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CASE REPORT

Transient Hypnic Headache-like Phenomenon in Guillain-Barre Syndrome: Lessons from a First Case Report

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ABSTRACT

Headache is an uncommon feature of Guillain-Barre syndrome (GBS), which is more frequently associated with severe limb and/or back pain. However, when it does it occur, headache in GBS may emanate from a range of causes, including raised intracranial pressure, reversible cerebral vasoconstriction syndrome, posterior reversible encephalopathy syndrome, or due to complications of intravenous immunoglobulin (IVIg) therapy, such as aseptic meningitis and cerebral venous sinus thrombosis. Hypnic headache (HH)-like phenomenon has not been thus far described in association with GBS. We report herein a patient with GBS who developed HH-like phenomenon during the recovery phase; she developed a cyclical nocturnal headache lasting around four hours and demonstrated exquisite response to caffeine. We postulate potential mechanisms for the same.

Keywords: Hypnic headache; reversible cerebral vasoconstriction syndrome; posterior reversible encephalopathy syndrome; IVIg

1 INTRODUCTION

While back pain and limb pains of moderate to severe intensity are a well-recognized feature of Guillain Barre syndrome (GBS), headache seems to be relatively unusual[1,2]. Most reports of headache as a prominent feature in GBS are based on the development of posterior reversible encephalopathy syndrome (PRES) or reversible cerebral vasoconstriction syndrome (RCVS) or raised intracranial pressure.[3–9] Headache in GBS may also be associated with the use of intravenous immunoglobulins (IVIg). IVIg may precipitate aseptic meningitis,[10] and rarely, a hypercoagulable state, leading to cerebral venous sinus thrombosis (CVST).[11] The development of typical hypnic headache in association with GBS has not been reported in literature so far. We describe a first case report of hypnic headache-like phenomenon in a patient recovering from GBS, and explore potential pathophysiological mechanisms, and treatment options.

2 CASE REPORT

A 42-years old female presented to our emergency services, with complaints of progressive weakness and pain involving the limbs and lower back for five days. She developed tingling of both hands and feet seven days prior to presentations. Two days later, she started to experience difficulty in walking and climbing up stairs. This weakness ascended over the next two days to involve the trunk, and she was unable to turn in bed without support. Over the next two days, she also began experiencing trouble with raising her upper limbs and grasping objects. There was no history of bowel or bladder involvement. At presentation to the emergency, she was non-ambulatory, and had also developed neck flexion weakness. She had history of upper respiratory tract infection two weeks prior to presentation. There was no history of insect bite, vaccination, drug intake, or previous history of significant medical illnesses. On examination, she was noted to have blood pressure of 130/80 mm Hg, regular pulse rate of 87 per minute, respiratory rate of 22 per minute. Oxygen saturation (SpO_2) was 95% on room air. She was

afebrile. Higher mental function assessment was normal. Cranial nerve examination revealed the presence of bilateral lower motor neuron type of facial palsy (Figure 1).

Fig. 1: Bifacial weakness at presentation in our patient

Extraocular movements were normal. Bulbar function was normal. She was found to have profound neck muscle weakness and was unable to raise her neck from the pillow. Motor system assessment revealed hypotonia involving all four limbs. Power examination using the Medical Research Council (MRC) scale showed: Bilateral shoulder=2/5; Elbow: 3/5; Wrist=2/5; Hip=1/5; Knee=2/5; Ankle=1/5. Deep tendon reflexes, including biceps, triceps, brachioradialis, knee and ankle jerks, were not elicitable. Sensory system examination was normal. She also had trunk muscle weakness and was unable to turn in bed or sit up by self. Single breath count was 17. There were no signs of meningeal irritation. Systemic examination was normal. Considering that she had an ascending pattern acute flaccid motor quadriparesis involving proximal and distal limbs, neck and trunk muscles, the clinical possibility of GBS with acute motor axonal neuropathy (AMAN) variant was considered. The patient was urgently admitted to intensive care services. Routine hemogram, hepatic and renal function, erythrocyte sedimentation rate, C-reactive protein, thyroid function tests, blood sugar, vasculitis profile, and viral markers for HIV, hepatitis B and hepatitis C were negative. Nerve conduction studies revealed the presence of axonal pattern of neuropathy involving all limbs, with prolonged F-wave response and H-reflex (Figure 2).

