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# GBS WITH NON-HODGKIN LYMPHOMA , A RARITY

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## ABSTRACT:

Patients of Non-Hodgkin's lymphomas may develop neurological signs and symptoms. This case is of a 76 year old male recently diagnosed with Non-Hodgkin's lymphoma and on chemotherapy who presented with sudden bilateral leg weakness and inability to walk. The signs and symptoms, neurological examinations and Nerve conduction studies revealed a polyneuropathy which was consistent with Guillain-Barré syndrome (GBS). This has been seen in patients with Hodgkin's lymphoma but is rare in NHL.

**Keywords:** Non-Hodgkin lymphoma (NHL), Guillain-Barré syndrome (GBS), demyelinating polyneuropathy, chemotherapy.

**INTRODUCTION:** Non-Hodgkin lymphoma (NHL) is considered as a malignancy which starts from white blood cells referred to as lymphocytes, which are undoubtedly an essential part of the body's defense system. NHL most frequently affects adults, however even children can be affected. NHL typically starts in lymph nodes or other lymphatic tissue but occasionally it can also affect the skin. Lymphomas can occur anywhere within the body where lymphatic tissue is present. Lymph nodes, bone marrow, adenoids and tonsils, spleen, thymus and alimentary canal are the major sites of the lymphoid tissue. The type of lymphoma depends on the kind of lymphocyte affected (B cells or T cells), how mature the cells are, when they become cancerous and some other factors. Indolent lymphomas develop and unfold gradually whereas aggressive lymphomas grow and advance rapidly. In NHL there's a subtle male to female preponderance and the incidence rises with age particularly after forty years<sup>(1)</sup>. The neurological symptoms of NHL may potentially include any sort of neurological symptom from headaches to paralysis and meningism<sup>(2)</sup>.

Different patterns of neurological disease in patients with NHL have been seen, including direct lymphomatous involvement of the peripheral nerves, cord compression, and meningeal infiltration, spread to cerebrum, as paraneoplastic lymphomatous involvement of the peripheral nerves. Peripheral neuropathy is commonly caused by the toxic effect of

chemotherapeutic drugs. Another reason behind central nervous system damage is radiotherapy (radiation myelopathy)<sup>(1,3)</sup>. Paraneoplastic syndromes in neurologic essence, such as Guillain-Barré syndrome (GBS), are rare in NHL<sup>(1)</sup>. Guillain-Barré syndrome (GBS) is an auto immune disorder damaging the peripheral nerves, manifesting as a rapid-onset muscle weakness. The inceptive prodromes are generally changes in sensation or pain in conjunction with muscle weakness. GBS Immunopathology suggests that this is sometimes prompted by infection or, less commonly by surgery and also scarcely by vaccination. The diagnosis is generally made by clinical exclusion of alternate causes, and supported by tests like nerve conduction studies (NCS) and examination of the cerebrospinal fluid. GBS is the most common form of acute flaccid paralysis, and has different clinical subtypes are Acute inflammatory demyelinating polyneuropathy (AIDP), Acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN) or Pharyngeal-cervical-brachial variant.<sup>(4)</sup>. We present a case of NHL with GBS.

## CASE REPORT:

A 76-years-old male with previous co-morbid of hypertension for the last 5 years, on diet control, came to the A n E of Shifa International Hospital in April 2019, with the complaint of lower back pain and

