Clinical Reasoning: A 65-Year-Old Woman With Cancer History and Wrist Drop

Author(s):
Rebecca Merrill, BS¹; Meaghan Puckett, BA¹; William Patrick Morrow, MD²; Eric D. Hsi, MD²; Jason Powell, MD³; Zhongyu Li, MD, PhD⁴; Rakhee Vaidya, MBBS⁵; Roy Strowd⁶

Corresponding Author:
Rebecca Merrill, rmerrill@wakehealth.edu


Equal Author Contribution:

Neurology® Published Ahead of Print articles have been peer reviewed and accepted for publication. This manuscript will be published in its final form after copyediting, page composition, and review of proofs. Errors that could affect the content may be corrected during these processes.

Copyright © 2022 American Academy of Neurology. Unauthorized reproduction of this article is prohibited
Abstract:
Wrist drop is a common presentation in neurology. To localize the lesion, clinicians can focus on testing finger extension, elbow flexion with semi-pronated forearm, and elbow extension among other muscle groups as well as identifying dermatomes of numbness. Once the lesion is localized, electrophysiology or imaging can guide to an underlying etiology. Here we describe a case that illustrates the importance of using a stepwise approach to diagnose the etiology of wrist drop in a patient with a cancer history. A 65-year-old woman with diffuse large B-cell lymphoma in remission presented with new onset wrist drop, severe pain, numbness, and tingling concerning for peripheral nerve injury. Imaging findings from PET, venous ultrasound, nerve conduction velocity study (NCV), and MRI were conflicting favoring deep venous thrombosis, cancer recurrence, or peripheral nerve sheath tumor. A biopsy was ultimately required to confirm the diagnosis.

SECTION 1
A 65-year-old woman with diffuse large B-cell lymphoma (DLBCL) presented with new wrist drop and severe pain in the left hand. Five months prior, she completed six cycles of R-CHOP (i.e., rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) and achieved complete remission. One month prior, she began having trouble gripping items and typing. She presented to the neurology clinic with progressive left wrist drop, numbness, tingling and pain. She denied history of arm or shoulder trauma. Neurologic examination showed 1/5 strength with wrist extension (i.e., extensor carpi radialis and extensor carpi ulnaris muscles), and 0/5 strength with finger extension (i.e., extensor digitorum, extensor indicis, and extensor digiti minimi). All other muscles showed no weakness including the brachioradialis, triceps, and deltoid. Sensation was diminished on the dorsum of the hand. Deep tendon reflexes were 2+ throughout.

Questions for Consideration:
1. How would you describe this presentation?
2. What is the localization?

SECTION 2
This patient presents with subacute onset of wrist drop. This most commonly arises from lesions involving the radial nerve and muscles of wrist extension. The radial nerve is the terminal continuation of the posterior cord of the brachial plexus and contains fibers from the C5-T1 nerve roots. Wrist drop can arise from abnormalities anywhere along its course (Fig 1).
When approaching patients with wrist drop, it is helpful to focus on four muscles: the extensor digitorum, brachioradialis, triceps, and deltoid. Isolated weakness of the extensor digitorum is seen in forearm radial nerve lesions. Involvement of the brachioradialis suggests pathology proximal to the forearm at the spiral groove. Prominent involvement of the triceps, brachioradialis, and extensor digitorum indicates pathology in the axilla. Deltoid weakness suggests a radial nerve lesion in the posterior cord. Patients with C7 root lesions present with weakness of extensor digitorum and triceps sparing the brachioradialis. There are also four sensory branches of the radial nerve: lower lateral cutaneous nerve of the arm, posterior cutaneous nerve of the arm, posterior cutaneous nerve of the forearm, and superficial branch.

Our patient’s exam best localizes to a lesion at the forearm or spiral groove.

**Question for Considerations**

1. What imaging modalities can be used to determine the etiology of wrist drop?

**SECTION 3**

Wrist drop can be evaluated with a variety of diagnostic tests, including nerve conduction study (NCV), electromyography (EMG), neuromuscular ultrasound (NMUS), magnetic resonance imaging (MRI), and in cancer patients, positron emission tomography (PET).

