The Tirzepatide Tingle: Worsening peripheral neuropathy during Mounjaro® treatment

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Background

Mounjaro®▼ (tirzepatide) is a dual GIP/GLP-1 receptor agonist used in type 2 diabetes (T2DM) and weight management for its effects on glycaemic control and weight reduction. Peripheral neuropathy is common in long-standing diabetes and may fluctuate or progress over time. However, worsening neuropathic symptoms during tirzepatide titration may raise concern for a suspected adverse drug reaction (ADR).

Aim

To explore a suspected ADR case involving worsening peripheral neuropathy during tirzepatide dose escalation and consider possible contributing factors.

Methodology

A retrospective case review and a literature search were undertaken in November 2025 using Embase, Cochrane Library and PubMed. Clinical findings were compared with published evidence to assess possible explanations for worsening neuropathy.

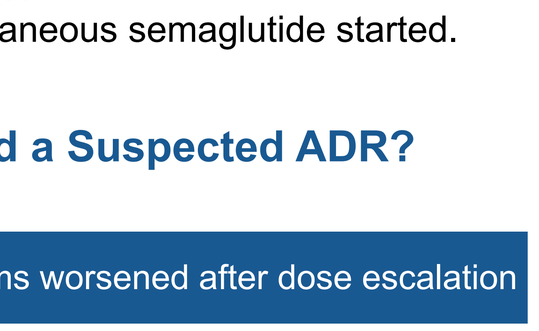
Case Report

- A 41-year-old man with long-standing T2DM and established diabetic peripheral neuropathy reported worsening neuropathic symptoms during tirzepatide titration.
- Symptoms worsened at 7.5 mg once weekly, deteriorated further at 10 mg, and became less severe after dose reduction to 5 mg.
- Previously tolerated oral semaglutide without similar neuropathic worsening.
- Over six months of tirzepatide treatment, HbA1c improved from 103 to 69 mmol/mol, and weight decreased from 106 kg to 91.6 kg, approximately 14% reduction.
- No recent medication changes or alternative acute cause for worsening neuropathy were identified.
- Tirzepatide discontinued and subcutaneous semaglutide started.

Why Was This Considered a Suspected ADR?

Timing	Symptoms worsened after dose escalation
Dose relationship	Symptoms deteriorated further at 10 mg
Improvement after reduction	Symptoms became less severe at 5 mg
Clinical impact	Patient reluctant to continue treatment
Yellow Card submitted	Medicine-related contribution could not be excluded

Dose changed? Symptoms changed? Consider a Yellow Card



Results

Evidence source	What was found	Interpretation for this case
SURPASS tirzepatide trial	Safety data mainly reported gastrointestinal adverse effects	Peripheral neuropathy not identified as a safety concern
Tirzepatide and GLP-1 receptor agonist case reports	Peroneal neuropathy and foot drop reported in association with rapid weight loss	Suggests weight loss related nerve compression as a possible explanation
Treatment induced neuropathy of diabetes literature	Rapid improvement in glycaemic control can trigger worsening neuropathic symptoms	Relevant because HbA1c improved from **103 to 69 mmol/mol** over six months
Diabetes related progression	Long-standing T2DM and established neuropathy increase the baseline risk of progression	Underlying diabetic neuropathy may have contributed

Discussion

- This case was reported as a suspected ADR because a medicine-related cause could not be excluded.
- The dose-related pattern and impact on treatment continuation supported Yellow Card reporting, particularly as tirzepatide is subject to additional monitoring.
- Causality remains uncertain as underlying diabetic neuropathy, rapid HbA1c improvement and significant weight reduction may also have contributed.
- Published evidence directly linking tirzepatide with peripheral neuropathy remains limited.

Practice change / wider learning

- Counselling now includes advice on new or worsening neuropathic symptoms when tirzepatide is initiated or the dose is increased.
- Patients are advised to report worsening pain, tingling, numbness or weakness.
- Clinicians should review symptoms promptly, consider metabolic and weight loss related explanations, and submit a Yellow Card report where appropriate.

Conclusion

This case highlights a practical pharmacovigilance challenge: neuropathic symptom changes during tirzepatide treatment may be multifactorial but should still prompt consideration of a suspected ADR when the timing and clinical impact are significant.

References
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