

# Diabetes and CIDP

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# Is it CIDP or Diabetic Neuropathy?

## 51-year-old Woman With Comorbid Type 2 Diabetes Mellitus

History	Case notes
<b>Presenting complaint</b>	<ul style="list-style-type: none"><li>• 10-year history of fatigue, worsening numbness in feet, and progressive loss of balance and difficulty walking, particularly severe in past 6 months</li></ul>
<b>Medical history</b>	<ul style="list-style-type: none"><li>• Height: 5' 2"; weight: 160 lb (72.6 kg)</li><li>• Diagnosed with diabetes mellitus at age 42<ul style="list-style-type: none"><li>– Partially controlled on metformin 1000 mg BID + glipizide 15 mg BID</li></ul></li><li>• Diagnosed with hypertension at age 48<ul style="list-style-type: none"><li>– Currently on losartan 50 mg QD (BP: 128/82 mm Hg)</li></ul></li></ul>
<b>Social history</b>	<ul style="list-style-type: none"><li>• Married; 3 children</li><li>• Works as housekeeper; requires moderate physical activity; had to stop working 2 weeks ago</li></ul>

# Physical Findings

Examination	Case notes
<b>Motor</b>	<ul style="list-style-type: none"><li>• Loss of bulk of intrinsic foot muscles</li><li>• 3/5 at ankle and toe movements</li><li>• 4/5 interossei in hands</li><li>• 5/5 at hip flexion and knee flexion/extension</li><li>• 5/5 at biceps, triceps, and finger abduction</li><li>• 5/5 at deltoid</li></ul>
<b>Sensory</b>	<ul style="list-style-type: none"><li>• Vibration sense absent at toe; moderately reduced at ankle, knee, and finger</li><li>• Proprioception absent at toe and ankle; normal at finger</li></ul>
<b>Reflexes</b>	<ul style="list-style-type: none"><li>• Absent ankles, reduced knee, wrist; normal biceps, triceps</li></ul>
<b>Function</b>	<ul style="list-style-type: none"><li>• Difficulty walking and sometimes uses a wheelchair</li><li>• Not able to work as a housekeeper</li></ul>

# Electrophysiology Suggests Demyelination

Nerve and site	Latency (ms)	Amplitude (mV)	CV (m/s)	F wave (ms)
L. median – APB (wrist)	6.8*	5.8	—	36.3*
L. median – APB (elbow)	9.1	4.4	42*	—
L. ulnar – ADM (wrist)	4.1*	4.0	—	Absent
L. ulnar – ADM (wrist to below elbow)	7.5	2.0*	41*	—
L. ulnar – above to below elbow)	12.3	1.6	27*	—

Absent responses: bilateral peroneal-EDB, bilateral sural, L. median sensory, L. ulnar sensory. \*Result is in demyelinating range.

Peroneal motor, tibial motor, and sural sensory  
are all absent.

# What Features Guide Diagnosis?

Work-up	Case notes
Physical exam	<ul style="list-style-type: none"><li>• Loss of bulk of intrinsic foot muscles, suggesting long-term weakness/disease consistent with diabetic neuropathy</li><li>• Distal but not proximal weakness</li><li>• Vibration sense absent at toe; moderately reduced at ankle; normal knee, and finger; moderate proprioception decrease</li><li>• Reflex loss in ankles</li><li>• Unsteady gait/unstable on standing</li></ul>
Labs	<ul style="list-style-type: none"><li>• HbA<sub>1c</sub>: 7.4%</li><li>• BUN/creatinine: normal</li><li>• CSF protein: 90 mg/dL</li></ul>
Electrophysiology	<ul style="list-style-type: none"><li>• Sensorimotor polyneuropathy</li><li>• Evidence consistent with segmental demyelination<ul style="list-style-type: none"><li>– Prolonged distal latency, L. median &gt; ulnar</li><li>– Moderate motor conduction velocity slowing, L. median and L. ulnar</li><li>– Slowing at compression sites: Median at wrist; ulnar at elbow</li></ul></li></ul>

