction study (Figs. 2A−C) were in keeping with an acute demyelinating and axonal sensorimotor illness.

Table 1: Results of laboratory investigations

Test	Day #1	Day #3	Day #5	Day #6	Day #14	Day #20
Haemoglobin (mg/dL)	8.9	9.1			7.8	8.3
Packed cell volume	0.25	0.25			0.23	0.25
Platelet count (x 10^9/Fl)	166	224			225	151
White blood cell count (x10^9/L)	10.9	8.2			5	7.9
Sodium (mmol/L)	126	126	119	134	134	138
Potassium (mmol/L)	2.5	4.5			4.7	4.3
Chloride (mmol/L)	89	97			103	111
Bicarbonate (mmol/L)	23	23			19	17
Urea (mmol/L)	3.3	2.5			18	15.3
Creatinine (ummol/L)	77	63			85	64
Creatine phosphokinase (U/L)	2317	1172	693	471	316	154
Erythrocyte sedimentation rate (mm/hr)	95					

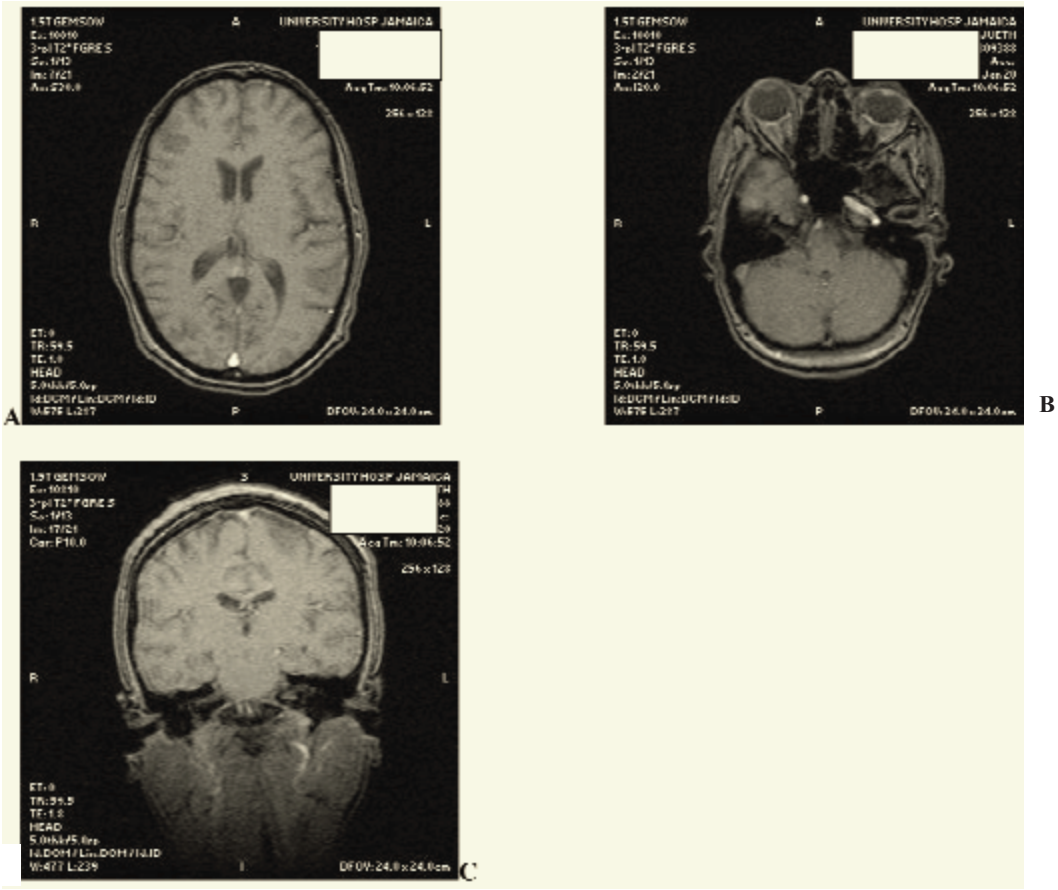

Fig. 1A–C: Magnetic resonance imaging of the brain one month after the patient became quadriparetic.

