# Polyradiculoneuropathies Associated with Immune Checkpoint Inhibitors: Are We Facing a New Nosological Entity?

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## Objectives

Immune checkpoint inhibitors (ICIs) such as ipilimumab, nivolumab, and Pembrolizumab have revolutionized the treatment of advanced malignancies. However, their expanding use has been paralleled by the emergence of immune-related adverse events (irAEs), including neurological complications affecting the peripheral nervous system (PNS). This study presents a case of ICI-induced polyradiculoneuropathy and reviews the current literature, with a focus on the diagnostic and therapeutic challenges in differentiating acute inflammatory demyelinating polyneuropathy (AIDP) from acute-onset chronic inflammatory demyelinating polyneuropathy (A-CIDP).

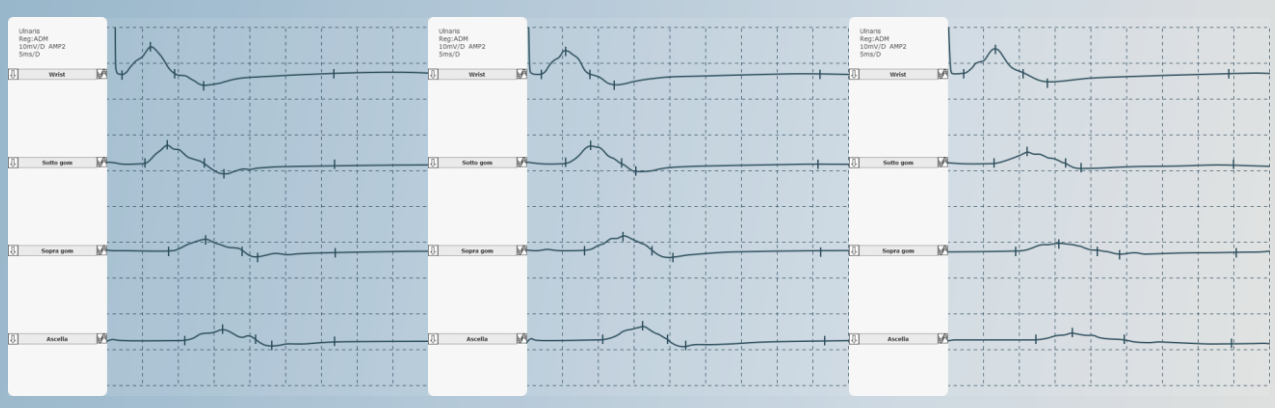
## Materials and methods

We report the case of a 48-year-old woman with metastatic melanoma treated with pembrolizumab who developed progressive motor and sensory symptoms consistent with polyradiculoneuropathy after two treatment cycles.

Clinical assessment, neurophysiological testing (nerve conduction studies and electromyography), and cerebrospinal fluid (CSF) analysis were performed to guide diagnosis and treatment. A literature review was conducted to identify reported cases of ICI-associated AIDP and CIDP, including demographic data, clinical features, diagnostic findings, and outcomes.

| | **Day of admission** | | | **Day 60** | | | **Day 100** | | | **Day 140** | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Lat (ms) | Amp (mV) | CV (m/s) | Lat (ms) | Amp (mV) | CV (m/s) | Lat (ms) | Amp (mV) | CV (m/s) | Lat (ms) | Amp (mV) | CV (m/s) |
| **SENSORY** | | | | | | | | | | | | |
| R SURAL | 2.5 | 7.8 | 50 | 2.6 | 7.8 | 59 | 2.7 | 11.4 | 43 | 2.5 | 10.4 | 44 |
| L ULNAR | 2.2 | 8.7 | 47.4 | 2.1 | 15.2 | 40 | 2.9 | 9.4 | **35** | 2 | 9.3 | 41 |
| **MOTOR** | | | | | | | | | | | | |
| R PERONEAL | | | | | | | | | | | | |
| *Ankle* | 3.8 | 9.9 | | 2.5 | 8.1 | | 3.6 | 8.0 | | 3.9 | 5.6 | |
| *Fib Head* | 9.6 | 5.9 | **38** | 8.7 | 7.9 | 48 | 8.8 | 5.4 | 37 | 9.6 | **3.8** | **38** |
| *Pop fossa* | 11.0 | 5.7 | **37** | 10 | 7.7 | 58 | 10.5 | 4.5 | **38** | 11.7 | **3.7** | **41** |
| L TIBIAL | | | | | | | | | | | | |
| *AH* | 4.5 | 14.2 | | 3.7 | 14.5 | | 5 | 13.5 | | 2.9 | 11 | |
| *Pop fossa* | 13 | 6.7 | 38 | 10 | 9.9 | 50 | 14.7 | 7.6 | **33** | 10 | 8 | 48 |
| *F wave* | **NR** | - | - | 52 | - | - | **NR** | - | - | 57 | - | - |
| R MEDIAN | | | | | | | | | | | | |
| *Wrist* | 2.7 | 11.9 | | 2.2 | 10.9 | | 3.7 | 11.9 | | 2.8 | 11.7 | |
| *Elbow* | 6.6 | 11.5 | 52 | 6.2 | 10.2 | 56 | 7.7 | 6.4 | **44** | 6.9 | 7.8 | 53.3 |
| L ULNAR | | | | | | | | | | | | |
| *Wrist* | **2.8** | 10.5 | | 2.1 | 11.3 | | 2.7 | 9 | | 2 | 7.4 | |
| *B. elbow* | 5.6 | 6.5 | **43** | 5.7 | 8.9 | 50.7 | 6.2 | **4.5** | **38** | 4.7 | 5.8 | **46** |
| *A. elbow* | 7.7 | 5.5 | **40** | 7.9 | 7.7 | 53.4 | 9.1 | **2.9** | **41,5** | 8 | 5 | **39** |
| *F wave* | **51** | - | - | 29 | - | - | **NR** | - | - | 30 | - | - |