**What imaging modalities were used?**

- **Step 1: PET**

  In a patient with a suspected lymphoma, focal uptake of fluorodeoxyglucose (FDG) in the lymph nodes of the axilla or along the course of the nerves suggests a neoplastic etiology. Low-grade diffuse FDG uptake may be seen with radiation induced brachial plexopathy or in rare cases of infectious brachial plexitis or thromboses.

  In our patient, PET showed linear uptake along the vascular bundle of the left axilla that was most consistent with an upper extremity deep vein thrombosis (DVT). There was no focal uptake to suggest tumor recurrence (Fig 2).

- **Step 2: Venous ultrasound**

  Due to concern for DVT, an upper extremity venous ultrasound was performed. Ultrasound suggested an enlarged lymph node adjacent to the axillary artery and vein but no DVT.

- **Step 3: NCV/EMG/NMUS**

  NCV/EMG is helpful in determining the location of nerve injury and acuity of pathology. In our patient, NCV revealed absent left radial sensory response and an abnormal radial motor response with a markedly low amplitude, slowed conduction velocity, and normal latency. NCV of the contralateral arm was normal. EMG showed fibrillation potentials in the extensor digitorum and extensor carpi radialis muscles consistent with active denervation. There was reduced muscle recruitment in the brachioradialis. No abnormalities of the triceps or deltoid muscles were noted. These findings were consistent with a severe focal left radial axonopathy at or distal to the spiral groove.

  NMUS is an increasingly available non-invasive diagnostic tool that can visualize the radial nerve at specific locations including the spiral groove. Compression is characterized by increased cross-sectional area or echogenicity. NMUS was not performed in this patient.

- **Step 4: MRI**
MRI is the modality of choice for lesions in the brachial plexus or axilla and allows for characterization of mass lesions through high-resolution anatomic imaging. MR neurography is used to identify peripheral nerve injury where nerves appear hyperintense and without a normal fascicular pattern. Mass effect from a lesion compressing the nerve or scarring from previous injury can also be seen (2). In a patient with cancer, MRI can demonstrate metastatic lesions, nerve sheath tumors, inflammatory lesions, or radiation injury. Metastatic lesions appear as contrast-enhancing masses. Malignant peripheral nerve sheath tumors restrict diffusion and are larger and more irregular than benign tumors. Peripheral neurolymphomatosis presents as enhancing, T2-weighted hyperintense lesions along the course of the nerve. Inflammatory etiologies (e.g. brachial plexitis) appear hyperintense diffusely on T2- weighted imaging with asymmetric thickening, and enhancement acutely (2).

In our patient, MRI revealed an enhancing, T2-hyperintense left axillary mass. A differential diagnosis of enlarged lymph node or nerve sheath tumor was reported (Fig. 2).

Questions for Consideration:

1. What is the next step to establish a diagnosis when imaging is inconclusive?
2. What treatment options are available?

SECTION 4

Due to high suspicion for a neoplastic process, the decision was made to proceed with open nerve biopsy. A mass was resected from the lateral cord of the brachial plexus to the proximal radial nerve. Histologic sections revealed extensive, diffuse infiltration of the peripheral nerve by clusters and sheets of large neoplastic lymphoid cells. The histologic results were consistent with relapse of her DLBCL. Immunostains showed that the lymphoid cells were B-cells expressing CD5, CD20, CD79a, MUM1, and BCL2 and negative for cyclin D1, CD10, BCL6, and MYC. Bone marrow biopsy, spinal fluid, and PET/CT scan was negative for malignant involvement.

The patient was started on salvage chemotherapy with R-DHAC (rituximab, dexamethasone, cytarabine, and carboplatin). PET/CT scan after salvage chemotherapy showed treatment response. The patient is undergoing high-dose chemotherapy and autologous stem cell transplant. Her wrist drop and weakness remained stable and is supported by a brace.