CASE MANAGEMENT

Initial supportive care included physical therapy, swallowing rehabilitation, prevention of decubitus ulcers *via* cushions and frequent turning in bed and bladder training. With the initial marked elevation of the creatine kinase levels, the possibility of a myopathy was entertained and pulse methyl prednisolone was administered at a dose of one gram per day for seven days but no improvement was noted. Four months after the onset of her illness, she was treated with a course of intravenous immunoglobulin 0.4 g/kg for five days. The late timing of this was based on financial constraints in procuring the nerve conduction studies.

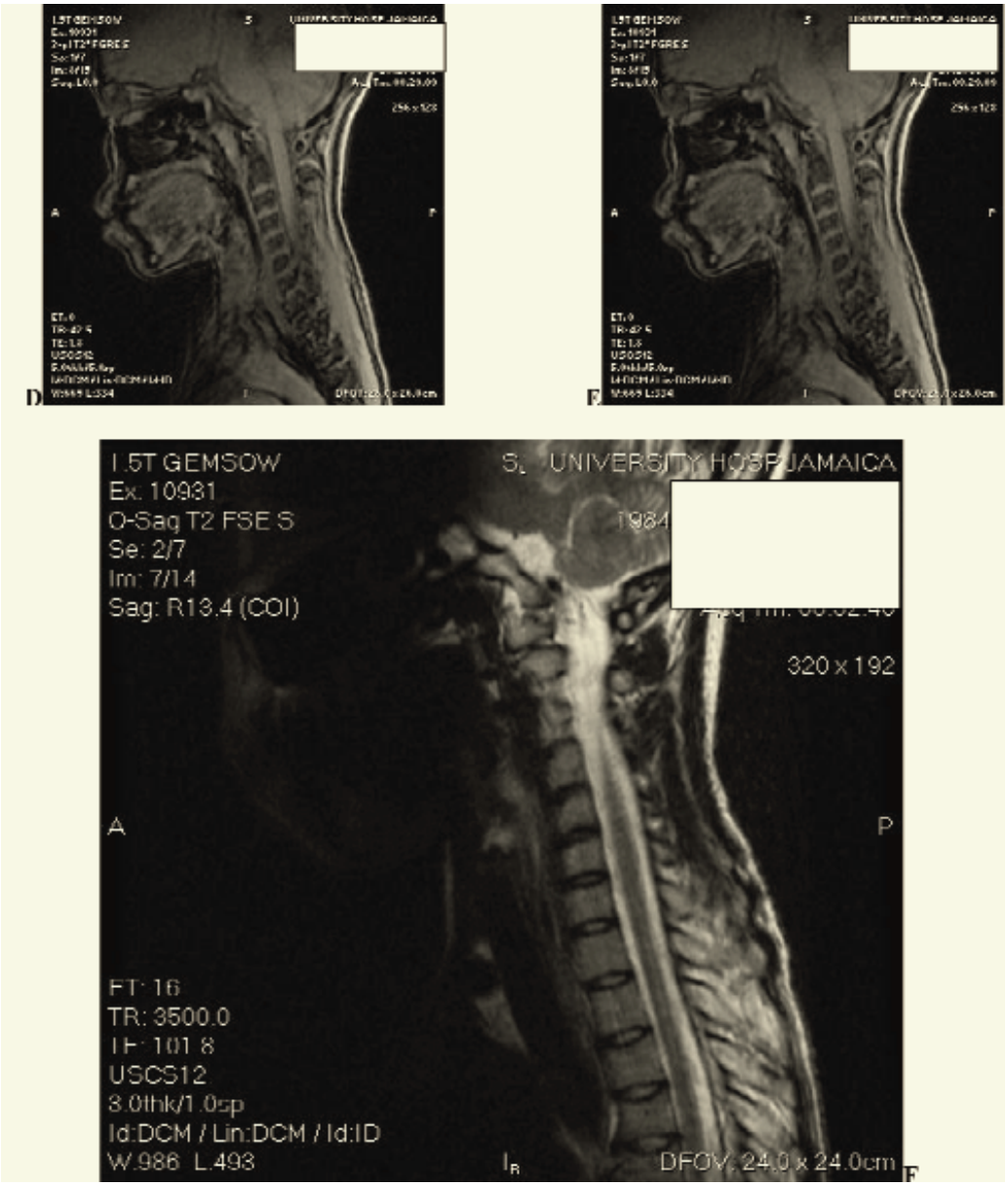

Fig. 1D–F: Cervical magnetic resonance imaging 10 weeks after initial diarrhoeal illness.