Magnetic resonance imaging of the brain and spinal cord was normal. The patient also underwent cerebrospinal fluid (CSF) analysis, which showed mild albuminocytologic dissociation (total leukocyte count=2 cells/mm^3; all lymphocytes; CSF sugar=72 mg/dL with concomitant blood sugar of 110 mg/dL; protein=98 mg/dL). CSF tests for Gram stain, bacterial culture, acid fast bacilli stain, fungal stain, India

Nerve / Sites	Muscle	Latency ms	Amplitude mV	Segments	Distance mm	Velocity m/s
R Median - APB						
Wrist	APB	4.06	2.9	Wrist - APB		
Elbow	APB	7.55	1.9	Elbow - Wrist	190	54
L Median - APB						
Wrist	APB	4.69	2.3	Wrist - APB		
Elbow	APB	8.59	1.4	Elbow - Wrist	190	49
R Ulnar - ADM						
Wrist	ADM	2.45	1.8	Wrist - ADM		
B.Elbow	ADM	7.03	1.1	B.Elbow - Wrist	200	44
L Ulnar - ADM						
Wrist	ADM	2.50	2.8	Wrist - ADM		
B.Elbow	ADM	6.09	2.3	B.Elbow - Wrist	200	56
R Peroneal - EDB						
Ankle	EDB	5.42	1.8	Ankle - EDB		
Fib head	EDB	13.85	1.5	Fib head - Ankle	280	33
L Peroneal - EDB						
Ankle	EDB	5.00	1.5	Ankle - EDB		
Fib head	EDB	13.54	1.0	Fib head - Ankle	280	33
R Tibial - AH						
Ankle	AH	5.05	2.9	Ankle - AH		
Pop fossa	AH	13.65	0.9	Pop fossa - Ankle	300	35
L Tibial - AH						
Ankle	AH	5.63	2.6	Ankle - AH		
Pop fossa	AH	13.13	1.1	Pop fossa - Ankle	300	40

Sensory NCS

Nerve / Sites	Rec. Site	Onset Lat ms	Amp µV	Segments	Distance mm	Velocity m/s
R Median - Digit II (Antidromic)						
Wrist	Dig II	2.19	24.3	Wrist - Dig II	120	55
L Median - Digit II (Antidromic)						
Wrist	Dig II	2.14	38.5	Wrist - Dig II	120	56
R Ulnar - Digit V (Antidromic)						
Wrist	Dig V	1.93	20.5	Wrist - Dig V	100	52
L Ulnar - Digit V (Antidromic)						
Wrist	Dig V	1.88	41.7	Wrist - Dig V	100	53
L Sural - Ankle (Calf)						
Calf	Ankle	1.61	26.9	Calf - Ankle	100	62
R Sural - Ankle (Calf)						
Calf	Ankle	1.46	18.5	Calf - Ankle	100	69

F Wave

Nerve	M Lat ms	F Lat ms
R Median - APB	NR	NR
R Ulnar - ADM	NR	NR
R Peroneal - EDB	5.73	48.65
R Tibial - AH	5.10	67.08
L Peroneal - EDB	NR	NR
L Tibial - AH	5.68	65.52
L Median - APB	4.01	28.28

Fig. 2: Nerve conduction studies demonstrating axonal neuropathy involving all four limbs