sudden onset of bilateral lower limb weakness associated with inability to walk on both legs for 3 days. This was preceded by leg pain. There were no other complaints of bowel or urinary dysfunction, no speech or swallowing difficulty, no upper limb weakness, seizures, LOC, or fever. He also gives a history of intermittent low back pain. This patient was already been diagnosed as Non-hodgkin's Lymphoma on right inguinal lymph node biopsy on 3.11.2018 which showed "Follicular lymphoma, WHO Grade 3A, Ki67 proliferative index 40%". He had history of inguinal hernia operated 20 years back. He was in his usual state of health when on 28.10.18 he noted a lump at the operation scar of herniotomy. Visited a local hospital for follow up with his surgeon. Initially an Ultrasound abdomen was done which showed "cholelithiasis, splenomegaly with hypoechoic areas in spleen and extensive abdomino-pelvic lymphadenopathy". He underwent submandibular lymph node FNAC on 30.10.18 which showed a "lymphoproliferative disorder". He was referred to Shifa International hospital on 5.11.2018 for further workup and treatment. CT Scan neck, soft tissues, chest, abdomen and pelvis with contrast performed on 17.11.2018 showed enlarged lymph nodes in neck, bilateral axilla, mediastinum, in abdomen and pelvis with mass effect on adjacent viscera and vessels, findings likely of a Lymphoma. Bone marrow biopsy and aspiration performed on 20.11.2018 showed a "hypercellular marrow involved by lymphoma". Immunohistochemistry showed CD20:positive, CD10:Positive, Ki67 (proliferative index) 30-40%. His first cycle of chemotherapy started on 21.11.2018. He had a total 6 cycles of R-CHOP (Rituximab, Cyclophosphamide, Vincristine, Doxorubicin, Prednisone) Repeat CT scan of chest, abdomen and pelvis on 9.2.2019 showed interval increase in disease in mediastinal, retrocaval, peripancreatic and left paraaortic region, Some of left axillary lymph nodes were reduced in number and size while some are unchanged. Interval significant reduction in size of lymph nodes in right axilla, along internal iliac vessel and inguinal region, overall findings were suggestive of a mixed response to treatment. Repeat CT scan done on 20.3.19 showed interval increase in size of cervical, left supraclavicular, left axillary and mediastinal lymph nodes, interval increase in lobulated necrotic nodular mass in left para aortic and aorto caval region, interval increase in retrocaval nodal mass. Overall findings suggestive of interval increase in disease process so the patient was shifted to GDP (Gemcitabine, Dexamethasone and Cisplatin) and had 1 cycle of GDP. His last session of chemotherapy was done 10 days ago before his acute

presentation in the emergency department.

On examination in ER the patient had a pulse of 99/min, breathing rate 18/min BP 100/65 mmHg, SpO2% 91%. Was afebrile, GCS 15/15 and was having a pain score of 2/10 on arrival. Chest had B/L equal air entry. Pupils bilaterally equally reactive, pallor present, had bilateral pedal edema but no specific findings in abdomen. Neurological examination revealed intact cerebellar and sensory sensations, mild thoraco-lumbar spine tenderness, plantars bilateral mute, hyporeflexia in reflexes of upper and lower limbs. Power was as follows Upper limbs 5/5, 5/5. Lower Limbs Knees both in flexion and extension 4+/5, 4+/5, Hips in extension and flexion 3/5, 3/5, ankles dorsi and plantar flexion 4/5, 4/5. Laboratory investigations were done which showed TLC 14,270/UL, Hb 7.9 g/dL, Platelet count 14000/UL, Sodium 135mEq/L, potassium 3.5 mEq/L, Chloride 99 mEq/L, Bicarbonate 24mmol/L. BUN 15mg/dL, Urea 32.1 mg/dL, creatinine 1.2 mg/dL. ALP 395 U/L. MRI Dorso lumbar spine with contrast showed diffused heterogeneous marrow signal with post contrast enhancement at L1, T11, T10 and T8 vertebrae. Disruption of the posterior cortex of L1 vertebrae with soft tissue epidural compression indenting the ventral thecal sac on right. Small enhancing posterior epidural component at level of L5. Multiple para aortic, retrocaval and peripancreatic lymph nodes, lumbar disc degenerative changes. Nerve Conduction studies were then done and the report showed an abnormal study findings were suggestive of mixed predominantly demyelinating polyneuropathy, given the clinical history, Guillain Barre Syndrome is a possibility. The results of the nerve conduction studies were as follows: 1) Bilateral median APB motor responses have moderately prolonged distal latency, severely reduced amplitude, conduction velocity and not recordable F wave. 2) Right ulnar ADM motor response has mildly prolonged distal latency, moderately reduced amplitude, conduction velocity and mildly prolonged F wave. 3) Left ulnar ADM motor response has normal distal latency, mildly reduced amplitude, normal conduction velocity and F wave. 4) Right tibial motor response has normal distal latency, severely reduced amplitude, conduction velocity and not recordable F wave. 5) Left Tibial and bilateral Peroneal EDB motor are not recordable. 6) Bilateral peroneal TA motor responses have normal distal latencies, severely reduced amplitudes and normal conduction velocities. 7) Bilateral median, sural and superficial peroneal sensory are not recordable. 8) Right ulnar sensory response has moderately reduced latency, severely reduced amplitude and moderately reduced conduction velocity. 9) Left ulnar sensory response has moderately

reduced latency, moderately reduced amplitude and severely reduced conduction velocity. 10) Right radial has technical difficulty. 11) Left radial sensory response has normal latency, mildly reduced amplitude and normal conduction velocity. The patient was diagnosed with GBS and was advised PLEX but the patient and his family refused Plasmapheresis, IVIG or any other aggressive management. So the patient was put on supportive care. On the 3rd day of admission the neurological examination revealed GCS 15/15. Speech and comprehension Normal, reflexes diminished, plantar right downgoing, left equivocal, Power Upper limbs 4+/5, 4+/5, lower limbs 4-/5, 4-/5. Patient was discharged home in stable condition.