Over the course of her hospitalization, there was mild improvement with swallowing capacity returning to almost normal and improved bowel and bladder function. She also had some improvement in motor function with her proximal muscle strength improving to grade 2/5 on the Medical Research Council (MRC) scale.

Antiepileptic medications were started after her initial presentation with seizures. After the correction of her electrolyte abnormalities, these were tapered and then discontinued. She started rehabilitative physiotherapy and was discharged for home after 90 days in hospital.

Approximately one week after discharge, the patient returned with recurrent seizures on a background of normal electrolytes and a urinary tract infection, confirmed by a positive urine culture. During this admission, she developed aspiration pneumonia and succumbed to her illness.

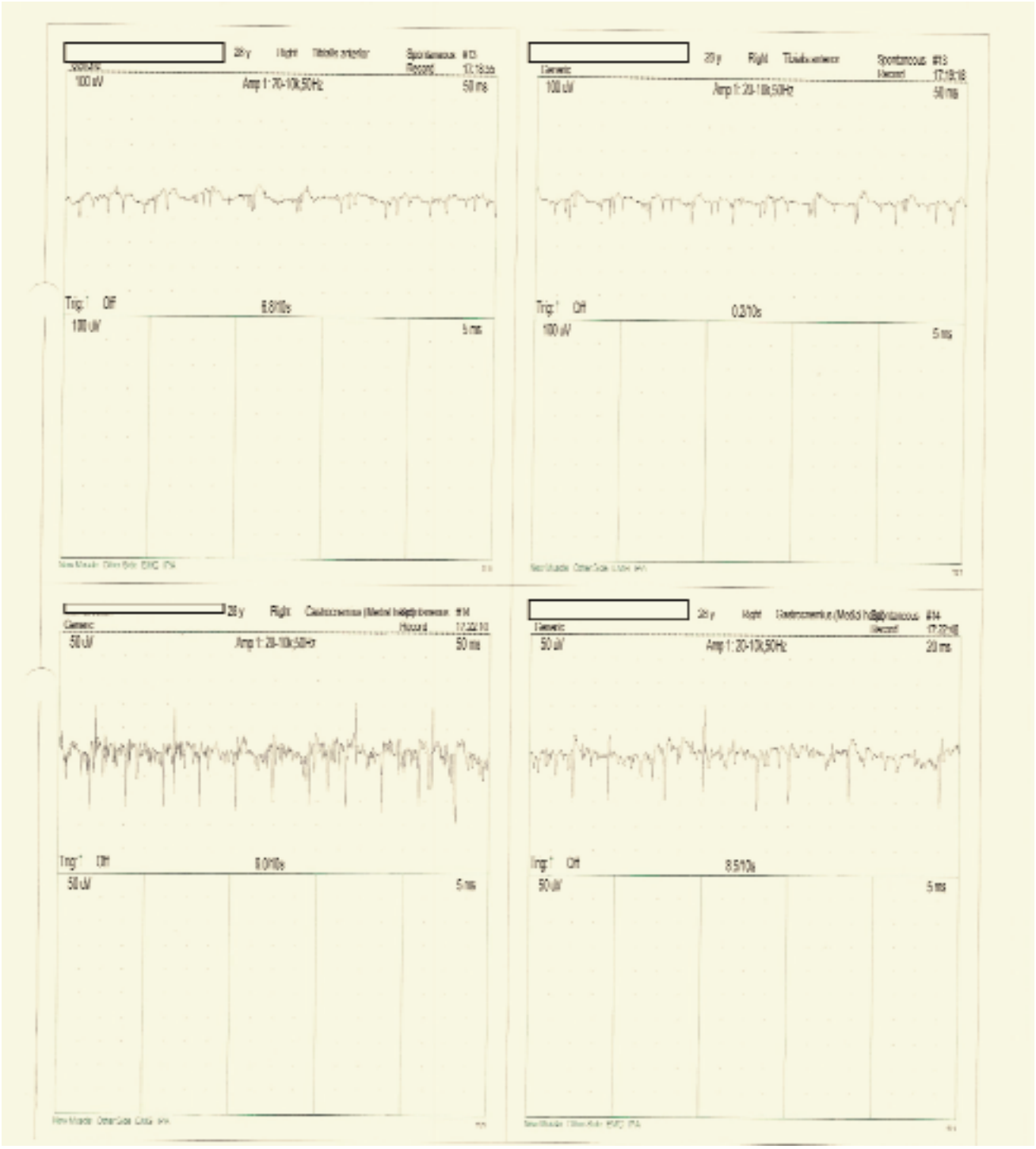

Fig. 2A: Findings on nerve conduction studies.

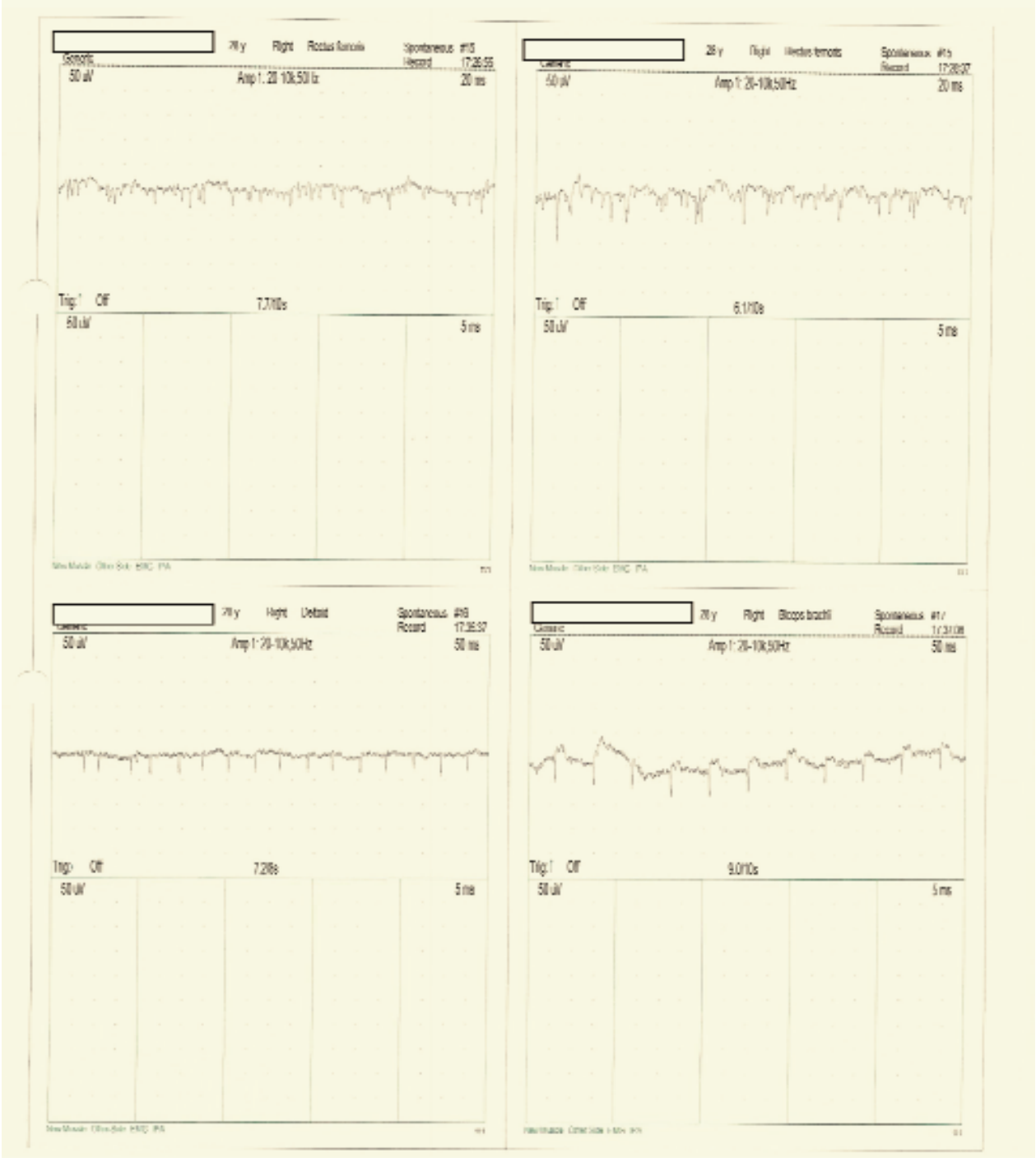

Fig. 2B: Findings on nerve conduction studies.

