GUILLAIN BARRE SYNDROME FOLLOWING ACUTE HEPATITIS A INFECTION: A CASE REPORT

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ABSTRACT

Guillain Barre Syndrome (GBS) is an acute inflammatory polyradiculopathy. It is a rapidly ascending motor weakness accompanied by areflexia with or without sensory deficit, often triggered by a respiratory or gastrointestinal infection. Although rare, there are a number of cases of hepatotrophic virus induced GBS. We report a case of a 58 year old Chinese who had acute onset of jaundice, tea colored urine and acholic stool. This was followed by paresthesias of the palms and soles and proximal bilateral upper and lower extremity weakness. He was diagnosed with acute hepatitis A and GBS. The patient was treated with intravenous immunoglobulin. However, bulbar symptoms rapidly progressed requiring tracheostomy and gastrostomy. He gradually recovered and after 2 months, he only had minimal neurologic symptoms. GBS is a neurological emergency that require a high index of suspicion to diagnose. It is important to be aware of the association of acute hepatitis A and GBS so that diagnosis and treatment are not delayed.

Keywords: Case Report, Guillain Barre Syndrome, Hepatitis A, Acute Inflammatory Polyradiculopathy

INTRODUCTION

Guillain-Barre Syndrome (GBS) is autoimmune in nature. It is an acute and fulminant polyradiculopathy. In 70% of the cases, symptoms of respiratory or gastrointestinal infection occur one to three weeks prior to the onset of GBS. Most cases are caused by *Camplyobacter jejuni*, Cytomegalovirus, Human Herpes virus and Epstein Barr virus.[1] Rarely, it has been associated with hepatotrophic virus. [2]

CASE REPORT

A 58 year old Chinese businessman from Manila was admitted due to bilateral proximal upper extremity weakness.

Ten days earlier, he noticed beginning tea colored urine, acholic stools and mild jaundice. There were no other accompanying symptoms. After a week, he sought consult and blood test showed reactive Anti-HAV (IgM and IgG), ALT 1646 U/L, AST of 332 U/L and elevated bilirubin levels (total bilirubin: 6.22mg/dL, direct bilirubin 5.42 mg/dL, indirect bilirubin 0.80 mg/dL). Patient was diagnosed with acute hepatitis A and treated supportively. After 3 days, the patient experienced paresthesias of both palms and soles followed several hours later by weakness of proximal upper extremities.

Patient has hypertension. He is a non-smoker, occasional alcoholic beverage drinker, with no illicit drug use nor exposure to radiation and chemicals. He denies any recent respiratory infection or bout of gastroenteritis.

Upon admission, the patient was conscious, coherent, not in distress and hemodynamically stable. He had icteric sclerae and jaundice. He was oriented to time, place and person. Manual Muscle Testing (MMT) grades were 2/5 on proximal upper extremities 4/5 on distal upper and lower extremities. There was absent deep tendon reflexes on all extremities. There were no cerebellar signs, cranial nerve deficits, sensory loss or Babinski. Initial consideration was acute inflammatory polyneuropathy.

On the second hospital day, the patient had rapid progression of neurologic symptoms with inability to ambulate accompanied by bulbar symptoms. MMT was 2/5 on proximal and 4/5 on distal upper and lower extremities. Electromyography and nerve conduction velocity (EMG-NCV) showed prolonged distal motor latencies of the left fibular and bilateral tibial nerves; reduced compound muscle action potential (CMAP) amplitudes of bilateral median, ulnar, fibular, and tibial nerves. Sensory nerve conduction studies showed no response over bilateral median, left ulnar and right fibular nerves; reduced sensory nerve action potential (SNAP) amplitudes of the right ulnar and left fibular nerves. Prolonged F wave latencies on bilateral tibial nerves. Needle EMG examination done on distal muscles of all extremities showed recruitment and active denervation potentials. The impression was mixed axonal and demyelinating polyneuropathy involving motor and sensory nerves with active denervation potentials. Lumbar puncture obtained a clear colorless cerebrospinal fluid with opening pressure of 180-190 mmHg, protein of 40.6 mg/dL, sugar of 66 mg/dL and WBC of 0. CSF was negative for acid fast bacilli and *Cryptococcus neoformans*. CSF IgG was elevated at 82.8 mg/L (normal value: 6.3 - 33.5 mg/L).