### **DISCUSSION:**

GBS is an autoimmune idiopathic acute demyelinating polyneuropathy. Two thirds of the cases are related to a recent upper respiratory tract infection and G.I.T. infection, most commonly associated with CMV, EBV virus and *Campylobacter jejuni*<sup>(5)</sup>. GBS has been associated with some systemic diseases like SLE, Hodgkin's Lymphoma and HIV. It is extremely rare in NHL, occurring in less than 0.3% of the cases<sup>(1,6)</sup>.

GBS presents as acute ascending polyneuropathy predominantly motor paralysis. Varying degree of sensory loss occurs but mostly in first few days and is sometimes hardly detectable. Death occur due to the involvement of the respiratory muscles. Oculomotor nerve involvement occur in very severe cases. It should be differentiated from other orthopedic and lumbar diseases causing back pain as many patients presents initially with generalized body and muscle aches specially in the back, hip, thighs and lower limbs. Clinically diminished and then absent deep tendon reflexes is the most consistent finding of GBS. The important investigations include Nerve conduction studies and CSF examination. CSF is acellular or contain a few lymphocytes while protein levels are elevated. EMG and NCS studies have the following findings consistent with GBS: slow conduction velocity, reduction in amplitude of muscular action potentials, conduction block in motor nerves, prolonged distal latencies ( indicative of distal conduction block) and prolonged or absent F waves ( indicative of involvement of proximal parts of nerves and roots). All of these showing focal demyelination<sup>(1)</sup>. Patients with NHL may present with neurological signs and symptoms. The peripheral neuropathy is mostly due to the local infiltration by lymphomatous cells or due to drug toxicity. Infiltration of the CNS is diagnosed usually by imaging techniques whereas peripheral nerve involvement may present with generalized motor,

sensory or sensory motor neuropathy, plexopathy, individual peripheral or cranial nerve deficit. Immune response in both CNS and PNS is attributed to be the most important cause of GBS. The tumors act as an antigen, which initiates an immunological response. Drugs causing neurological abnormalities are Vinca alkaloids causing sensorimotor polyneuropathy, cytarabine causing cerebellar dysfunction and intrathecal methotrexate and cytarabine may cause myelopathy<sup>(9)</sup>. Pal PK studied clinical and electrophysiological characteristics in vincristine induced neuropathy. NCS show prolonged mean distal latencies, decreased amplitude of Action potential, unchanged conduction velocities concluding that vincristine produces distal axonal sensorimotor neuropathy predominantly involving large diameter fibers<sup>(9,10)</sup>. In our case the differentials included demyelinating polyneuropathy (GBS), chemotherapy drug toxicity, Cauda equina syndrome or intramedullary lymphoma of the spinal cord. The clinical presentation of no bladder or bowel dysfunction and MRI findings excluded cauda equine syndrome. Also the MRI dorsolumbar spine with contrast was not consistent with intramedullary lymphoma of the spinal cord. Toxin mediated polyneuropathy was ruled out based on clinical features of diminished reflexes and NCS studies. The NCS studies showed mixed but predominantly demyelinating polyneuropathy consistent with GBS. Plasma Exchange is recommended as gold standard of care for the treatment of GBS but randomized control trials have shown that IVUG are at least equally effective. Plasma exchange leads to faster improvement compared to supportive care alone and is most effective when treatment is initiated in the first 7 days after the start of symptoms<sup>(8,11)</sup>. In our case unfortunately the patient refused treatment with either IVIG or PE and demanded supportive care.

### **CONCLUSION:**

We believe that GBS though extremely rare in NHL, was developed in this patient due to the immune mechanisms triggered by NHL. GBS is commonly seen in Hodgkin's Lymphoma and post transplantation but extremely rare in NHL. A few cases have been reported showing GBS in association with diffuse large B cell lymphoma, Burkitt Lymphoma and T/NK-cell lymphoma<sup>(1,6,11,12)</sup>. In our case GBS was associated with Follicular lymphoma ( grade 3A).

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**Javaria Munir:** Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review.

**Umer Aziz Qazi:** Study concept and design, data collection, data collection, data