ELECTROMYOGRAPHY

MUSCLE	SPONTANEOUS ACTIVITY pos. waves/fibs	fasciculations	VOLUNTARY MOTOR UNIT POTENTIAL
Right tibialis anterior	4+	0	No voluntary motor unit action poter (MUAP)
Right medial gastrocnemius	4+	0	No voluntary motor unit action poter (MUAP)
Right tibialis posterior	3-4+	0	No voluntary motor unit action poter (MUAP)
Right ext. digit. brevis	4+	0	No voluntary motor unit action poter (MUAP)
Right rectus femoris	3-4+	0	Few, polyphasic MUAPs
Right biceps femoris (short head)	3-4+	0	No voluntary MUAPs
Left tibialis anterior	3-4+	0	No voluntary MUAPs
Left medial gastrocnemius	3-4+	0	No voluntary MUAPs
Right deltoid	3-4+	0	No voluntary MUAPs
Right biceps brachii	3-4+	0	No voluntary MUAPs

Fig. 2C: Electromyography.

Table 2: Neurophysiological criteria for AIDP, AMSAN and AMAN*

AIDP — Acute Inflammatory Demyelinating Polyneuropathy
At least one of the following in each of at least two nerves, or at least two of the following in one nerve if all others inexcitable and dCMAP > 10% LLN:
Motor conduction velocity < 90% LLN (85% if dCMAP <5 0% LLN)
Distal motor latency >110% ULN (> 120% if dCMAP < 100% LLN)
pCMAP/dCMAP ratio < 0·5 and dCMAP > 20% LLN
F-response latency > 120% ULN

AMSAN* — Acute Motor-sensory Axonal Neuropathy
None of the features of AIDP except one demyelinating feature allowed in one nerve if dCMAP < 10% LLN
Sensory action potential amplitudes < LLN

AMAN* — Acute Motor Axonal Neuropathy
None of the features of AIDP except one demyelinating feature allowed in one nerve if dCMAP < 10% LLN
Sensory action potential amplitudes normal

Inexcitable
dCMAP absent in all nerves or present in only one nerve with dCMAP < 10% LLN

*dCMAP = compound muscle action potential amplitude after distal stimulation; pCMAP = compound muscle action potential amplitude after proximal stimulation; LLN = lower limit of normal; ULN = upper limit of normal. *In the original definitions the difference between AMSAN and AMAN proposed here is implied but not stipulated.*

*Source: 12

DISCUSSION

Guillain-Barré syndrome is an acute polyneuropathy with various subtypes. Acute inflammatory demyelinating polyradiculoneuropathy, the classic demyelinating form of GBS, accounts for 90% of all GBS cases in the Western world. Acute motor axonal neuropathy and AMSAN are axonal forms of GBS that are more prevalent in Asia, South and Central America and often preceded by *Campylobacter jejuni* (*C jejuni*) infection, as proven by serological studies (7).

The present case, as previously mentioned, had stool culture done late as the results of stool cultures usually do not remain positive beyond two weeks (6). More specific methods such as real time polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assay (ELISA) techniques for campylobacter species are not offered at the University Hospital of the West Indies.

While immunologic evidence is strongest for antecedent *C jejuni* infection, other infectious agents have been temporally associated with subsequent GBS and have included influenza viruses, *Mycoplasma pneumoniae*, human immunodeficiency virus, Epstein-Barr virus and cytomegalovirus (9). In rare cases, haematological malignancies (10) may also be linked to GBS. The relationship between vaccinations and GBS is not thought to be directly casual (5). Although host genetic or other phenotypic factors are likely to influence susceptibility to development of GBS in certain individuals, an association with specific HLA subtypes or other immunogenetic susceptibility factors has not been consistently identified by existing studies. Our literature review did not reveal any reports of an association of ethnicity with these HLA subtypes. The association between HLA-DR and -DQ and GBS is not strong, but some studies have found that polymorphisms of CD1E and CD1A genes may be linked to occurrence of GBS (11).