Ink, cryptococcal antigen, and cytology for malignant cells were negative. She was initiated on IVIg at a dose of 2 g/kg over 5 days (total dose=140 g; Patient's weight=70 kg). She began to demonstrate improvement on the third day of IVIg therapy, and power of both lower limbs improved to 2/5 at the hips and ankles, and neck flexor power also improved mildly on day 5 of IVIg. Single breath count improved to 40. There were no immediate complications noted with IVIg therapy. Two days following completion of IVIg therapy, the patient developed nocturnal headache. She had no prior history of headache. The headache would begin at 11 PM and subside by 2 AM, and interrupted sleep. It was holocranial, moderate in intensity, and non-throbbing. It was not associated with nausea, vomiting, photophobia or phonophobia, conjunctival tearing, eyelid edema, nasal congestion, or visual complaints. Fundus examination was normal. There were no features of meningeal irritation. Her SpO_2 at this time was 92-93% and blood pressure was normal. A repeat MRI brain and MR venography with contrast was normal. The headache was not responsive to intravenous diclofenac, tramadol, or oral naproxen. Indomethacin 50 mg led to mild reduction. Finally, intake of coffee led to dramatic resolution of headache on the third

night of headache. Thereafter, the patient continued to have headaches every night for the next ten days responsive to caffeine, after which they resolved completely.

3 DISCUSSION

A diagnosis of typical hypnic headache (HH) as per the International Classification of Headache disorders requires the development of headache during sleep, leading to awakening. Headaches should occur for at least ten days per month, for three months, should last for up to 15 minutes to four hours after awakening, and should not be accompanied by autonomic dysfunction or restlessness. HH was initially described by Raskin in 1988.[12] It is a rare headache disorder, reported to comprise 0.07% to 0.1% of all headache patients in various series.[13]

Because of the cyclical tendency of HH to occur at the same time, it has been also termed clockwise headache or alarm clock headache. Compared to typical HH, our patient harbored several unusual features. HH is more common after the age of 50 years, unlike our patient, who was 42 years, although it has been reported to occur in younger patients including pediatric patients as well. In the largest series of patients with HH, a review of 348 cases, Silva-Neto et al. observed that the pain was usually bilaterally located (in 55.5%), of moderate intensity (in 61.5%), and of a dull character (in 74.4%).[12] Autonomic features were reported by 7.6% of patients and were dominated by lacrimation and rhinorrhea.

Our patient had resolution of symptoms, after a short symptomatic spell of 14 days. Spontaneous resolution has been reported with HH in 17% patients. However, the short duration of symptomatic period in our patient suggests that her preceding illness and recovery from it probably contributed to the development of this HH-like phenomenon.

Our patient experienced desaturation of 3% at night, possibly suggesting the contribution of hypoxia to the development of headache. This may have been the result of respiratory muscle weakness or central hypoventilation. In this respect, the development of HH-like phenomenon may be a harbinger of incipient respiratory muscle weakness. Caffeine may have helped due to its weak bronchodilator properties, leading to improvement in hypoxia. However, the converse argument would be that the onset was during the recovery phase, with definite improvement in limb muscle power and single breath count. Another possibility was the development of nocturnal hypertension contributing to headache, but blood pressure monitoring continued to be normal through the night.

We also considered whether IVIg therapy may have contributed the headache. However, the onset of headaches was after completion of uneventful and well tolerated IVIg treatment. She had no features to suggest aseptic meningitis, and repeat neuroimaging ruled out the development of CVST, PRES or RCVS. Another possible cause of headache in patients with GBS is raised intracranial pressure, which may even precede the development of limb weakness. These patients usually harbor elevated CSF protein and may present with significant visual diminution.[9] However, our patient demonstrated no features of elevated intracranial pressure.

Our patient had exquisite response to caffeine intake. Caffeine has anti-nociceptive properties due to adenosine blocking properties, leading to cerebral vasoconstriction, along with its peripheral actions.[14]

4 CONCLUSIONS

Our case report highlights several important considerations of new-onset headache in a patient with GBS. Hypnic headache-like phenomenon is described for the first time in association with GBS, and putative mechanisms discussed. Clinicians must be aware of this entity, and certainly screen the patient for impending respiratory failure.

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