With the above clinical findings patient was diagnosed with GBS associated with acute hepatitis A infection. Intravenous immunoglobulin (IVIg) was started at 0.4g/kg/day for five days. However, bulbar symptoms progressed further and he underwent tracheostomy and gastrostomy tube insertion. After the course of IVIg, his neurologic progression abated. He then underwent physical and speech therapy with gradual improvement in neurologic symptoms. Follow up EMG-NCV after one month revealed improvement of the CMAP amplitudes of the left fibular nerve, and the sensory responses of bilateral median, left ulnar, and bilateral superficial fibular nerves as compared to the previous EMG NCV report. After two months, the patient was able to tolerate regular diet. He still had weakness of the right hand with minimal numbness of both hands and electric sensation of the left foot. MMT: 4/5 on finger flexors and 5/5 on other extremities. Deep tendon reflex: +1 on bilateral biceps jerk and 0 on all other extremities. He had no sensory loss. The patient can do activities of daily living by himself. He attends regular physical therapy three times a week.

DISCUSSION

The most frequent cause of acute flaccid paralysis is GBS. [3] It occurs with an annual incidence rate of 1 to 4 cases per 100,000. It occurs more often in men than in women and more frequently in adults than children. [1] GBS develops after 1 to 3 weeks of respiratory or

gastrointestinal infection. *Campylobacter jejuni* is the most common triggering agent (13% to 39%) followed by cytomegalovirus (5% to 22%), Epstein Barr Virus (1% to 13%) and *Mycoplasma pneumoniae* (5%). [3] It has rarely been associated with hepatitis A, B, C, D and E. [2,4] In a series of 1,100 GBS cases, 11 out of 1100 (1%) cases were triggered by viral hepatitis.[5] This syndrome is an immune mediated attack on peripheral nerve specifically in the myelin sheath or Schwann cells of sensory and motor nerves. [3] Conduction block is the cause of flaccid paralysis and sensory disturbance. [1]

GBS usually presents as a rapidly ascending motor weakness accompanied by areflexia with or without sensory deficit. In contrast, our patient presented with a descending motor weakness accompanied by areflexia with no sensory deficit. Early stages of GBS would manifest as pain in the neck, back or shoulder which were felt by the patient. [1] Bulbar symptoms are also seen and is due to involvement of lower cranial nerves manifested as difficulty handling secretions, maintaining an airway and difficulty of breathing which were experienced by the patient which led to the need for tracheostomy and gastrostomy tube insertion.

The exact mechanism of hepatitis A association with GBS is still unknown but it may be associated with direct cytotoxicity and vasculitis of vasa nervorum.[4] Another possibility is a cross reaction between Schwann cells, myelin or other peripheral nerve antigens leading to peripheral nerve damage.[6, 7]

Laboratory features of GBS include: CSF findings of cytoalbuminologic dissociation: elevated CSF protein without accompanying pleocytosis. CSF protein can still be normal when the symptoms have been present for only 2 days and will start to rise at the end of the first week. In the patient's case, lumbar puncture was performed on the third day of onset of neurologic symptoms. This could explain why the CSF protein level was normal. His EMG-NCV findings of prolonged F wave latencies, prolonged distal latencies and reduced amplitudes of compound muscle action potentials and reduced sensory nerve action potential were compatible with GBS with an Acute Motor Sensory Axonal Neuropathy (AMSAN) subtype. [1]

Early observations on the clinical manifestations of GBS following hepatitis A infection were summarized by Ono et al (1994)[5] after a review of 9 reported cases. These were: 1) most cases were men; 2) the onset of hepatitis to the development of neurologic symptoms is less than 14 days; 3) facial nerve palsy is common; 4) frequently impaired joint position, vibratory sense and superficial sensation; 5) good outcome of neuropathic symptoms independent of ALT levels. In our case, three of the clinical manifestations can be seen. His gender, the onset of neurologic symptoms was within 10 days of noticing signs of acute hepatitis A infection and his favourable neurologic outcome.