The electrophysiologic evaluation of a suspected case of GBS remains a key extension of the clinical examination. Standard parameters of the motor nerve include the distal motor latencies, CMAP amplitudes, conduction velocities, waveform duration and morphology and F waves. Sensory nerve action potentials is the electrophysiologic correlate for the sensory nerve. The findings may be quite variable and beyond the nuances of GBS variants, and are often a function of the time during the disease course that the patient is evaluated.

The hallmark of the classic GBS variant of AIDP rests in the basic pathophysiology of demyelination with occasional or variable secondary axonal degeneration. These patients exhibit prolonged distal latencies, slow conduction velocities, temporal dispersion, conduction block and prolonged F waves. At least three motor and sensory nerves with multi-site stimulation F waves and bilateral tibial H reflexes should be assessed on nerve conduction testing. Hughes and Cornblath outlined the electrophysiologic classification of GBS (12) [Table 2]. In that criterion, at least one of the defined markers of demyelination should be observed in each of at least two nerves. The entity of conduction block represents loss of myelin with neural conduction failure, which may lead to acute weakness and sensory loss. It is embodied in > 20% reduction in baseline to peak CMAP from proximal to distal stimulation sites. Conduction block may be seen in 74% of patients with AIDP within the first two weeks of their disease course. Approximately 40−60% of AIDP patients eventually demonstrate SNAP amplitude reduction or absence by the third or fourth week of the illness. This may be attributable to conduction block or secondary axonal degeneration (13).

The variant AMSAN shows no electrophysiologic evidence of demyelination, instead exhibiting an axonal pattern of reduced or absent peak to baseline amplitude in sensory and motor with relatively preserved conduction velocity in excitable nerves. Nerve conduction studies in AMSAN reveal markedly diminished amplitudes or absent CMAP within 7−10 days of onset of the illness. Sensory nerve action potentials are also profoundly reduced or absent. Low amplitude or absent CMAPs do not necessarily imply axonal degeneration. Distal conduction block can account for distal reduced or absent CMAPs. In fact, it may be impossible to distinguish AIDP and AMSAN initially, purely on nerve conduction studies (14). The index case would have benefitted from serial nerve conduction studies to formally distinguish AIDP with secondary axonal loss from AMSAN, but her poor outcome leads one to clinically assume the latter diagnosis of AMSAN.

The efficacy of plasmapheresis and intravenous immunoglobulin has been established in large international randomized trials and case reports, with corticosteroids proven ineffective (15). Despite reported improvement with immunoglobulin therapy (16), the prognosis and recovery of AMSAN is generally poorer than the other subtypes and the main stay of treatment is supportive care (17). This entails prompt diagnosis based on history and examination. One must address issues of swallowing, aspiration, ventilation, decubitus ulcers, limb physiotherapy, autonomic dysfunction, bladder and bowel care, analgesia, deep vein thrombosis prophylaxis, and education of involved family members and the patient.

Poor prognostic factors include older age, rapid onset (less than seven days) prior to presentation, severe muscle weakness on admission, need for ventilatory support, an average distal motor response amplitude reduction to < 20% of normal, and preceding diarrhoeal illness (18). As realized from this case, the cause of demise in this illness may be related to the sequelae of complications. Supportive and rehabilitative care is of paramount importance.

We acknowledge that several questions remain unanswered in this complicated case. The aetiology of her hyponatraemia might have been initially dehydration related to vomiting, but the persistence even in her euvolaemic state leads one to believe she may have had SIADH. This hyponatraemia may have led to her seizures. We are unsure of the cause of her dark urine. The elevation of her CPK makes this likely myoglobinuria, but confirmatory test were unavailable. The absence of cytoalbuminologic dissociation on her CSF does not exclude the diagnosis of GBS. The normalization of her CPK was also on the background of hydration and steroid use before the late timing of her muscle biopsy. One may wonder if the muscle atrophy may still represent an underlying chronic myopathy. Again, the axonal loss may indicate another differential of AIDP with secondary axonal loss but her poor outcome supports AMSAN.

