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Miller Fisher Syndrome Induced by Chemotherapy in Known Case of Acute Lymphocytic Leukaemia: A Case Report

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Abstract

Introduction: Guillain-Barre Syndrome (GBS) is an acute-onset autoimmune-mediated neuropathy. Guillain-Barre Syndrome can be divided into three subtypes: acute inflammatory demyelinating poly-radiculo-neuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor sensory axonal neuropathy (AMSAN). About 20% of patients with GBS develop respiratory failure and require mechanical ventilation. We are presenting a variant of GBS (Miller Fisher Syndrome, or MFS), which has been confirmed by nerve conduction studies along with the triad of ophthalmoplegia, ataxia, and areflexia. The objective of this study is to present a rare case of chemotherapy-induced GBS. Important clinic findings: A 25-year-old gentleman with acute lymphocytic leukemia on active chemotherapy treatment presented with lower limb weakness. This weakness started after his fifth chemotherapy session. After the sixth chemotherapy, he developed complete paralysis of the left lower limb. Later, he developed right lower limb paralysis. He was also complaining of eye dryness and incomplete closure of both eyes. While inpatient, he developed upper-limb weakness. His chemotherapy consisted of MESNA, cyclophosphamide, doxorubicin, vincristine, cyorabine, and methotrexate. He had ptosis and ophthalmoplegia in the left abducent and right oculomotor regions. He had bilateral facial nerve palsy. He was hypotonic with power grade 3 in the upper limbs and grade 0 in the lower limbs with areflexia. His sensation was intact in the upper limbs but lost in the lower limbs. His planter reflexes were mute. Diagnoses and Management: Intra-

venous immunoglobulins were given for 5 days. A nerve conduction study showed severe demyelinating sensorimotor polyradoculoneuropathy with secondary axonal loss. The triad of ataxia, ophthalmoplegia, and areflexia was consistent with MFS. The patient improved over the course of the hospital stay but did not reach full recovery. Conclusion: Although GBS is uncommon, it must be taken into account when making a differential diagnosis for any patient presenting with progressive weakness. Drug history is important in all GBS cases.

Keywords

Guillain-Barre Syndrome Variant, Miller Fisher Syndrome, Chemotherapy, Acute Lymphocytic Leukaemia

1. Introduction

Guillain-Barré syndrome (GBS) is an inflammatory disease of the polyneuropathies and is the most common cause of acute flaccid paralysis, with an annual global incidence of approximately 1 - 2 per 100,000 person-years. It is more common in males than females [1]. GBS has three subtypes: acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor-sensory axonal neuropathy (AMSAN). Miller Fisher Syndrome (MFS) is a variant of GBS. 76% of patients report a triggering event four weeks prior to the presentation [2]. This includes an upper respiratory infection in 35% and gastroenteritis in 27% [2]. Other triggers, including medications, have been reported, such as tumor necrosis factor-alpha antagonist therapy, tacrolimus and suramin, isotretinoin, and immune checkpoint inhibitors [3]. Plasma exchange and intravenous immunoglobulin are effective treatments [4].

2. Case Report (Patient Information and Clinical Findings)

25-year-old military soldier from the southern part of Sudan had been recently diagnosed with acute lymphocytic leukemia nine months prior to this presentation. He presented with sudden-onset acute flaccid paralysis. He was scheduled for eight chemotherapy sessions. His chemotherapy sessions consisted of MESNA, cyclophosphamide, doxorubicin, vincristine, cyorabine, and methotrexate. He started to develop his symptoms after his fifth chemotherapy session, with a numbness sensation in the left leg associated with muscle cramps. Then he developed a foot drop and an unsteady ataxic gait. After the sixth chemotherapy, he developed complete flaccid paralysis of the left lower limb. Later, he developed right lower-limb flaccid paralysis. He was also complaining of eye dryness and incomplete closure of both eyes. He had a mouth deviation. While inpatient, he developed upper limb weakness and cranial nerve palsy, along with difficulty swallowing and drawling. He had fecal impaction and constipation in spite of the sensation of urgency. He had lost his appetite. He also had back and hip

pain. He had no other relevant past medical history. He was ill and cachexic. He had muscle wasting. He was slightly hypotensive, with a blood pressure of 100/60. He was bald and had lost his facial hair completely. He was slightly pale. He had ptosis and ophthalmoplegia in the left abducent and right oculomotor regions. He had bilateral facial nerve palsy, which was clear due to his inability to blow, and he was drooling saliva and fluids when asked to drink. He was hypotonic with power grade 3 in the upper limbs and grade 0 in the lower limbs with areflexia. Initially, his sensation was intact on the upper limbs but lost in the lower limbs up to mid-thighs, but later he lost sensation in his upper limbs. His planter reflexes were mute.

2.1. Diagnosis

Initially, it was thought to be cauda equine due to metastic carcinoma of the vertebral column, but an urgent MRI of the spine was done, and it was unremarkable. An MRI of the brain was also done, and it was unremarkable apart from hypertrophied sinuses. His blood investigations showed anemia and high white blood cells related to his acute lymphocytic leukemia (ALL) (Table 1). He was under close monitoring by the rapid response team while in the hospital and before completing the intravenous immunoglobulins. His monitoring consisted of measuring his peak expiratory flow rate every four hours. A final diagnosis was made after completing a 2-week inpatient nerve conduction study.