DISCUSSION

This case highlights important teaching points, including: (1) localizing wrist drop to the spiral groove should prompt imaging evaluation, (2) individual anatomical variants may result in unique localization, so there should be a low threshold to search in a wider area for a lesion, (3) in a lymphoma patient, even when imaging favors an alternative etiology, clinicians must have a high index of suspicion for cancer recurrence and pursue tissue for definitive diagnosis; and (4) perineural spread of lymphoma is a rare peripheral presentation of non-Hodgkin's lymphoma.

This case addresses several questions for clinicians and trainees caring for cancer patients with wrist drop:

What is wrist drop?

In patients with wrist drop, the wrist and finger extensor muscles become weak. Without wrist and finger extension, the flexor muscles are unopposed causing the appearance of a dropped wrist with the fingers curling under the wrist when the patient holds out the arm. The most common localization of wrist drop is a lesion to the radial nerve at the spiral groove. Once the lesion is localized, using imaging in a step-wise approach is essential to determine the etiology.

How does lymphoma affect the peripheral nervous system?

Lymphoma can affect the PNS directly or secondarily due to infectious, metabolic, treatment-related complications, or paraneoplastic neurological disorders (3). Compression from mass-like lesions can affect any nerve including the brachial plexus or radial nerve. Direct spread of lymphoma into the PNS (e.g. neurolymphomatosis) occurs when tumor cells...
invade the perineural space. Neurotrophic factors promote the spread of cancer along the nerve and are upregulated by cancer and neuronal cells (4,5). Lymphoma can also spread to the leptomeninges resulting in neoplastic meningitis.

In secondary involvement of the PNS, treatment toxicity due to chemotherapy is one of the most common causes. Neurotoxic chemotherapies used in patients with lymphoma include vinca alkaloids, proteosome inhibitors, brentuximab vedotin, and immune checkpoint inhibitors (3). Paraneoplastic neurological syndromes mostly involve the central nervous system (e.g., limbic encephalitis, encephalomyelitis). PNS paraneoplastic syndromes are rare.

**What is neurolymphomatosis?**

Neurolymphomatosis is the histologically documented infiltration of the peripheral nervous system by lymphoma and can present at diagnosis or recurrence (7). Common presentations of neurolymphomatosis include painful, asymmetric peripheral neuropathy, cranial neuropathy, painless polyneuropathy, peripheral mononeuropathy, plexopathy, or mononeuropathy multiplex (6,7). A high index of suspicion is required as presenting signs and symptoms are heterogeneous. Neurolymphomatosis should be considered in any lymphoma patient not receiving neurotoxic chemotherapy with unexplained PNS symptoms. Nerve biopsy is the gold standard of diagnosis. Neurological deficits rarely recover, and prognosis is poor, particularly with delayed diagnosis. It is unclear whether multi-drug chemotherapy regimens (e.g., R-CHOP) are superior to single-drug regimens (e.g. high-dose methotrexate).

References:

Figure 1: Etiologies, Symptoms, and Localization of Wrist Drop

Diagram demonstrating the possible etiologies of wrist drop with the associated signs and symptoms at each of the common localizations—C7 root, axilla, spiral groove, and forearm. Elbow flexion in the figure represents the brachioradialis’ action while the forearm is supinated. Patients may report paresthesias or sensory loss. A thorough examination of pinprick, temperature, and light touch should be conducted in patients with suspected lesions. All four sensory nerves are affected with lesions in the axilla. Lesions at the forearm spare sensation over the dorsal arm and forearm because the posterior cutaneous nerve of the forearm branches proximally. In our patient, sensory loss over the dorsum of the hand is consistent with a lesion in the spiral groove.