This case illustrates the need for complete evaluation with appropriate diagnostic tests in patients who present with an unclear diagnosis or experience an unexpected complication while in hospital. Working through the various differentials including osmotic demyelination, acute myopathy and GBS required investigations along disparate lines and as such delayed the diagnosis. Difficulty in obtaining the required investigations in our resource-limited setting also contributed to the delay in diagnosis. The final diagnosis serves as a reminder that GBS is now the most common cause of acute flaccid paralysis and should be considered early in all patients presenting with flaccid quadriparesis.

REFERENCES

1. Prineas JW. Pathology of the Guillain Barre Syndrome. Ann Neurol 1981; **9:** 6.
2. Seneviratne U. Guillain-Barré syndrome. Postgrad Med J 2000; **76:** 774–82.
3. Yuki N, Hartung H. Review article: medical progress in Guillain Barre Syndrome. N Engl J Med 2012; **366:** 2294−304.
4. National Institute of Neurological Disorders and Stroke. NINDS Guillain-Barré syndrome information page. National Institute of Neurological Disorders and Stroke; 2011. Available from: www.ninds.gov/disorders/gbs/gbs.htm
5. Sejvar J, Kohl K, Gidudu J, Amato A, Bakshi N, Baxter R et al. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine 2011; **29:** 599–612.
6. Bloom S, Webster G, Marks D. Oxford Handbook of Gastroenterology and Hepatology. First edition. Oxford: Oxford University Press; 2011.
7. Vucic S, Kiernan MC, Cornblath DR. Guillain-Barré syndrome: an update. J Clin Neurosci 2009; **16:** 733−41.
8. Bessède E, Delcamp A, Sifré E, Buissonnière A, Mégraud F. New methods for detection of campylobacters in stool samples in comparison to culture. J Clin Microbiol 2011; **49:** 941–4.
9. Tam CC, O'Brien SJ, Rodrigues LC. Influenza, campylobacter and mycoplasma infections, and hospital admissions for Guillain–Barre syndrome, England. Emerg Infect Dis 2006; **12:** 1880–7.
10. Wanschitz J, Dichtl W, Budka H, Loscher WN, Boesch S. Acute motor and sensory axonal neuropathy in Burkitt-like lymphoma. Muscle Nerve 2006; **34:** 494–8.
11. Zhong M, Cai F. Current perspectives on Guillian-Barre Syndrome. World J Pediatric 2007; **3:** 187−94.
12. Hughes RA, Cornblath DR. Guillain Barre Syndrome. Lancet 2005; **366:** 1653−66.
13. Haddden RD, Cornblath DR, Hughes RA, Zielasek J, Hartung HP, Toyka KV et al. Electrophysiological classification of Guillain Barre Syndrome: clinical associations and outcomes. Plasma Exchange/Sandoglobin: Guillain-Barré Syndrome Trial Group. Ann Neurol 1998; **44:** 780−8.
14. Van Den Bergh PY, Pieret F. Electrodiagnostic criteria for acute and chronic inflammatory demyelinating polyradiculopathy. Muscle Nerve 2004; **29:** 565−74.
15. Rostásy KM, Huppke P, Beckers B, Brockmann K, Degenhardt V, Wesche B et al. Acute motor and sensory axonal neuropathy (AMSAN) in a 15-year-old boy presenting with severe pain and distal muscle weakness. Neuropediatrics 2005; **36:** 260−4.
16. Hughes RA, Wijdicks EF, Benson E, Cornblath DR, Hahn AF, Meythaler JM et al. Supportive care for patients with Guillain-Barré syndrome. Arch Neurol 2005; **62:** 1194−8.
17. Rees JH, Soudain SE, Gregson NA, Hughes RA. Campylobacter jejuni infection and Guillain-Barré syndrome. N Engl J Med 1995; **333:** 1374−9.
18. Walgaard C, Lingsma HF, Ruts L, van Doorn PA, Steyerberg EW, Jacobs BC. Early recognition of poor prognosis in Guillain-Barre syndrome. Neurology 2011; **76:** 968.