Subacute Weakness in the Setting of Non-Hodgkin Lymphoma

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INTRODUCTION

Paraneoplastic neurological syndromes associated with Hodgkin (HL) and non-Hodgkin lymphomas (NHL) are uncommon and occur mostly with NHL rather than HL, with higher grade tumors leading to greater rates of nervous system involvement. It has been hypothesized that paraneoplastic syndromes are caused by an immune reaction to protein antigens expressed by the tumor, which are shared but sequestered in nervous system tissue. Paraneoplastic motor neuronopathies were first reported in 1963 with a disease course independent of the underlying malignancy. Patients with this syndrome typically develop proximally-predominant lower greater than upper extremity weakness, with a diagnosis of lymphoma usually following the neurological presentation. We present a case of an elderly man who developed a subacute motor neuronopathy after a diagnosis of NHL.

CASE PRESENTATION

A 70-year-old Caucasian man with a history of well-controlled diabetes mellitus, treated hypothyroidism, cervical spine degeneration, and marginal zone B-cell lymphoma presented to clinic for evaluation of possible chronic inflammatory demyelinating polyneuropathy (CIDP). Clinical course is described below in months prior to presentation to the neurology clinic:

•**7 months prior**: symmetric tingling in his hands, then two weeks later tingling in feet
•**4-3 months prior**: noted progressive weakness involving all limbs with worsening ambulation and balance, and falls
- no evidence of prodromal infection
- C3-6 cervical laminectomy with fusion, post-operatively complicated by a urinary tract infection that progressed to septic shock
- no improvement in weakness
- patient became wheelchair-bound with only slight improvement in function with physical therapy
- nerve conduction studies (NCS) and concentric needle electromyography (EMG) performed at outside institution

•**3 months -1 month prior:** given minimal improvement, patient received a 2 gm/kg induction dose of intravenous immunoglobulin (IVIg) followed by two monthly doses of 2 gm/kg plus prednisone 40 mg total daily for presumed CIDP

•**Clinical course:** no more than minimal improvement with these therapies
•**Family history**: Father- leukemia
Mother- NHL and follicular lymphoma grade III of intrathoracic lymph nodes

Neurologic Examination

•Mental status was normal with mild dysarthria
•No facial or tongue weakness or atrophy
•Severe diffuse symmetric limb weakness and atrophy (**Table 1**) with general hypotonicity
•No fasciculations were observed in cranial or limb muscles
•Deep tendon reflexes were absent except for 1+ biceps responses
•Sensation to large and small fiber modalities was intact except for slight reduction in timed vibration at his toes

Diagnostic Study Results:

•**NCS:** low amplitude motor response with preserved distal latencies and conduction velocities; absent sensory responses
•**EMG:** diffuse denervation in upper and lower limbs including thoracic paraspinal muscles (Table 2)
•**Cervical spine MRI postoperatively**: canal stenosis at C3-4 levels with flattening of cord and no abnormal enhancement
•**Labs:** erythrocyte sedimentation rate (ESR) elevated at 65 mm/hr, Vitamin B1 (65 nmol/L) and Vitamin B6 (11.7 nmol/L) had been low in the past, and he was placed on replacement
•**Cerebrospinal fluid (CSF):** elevated protein of 104 mg/dL, 3 WBCs, 3 RBCs, and was negative for cytology and oligoclonal bands
•**Whole body positron emission tomography scan:** left apical loculated pleural effusion without evidence of malignancy

Table 1. Muscle Strength

Muscle group	Initial consultation*	4 Months later*	8 Months later*
Shoulder Abduction	2/2	1/1	1/1
Biceps Strength	1/2	3/3	3/3
Triceps Strength	2/2	3/3	2/2
Wrist Extension	2/2	3/4-	2/2
Finger Flexion	3/3	4/4	4-/4-
Finger Abduction	1/1	1/1	1/1
Hip Flexion	2/2	1/1	1/1
Knee Flexion	2/2	2/2	1/1
Knee Extension	4/4	4-/4-	2/2
Foot Plantar Flexion	2/2	3/3	2/1
Foot Dorsiflexion	0/1	3/3	-/1

* Strength measured in MRC scale. Initial consultation is seven months after symptom onset.

Table 2. Summary of Needle Electromyography Performed 3 Months Prior to Presentation to Neurology Clinic

Muscle examined (left side)	Ins act.	Fib	PW	Fasc	Phases	Dur	Amp
1st Dorsal Interosseous	Normal	3+	0	0	Normal	1+	Normal
Abductor polices brevis	Normal	2+	0	0	Normal	1+	1+
Abductor Digit Minimi	Normal	1+	1+	0	Normal		
Flexor Pollicus Longus	Normal	0	3+	0	2+	1+	1+
Extensor indices proprius	Normal	2+	0	0	Normal	1+	Normal
Triceps	Normal	0	0	0	Normal	1+	Normal
Deltoid	Normal	1+	0	0	Normal	1+	Normal
Tibialis Posterior	Normal	0	0+	0	2+	1+	1+
Tibialis Anterior	Normal	2+	0	0	Normal		
Gastrocnemius	Normal	1+	0	0	Normal		
Vastus Lateralis	Normal	0	0	0	1+	1+	1+
Gluteus Medius	Normal	1+	0	0	Normal		
Lumbar Paraspinal	Normal	2+	1+	0	Normal		
Thoracic Paraspinal	Normal	1+	0	0	Normal		

Ins Act., insertion activity; Fib, fibrillation; PW, positive wave; Fasc, fasciculations; Recruit, recruitment; Dur, duration; Amp, amplitude.

DISCUSSION

The patient's presentation was complicated as it included a prior history of cervical stenosis and presumed diagnosis of CIDP. However, he continued to deteriorate after cervical spinal decompression, never developed myelopathic features, and his electrodiagnostic studies did not support a diagnosis of demyelinating neuropathy. Furthermore, immunomodulatory therapy with IVIg and corticosteroids over one year failed to result in significant improvement. Diffuse denervation patterns on EMG, including thoracic paraspinal musculature, support the final diagnosis of motor neuronopathy.

Treatment responses in paraneoplastic motor neuronopathy associated with lymphoma and other cancers have been variable.

Compared to NHL, the motor neuronopathy associated with HL appears to have a more favorable response to therapy.

Chemotherapy or radiation treatments may confound the extent of weakness and atrophy attributable to a paraneoplastic syndrome.

Many of these patients have risk factors for sensory neuropathy such as diabetes or chemotherapy exposures that may further cloud the clinical picture, complicating proper classification of the peripheral neuropathic process.

Alternative explanations for the underlying weakness often precede the ultimate diagnosis of a paraneoplastic process and may be accompanied by both medical and surgical interventions that produce little or no benefit, a pattern seen in our patient.

CONCLUSION

Paraneoplastic motor neuronopathy, although rare, should be considered in the differential diagnosis of patients with NHL presenting with a motor-predominant peripheral nerve disorder. Although severe and diffuse weakness usually precedes the diagnosis of malignancy, this case provides an example of motor neuronopathy following the diagnosis of NHL. Early identification of paraneoplastic neuronopathy is important as it may prevent unnecessary interventions and may guide therapeutic strategies.

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