Table 1. The most significant blood investigations that were carried out during the hospital stay.

	Date	12/06	16/06	19/06
1	WCC	33.5	Over	24
2	HB	12.9	12.5	13.3
3	MCV	108	105	103
4	MCH	34.4	32.7	36.9
5	MCHC	31.6	31	35.8
6	Platelets	104	39	94
7	Neutrophils	24.1	-	-
8	ESR			
9	CRP			
10	Sodium	131	127	132
11	Potassium	3.1	3.2	3.12
12	Urea	29	31	
13	Creatinine	0.8	0.6	
14	Protein	8	5.9	
15	GGT	74	117	
16	ALT	35	46	

2.2. Management and Follow-Up

The mainstay treatment was composed of dexamethasone and IVIg. The patient received five days of IVIg. After he received the treatment, his facial nerve palsy improved, as did his upper limb weakness. He was referred back to the oncology hospital to decide on the continuation of his chemotherapy treatment. It was decided to book him for follow-up in one month. The aim of follow-up was to assess his recovery, which was very slow. It is reported that GBS may have a very slow recovery for up to one year [5].

3. Nerve Conduction Study

Severe demyelinating sensorimotor polyradiculoneuropathy with secondary extremely severe axonal loss. It also showed conduction block with partial sural sparing. When combining the triad of ataxia, ophthalmoplegia, and areflexia, a diagnosis of Miller Fisher Syndrome (MFS) is made. It does not exclude the fact that there might be severe axonal neuropathy induced by chemotherapy.

4. Discussion

4.1. Scientific Discussion of the Strengths and Limitations Associated with This Case Report

The limitation of this study is the difficulty in determining if the chemotherapy is inducing and triggering the MFS presentation or if it is just superimposing the motor and sensory demyelination by axonal neuropathy. The strength is that the typical presentation of ataxia, ophthalmoplegia, and areflexia is supported by the nerve conduction study along with the clear MRI results of the brain and whole spine.

4.2. Discussion of the Relevant Medical Literature

Guillain-Barré syndrome (GBS) is an inflammatory disease of the polyneuropathies and is the most common cause of acute flaccid paralysis, with an annual global incidence of approximately 1 - 2 per 100,000 person-years. It is more common in males than females [1]. GBS has three subtypes: acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor-sensory axonal neuropathy (AMSAN). 76% of patients report a triggering event four weeks prior to the presentation [2]. This includes an upper respiratory infection in 35% and gastroenteritis in 27% [2]. Other triggers, including medications, have been reported, such as tumor necrosis factor-alpha antagonist therapy [3]. Tacrolimus and suramin, isotretinoin, and immune checkpoint inhibitors

In this case, chemotherapy is believed to be the cause of the Miller-Fischer syndrome. Interferon alpha, tumor necrosis factor alpha antagonist therapy, anticancer drugs, and some of the quinolones have been reported to cause peripheral neuropathy. Vincristine is also associated with sensory disorders [6]. Other than chemotherapy-induced peripheral neuropathy, the cause of GBS in this

case could be reduced immunity, which can make the patients more prone to infections, and thus the antibodies produced can cause nerve damage. In our case, no prior symptoms of infection were reported.

The clinical hallmark of MFS is a triad of acute ophthalmoplegia, areflexia, and ataxia in the setting of preceding causation. There may be associated symptoms, including diplopia or blurred vision, dysarthria, dizziness, and extremity tingling. Clinical signs include facial paresis and distal hyporeflexia without signs of upper motor neuron dysfunction [7]. In our case, the triad was present along with dysarthria and extremity tingling initially. The clinical exam showed areflexia.

The diagnosis of MFS is usually clinical-based, but supporting investigations are especially important to rule out other differentials. Other differentials include brainstem encephalitis and other neuromuscular auto-immune disorders. MRI imaging of the spine and brain showed no signs of encephalitis. A nerve conduction study aided in the diagnosis of MFS.

The management of MFS is mainly supportive care. IVIG and plasmapheresis are mainstay therapies [5] [8]. Monitoring was carried out for this case using the peak expiratory flow rate to determine the need for respiratory support. It was carried on by the rapid support team. The patient was started on IVIG. Although corticosteroids are no longer recommended, they were used along with IVIG to cover auto-immune neuromuscular disorders until nerve conduction studies.

In conclusion, based on the classical presentation of MFS, the nerve conduction study, and the chemotherapy regime that has been used, the diagnosis of drug-induced MFS was a solid one.

5. The Scientific Rationales for Any Conclusions

Although GBS is uncommon, it must be taken into account when making a differential diagnosis for any patient presenting with progressive weakness. As about 25% of patients require mechanical ventilation during a period of days to months, about 20% of patients are still unable to walk after 6 months, and 3% - 10% of patients die. It is critical to understand the range and severity of GBS-related neurologic symptoms [5]. A proper history, including medications and social history, is always important. Even if the patient is not responding to the initial management, that does not mean to change the diagnosis, as sometimes they are slow to respond. Usually, if the patient is not responding to IVIg, a repeat IVIg should be considered if the EGOS score is 6 or above. Plasmapheresis and IVIg combined treatment have no significant differences [8].

Patient Consent

The patient's consent was required to publish this case report.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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