**Diagnosis: Diabetic neuropathy with both demyelinating and axonal abnormalities.**

# Typical CIDP Differs From Diabetic Neuropathy

Typical CIDP <sup>1,2</sup>	DPN/DSP <sup>3,4</sup>
<ul style="list-style-type: none"> <li>• Distal and proximal weakness</li> </ul>	<ul style="list-style-type: none"> <li>• Distal weakness mainly in the feet</li> </ul>
<ul style="list-style-type: none"> <li>• Motor <math>\geq</math> Sensory loss</li> </ul>	<ul style="list-style-type: none"> <li>• Sensory <math>\geq</math> Motor loss</li> </ul>
<ul style="list-style-type: none"> <li>• Reduced or absent reflexes</li> </ul>	<ul style="list-style-type: none"> <li>• Most have absent DTRs at ankles</li> </ul>
<ul style="list-style-type: none"> <li>• Symptoms evolve over months</li> </ul>	<ul style="list-style-type: none"> <li>• Symptoms evolve over years</li> </ul>
<ul style="list-style-type: none"> <li>• Pain less common</li> </ul>	<ul style="list-style-type: none"> <li>• Pain more common</li> </ul>

DPN = diabetic peripheral neuropathy; DSP = diabetic sensory polyneuropathy; DTR = deep tendon reflex.

1. Dalakas MC. *Nat Rev Neurol*. 2011;7(9):507-517. 2. Köller H, et al. *N Engl J Med*. 2005;352(13):1343-1356.

3. Llewelyn JG. *J Neurol Neurosurg Psychiatry*. 2003;74(suppl II):ii15-ii19. 4. Zilliox L, et al. *Curr Treat Options Neurol*. 2011;13(2):143-159.

# Association of Diabetes and CIDP Remains Unresolved

- The literature is inconclusive<sup>1,2</sup>

Prevalence of CIDP in diabetic patients <sup>1</sup>	Prevalence of diabetes in CIDP patients <sup>2</sup>
<ul style="list-style-type: none"> <li>• Prospective study of patients referred to an electrophysiology laboratory (Miami, Florida)</li> </ul>	<ul style="list-style-type: none"> <li>• Retrospective analysis of medical records within a well-defined community (Rochester, Minnesota)</li> </ul>
<ul style="list-style-type: none"> <li>• N = 1127 in study period 2</li> </ul>	<ul style="list-style-type: none"> <li>• N = 1581</li> </ul>
<ul style="list-style-type: none"> <li>• In patients with diabetes               <ul style="list-style-type: none"> <li>– Prevalence of CIDP was 9.9% (32 of 189 patients) vs</li> </ul> </li> <li>• In patients without diabetes, the prevalence of CIDP was 1.8% (17 of 938 patients)</li> </ul>	<ul style="list-style-type: none"> <li>• In age and sex matched controls, the prevalence of diabetes was 12% (14 of 115 patients), but among CIDP patients, the prevalence of diabetes was 4% (1 of 23 patients)</li> </ul>
<ul style="list-style-type: none"> <li>• <b>Conclusion:</b> Prevalence of CIDP appeared to be increased in patients with diabetes mellitus</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Conclusion:</b> Prevalence of diabetes mellitus was not felt to be increased in CIDP</li> </ul>

# Dr Levine's Pearls:

## When to Consider CIDP in Diabetics

- Classic CIDP symptoms and signs
  - Symmetric proximal and distal weakness
  - Global hyporeflexia
- Aggressive clinical course
  - Diabetic neuropathy is slowly progressive
- Prominent motor signs
  - Although foot dorsiflexion weakness can occur in diabetic neuropathy, it is not common and one should consider alternative diagnoses, including CIDP
- Conduction block, marked temporal dispersion, or slowing of conduction velocity  $\geq 30\%$



# Dr Levine's Pearls (cont.): CIDP Can Be Misdiagnosed in Diabetics

- Diabetic neuropathy may have conduction slowing out of proportion to amplitude reduction
  - Diabetic neuropathy is both axonal and demyelinating
- Diabetics have predisposition to conduction slowing at sites of compression
- CSF protein increased in diabetics up to 100 mg/mL

# Alternative View: CIDP Is Being Missed in Diabetics

- CIDP patients with diabetes (CIDP + DM) may present with a different clinical phenotype and electrophysiological profile than CIDP patients without diabetes (CIDP – DM)
  - CIDP + DM patients likely to have more severe abnormalities
  - But they are less likely to receive appropriate treatment
- Response rates to CIDP therapies are similar with or without DM; clinicians need to consider the possibility of CIDP + DM

# Recommendations

- Avoid diagnosis of CIDP in patients with length-dependent, slowly evolving neuropathy
- Do not base diagnosis of CIDP on peroneal nerve conduction slowing alone
- Do not base diagnosis of CIDP on conduction slowing at compression sites
- If symptoms and signs lead to diagnosis of CIDP, give a limited trial of first-line therapy and have objective signs of improvement before continuing
- Seek second opinion