<table>
<thead>
<tr>
<th>Wrist drop localization</th>
<th>Associated symptoms</th>
<th>Common etiologies</th>
<th>Sensory disturbance</th>
<th>Finger and wrist extension</th>
<th>Elbow flexion with semi-pronated forearm</th>
<th>Elbow extension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical root</td>
<td>C5 C6 C7 T1</td>
<td>• Herniated disc • Inflammatory polyradiculopathy • Shoulder pain • Trauma or traction of nerve</td>
<td>• Posterior arm • Lateral arm • Posterior forearm • Dorsoradial hand</td>
<td>Abnormal</td>
<td>Abnormal</td>
<td></td>
</tr>
<tr>
<td>Axilla</td>
<td>• Triceps extension weakness</td>
<td>• Brachial plexitis • Proximal humerus fracture • Crutch palsy • Overuse injury</td>
<td>• Posterior arm • Lateral arm • Posterior forearm • Dorsoradial hand</td>
<td>Abnormal</td>
<td>Abnormal</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Spiral groove</td>
<td>• Finger extension weakness • Weak forearm supination</td>
<td>• Nerve compression • Humeral shaft fracture • Prolonged blood pressure cuff inflation • Saturday-night palsy</td>
<td>• Posterior arm • Dorsoradial hand</td>
<td>Abnormal</td>
<td>Abnormal</td>
<td></td>
</tr>
<tr>
<td>Forearm</td>
<td>• Finger extension weakness • Partial or no wrist drop • Forearm and wrist pain</td>
<td>• Nerve compression • Elbow dislocation/subluxation • Overuse injury • Tight casts • Distal autoimmune neuropathy</td>
<td>• Dorsoradial hand</td>
<td>Abnormal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 2: Coronal PET imaging showing increased fluorodeoxyglucose (FDG) uptake along the left axillary neurovascular bundle (2A, 2B). Coronal T1-weighted post-contrast left upper arm and humerus MRI showing an enhancing left axillary mass measuring 2.1 x 1.6 cm along the neurovascular bundle (2C).
## Clinical Reasoning: A 65-Year-Old Woman With Cancer History and Wrist Drop

Rebecca Merrill, Meaghan Puckett, William Patrick Morrow, et al.

*Neurology* published online July 18, 2022
DOI 10.1212/WNL.0000000000201039

This information is current as of July 18, 2022

<table>
<thead>
<tr>
<th>Updated Information &amp; Services</th>
<th>including high resolution figures, can be found at:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><a href="http://n.neurology.org/content/early/2022/07/18/WNL.0000000000201039.full">http://n.neurology.org/content/early/2022/07/18/WNL.0000000000201039.full</a></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subspecialty Collections</th>
<th>This article, along with others on similar topics, appears in the following collection(s):</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Imaging</td>
<td><a href="http://n.neurology.org/cgi/collection/all_imaging">http://n.neurology.org/cgi/collection/all_imaging</a></td>
</tr>
<tr>
<td>Clinical neurology examination</td>
<td><a href="http://n.neurology.org/cgi/collection/clinical_neurology_examination">http://n.neurology.org/cgi/collection/clinical_neurology_examination</a></td>
</tr>
<tr>
<td>Metastatic tumor</td>
<td><a href="http://n.neurology.org/cgi/collection/metastatic_tumor">http://n.neurology.org/cgi/collection/metastatic_tumor</a></td>
</tr>
<tr>
<td>Nerve tumor</td>
<td><a href="http://n.neurology.org/cgi/collection/nerve_tumor">http://n.neurology.org/cgi/collection/nerve_tumor</a></td>
</tr>
<tr>
<td>Surgical therapy-tumor</td>
<td><a href="http://n.neurology.org/cgi/collection/surgical_therapytumor">http://n.neurology.org/cgi/collection/surgical_therapytumor</a></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Permissions &amp; Licensing</th>
<th>Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><a href="http://www.neurology.org/about/about_the_journal#permissions">http://www.neurology.org/about/about_the_journal#permissions</a></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reprints</th>
<th>Information about ordering reprints can be found online:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><a href="http://n.neurology.org/subscribers/advertise">http://n.neurology.org/subscribers/advertise</a></td>
</tr>
</tbody>
</table>