The exact number of cases of GBS following Hepatitis A infection is difficult to ascertain since acute Hepatitis A can present with minimal symptoms and this can be overshadowed by the rapid and dramatic neurologic symptoms of GBS. Table 1 summarizes the available reported cases of GBS following acute Hepatitis A infection.

Table 1 Summary of reported cases of Guillain Barre Syndrome associated with Hepatitis A infection

Author	Publication Year	Age	Sex	Presentation	Interval*	Maximum ALT levels (U/L)	CSF protein (mg/dL)	Recovery Period	Treatment
Present Case	2018	58	M	Descending weakness	1 week	1646	40	2 months	IVIg
Jung[10]	2016	28	M	Progressive quadriparesis	1 week	◊	0.51	CIDP	IVIg
Patel[2]	2015	25	F	Ascending weakness	1 week	1206	◊	3 weeks	IVIg
Nomani[8]	2015	24	F	Ascending weakness	1 week	717	25	6 months	PE
Sharma[9]	2013	25	M	Asymmetric weakness Left > Right	30 days	◊	◊	1 month	none
Yoon[6]	2013	21	M	Progressive weakness	1 week	385	156	>4 months	IVIg
Bae[14]	2007	32	M	Ascending weakness	9 days	◊	◊	3 months	IVIg
Lee[11]	1997	43	F	Ascending weakness	5 days	1748	◊	70 days	PE
Jenkins[12]	1997	48	M	Quadriparesis	3 days	237	300	2 months	none
Ono[5]	1994	62	M	LE>UE	11 days	5,062	181	3 months	Prednisolone
Endoh[5]	1991	39	M	Muscle weakness	14 days	503	108	After 50 days	◊
Mares-Sgura[15]	1986	34	F	Muscle weakness	7 days	314	156	3 months	◊
Grover[5]	1986	31	M	No muscle weakness	7 days	8,760	◊	After 30 days	◊
Igarashi[13]	1983	49	M	Tetraplegia	◊	412	165	3 months	◊
Dunk[5]	1982	48	M	Muscle weakness	3 days	273	30	Ambulatory after 12 days	◊
Johnston[5]	1981	37	M	No muscle weakness	14 days	617	29	Ambulatory after 2 weeks	◊

*Interval: the time from the onset of neurologic symptoms after onset of acute hepatitis A infection

◊No mention in article

Among the reported cases, our patient belonged to the older age group, with most of the reported cases occurring in their 20's-40's. There is a male predominance. Most of the patients received IVIg treatment. The maximum level of ALT and CSF protein level cannot predict the outcome of the patient. Most of the patients reported had full recovery from GBS.

In general, GBS following acute Hepatitis A have a favourable prognosis and would rarely have long term neurologic sequelae[6].

Except for the mildest of cases, the treatment for GBS should be started as soon as diagnosed. Either high dose IVIg: 0.4g/kg/day for five daily infusions (total dose of 2g/kg body weight) or PE (~40-50mL/kg PE 4 to 5 times per week) can be initiated and they are equally effective.[1]

CONCLUSION

GBS is a neurological emergency. GBS associated with Hepatitis A is rare and is seen in <1% of patients with GBS. As clinicians, we should have a high suspicion for GBS in patients with a preceding acute hepatitis A infection followed by sudden onset of paresthesias and acute flaccid paralysis.

Our patient was diagnosed with acute Hepatitis A associated GBS. He was treated with IVIg and displayed a favourable prognosis.

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