The electrodiagnostic study performed at baseline and at different follow-up times in the A-CIDP patient




**L ULNAR** motor NCS recording from abductor digiti minimi

**A,** above; **AH,** abductor hallucis; **Amp,** amplitude; **B,** below; **CV,** conduction velocity; **Fib,** fibular; **L,** left; **Lat,** latency; **m/s**, meter per second; **ms,** milliseconds; **Pop**, popliteal; **NCS,** nerve conduction studies; **NR,** no responses; **R,** right; **S,** superficial.

**Sensory nerve conduction studies: latency represents the peak latency, and amplitude is measured in microvolts. Motor nerve conduction studies: latency represents the onset latency, and the amplitude is measured in millivolts. Normal values: sural (amp ≥ 6 mV, CV ≥ 40,6 m/s); sensory ulnar (amp ≥ 8 mV, CV ≥ 39,2 m/s); motor peroneal (lat ≤ 4.7 ms, amp ≥ 4 mV, CV fib head ≥ 41,6 m/s – CV pop fossa ≥ 39,1 m/s); motor tibial (lat ≤ 5.1 ms, amp ≥ 5 mV, CV pop fossa ≥ 34,6 m/s – F wave latency 58-69.9 ms); motor median (lat ≤ 3.6 ms, amp ≥ 5 mV, CV elbow ≥ 49,9 m/s – F wave latency 29.6-37.8 ms); motor ulnar (lat ≤ 2.5 ms, amp ≥ 5 mV, CV B. elbow ≥ 50,6 m/s, CV A. elbow ≥ 43,8 m/s – F wave latency 29.8-35.3 ms).*

## Results

The patient was initially diagnosed with AIDP and treated with intravenous immunoglobulin (IVIg), with partial improvement. However, a relapse occurred 60 days later, characterized by diffuse weakness and progression of symptoms, prompting reclassification as A-CIDP. Discontinuation of pembrolizumab and initiation of immunosuppressive therapy stabilized the disease course. The literature review identified 51 cases of ICI-associated AIDP and 10 of CIDP. Common symptoms included limb weakness, paresthesia, and gait disturbances. Electrophysiological studies often showed demyelinating patterns. While most patients responded to corticosteroids or IVIg, a subset experienced relapses suggestive of A-CIDP, raising concerns about diagnostic accuracy.

## Discussion

ICI-associated polyradiculoneuropathies present a diagnostic dilemma, particularly when clinical evolution reveals features consistent with A-CIDP. The overlap between monophasic and chronic demyelinating neuropathies in this context underscores the need for early, dynamic diagnostic reassessment and individualized treatment strategies. Timely discontinuation of ICI therapy and initiation of immunomodulatory treatment are critical to prevent irreversible neurological damage.

## Conclusions

This case and literature review suggest that ICI-induced polyradiculoneuropathies may represent a distinct nosological entity, often mimicking or transitioning from AIDP to A-CIDP. Clinicians should maintain a high index of suspicion for evolving disease courses and consider extended monitoring and tailored immunotherapy in affected patients.

## References

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2. *Doneddu PE et al.; Italian CIDP Database study group. Atypical CIDP: diagnostic criteria, progression and treatment response.*

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