A case of burning feet

Finn O'Sullivan, Jason Yu, Bosco Wu, Tim Tse, Jessica Qiu

CASE

A man, aged 71 years, presented with a three-month history of new onset bilateral distal lower limb paraesthesia. He described a burning sensation on the plantar surface of his feet. It had begun to disrupt his sleep as it was worse at night. He did not have any weakness or gait disturbances. This was on a background of hypertension and osteoarthritis, adequately managed with amlodipine/valsartan and meloxicam. He consumed a balanced diet and denied any major changes to his lifestyle. Inspection of the lower limbs revealed no signs of peripheral vascular disease or infection. A lower limb neurological examination revealed impaired temperature sensation bilaterally below the ankles with normal sensation to proprioception, vibration and light touch. There were no neurological deficits in tone, power and reflexes.

QUESTION 1

What is the most likely cause of his symptoms?

QUESTION 2

What type of sensory neuropathy is most likely?

QUESTION 3

What are some common aetiologies of small fibre neuropathy and their clinical features?

QUESTION 4

Which initial investigations should be performed?

ANSWER 1

The patient described new symmetrical burning feet, which is highly suggestive of neuropathic pain secondary to an acute distal symmetrical polyneuropathy (DSP). Neuropathic pain can localise to the central or peripheral nervous system.[1] The onset, progression of symptoms and distribution pattern, as well as distinguishing if the nerve fibre/s involved are motor, sensory and/or autonomic can help narrow the differential diagnosis.[2] Given the absence of weakness, a sensory DSP needs to be considered.

ANSWER 2

This is most likely a small fibre neuropathy (SFN). SFN predominantly or entirely affects the small (Aδ) fibres or unmyelinated C fibres that exist in nociception, thermal perception and autonomic pathways.[3] Salient features include prominent nocturnal burning pain affecting the feet, loss of pinprick and temperature sensation with preserved deep tendon reflexes, whereas in large fibre sensory axonal neuropathies, pain is less prominent.[4] Vibration and joint proprioception at the great toe might be affected, and ankle jerks might be diminished (though age might also affect the latter).[4]

ANSWER 3

It is important to recognise patterns of SFN to help guide initial investigations (Table 1).[4,5] Most SFNs present as DSP with common aetiologies shown in Table 1.[4,5] However, up to 50% of cases are idiopathic, especially in elderly patients.[2,3]

ANSWER 4

Initial targeted blood tests should be performed (Table 2).[2] Referral to a neurologist for nerve conduction studies should be considered if the symptoms exhibit sudden onset, rapid progression, asymmetrical patterns and/or have predominantly motor or autonomic features.[2] Conventional nerve conduction studies cannot detect isolated small fibre neuropathy without large fibre involvement, though autonomic testing can be considered.

CASE CONTINUED

The patient's vitamin B6 (pyridoxine) level was 923 nmol/L (35–110 nmol/L), more than eight-fold the upper limit of normal. All other tests were within normal range.

Upon further questioning, it was revealed that the patient had commenced a men's multivitamin a few weeks prior to symptom onset.

QUESTION 5

What are the causes of the elevated vitamin B6 levels and how is it managed?

ANSWER 5

Vitamin B6 (pyridoxine) toxicity commonly presents as a DSP with predominantly sensory features.[6] It can affect both small and large nerve fibres. The primary cause of vitamin B6 toxicity is from supratherapeutic dosing, typically from taking multiple over-the-counter supplements or excessive consumption of energy drinks.[7] The recommended daily intake of dietary vitamin B6 is 1.6–2 mg/day.[6] Severe sensory peripheral neuropathies from vitamin B6 toxicity are associated with intake above 200 mg/day;[7] however, reports have shown a correlation

with long-term intake of just 6 mg/day.[8] Inter-individual differences in the metabolism of vitamin B6 can predispose people to toxicity at the recommended daily intake.[9]

There is no specific treatment as ceasing supplement intake is typically sufficient to resolve symptoms within six months.

CASE CONTINUED

The patient was taking the multivitamin as directed on the bottle, which provided a daily dose of 6 mg of vitamin B6. The patient was recommended to cease the supplement and to have a follow-up in one month to evaluate if his symptoms had improved.

On follow-up, his symptoms have begun to improve but are not completely resolved.

Interestingly, the Therapeutic Goods Administration (TGA) made regulatory changes in March 2023 regarding vitamin B6 supplementation (Box 1).[10]

Table 1. Clinical presentations of SFN[4,5]

Presentation	Clinical features	Linked aetiologies
Classic SFN (distal symmetric polyneuropathy)	• Paraesthesia described as burning, pins and needles or electric shock-like • Worse at night • Symmetrical stocking–glove distribution (length-dependent) • Slow progression • Motor strength, proprioception and deep tendon reflexes usually preserved	• Diabetes mellitus and metabolic syndrome • Immune mediated (eg sarcoidosis, Sjögren's syndrome) • Thyroid dysfunction • Alcohol toxicity • Vitamin B12 deficiency • HIV • Neurotoxic medication (eg chemotherapy) • Coeliac disease • Paraneoplastic syndrome • Paraproteinemia
Non-length-dependent SFN (20–25%)	• Sensory symptoms are patchy, asymmetrical, migrating or diffuse • Involves trunk and face in addition to limbs • More common in women • Presents in younger patients	• Immune mediated (eg sarcoidosis, Sjögren's syndrome) • Paraneoplastic syndrome
SFN with autonomic dysfunction	• Autonomic features: palpitations, orthostatic hypotension, urinary retention, gastroparesis, sicca syndrome, skin discolouration • Erectile dysfunction	• Diabetes mellitus • Amyloidosis • Immune mediated (eg sarcoidosis, Sjögren's syndrome)
Painful SFN	• Painful paraesthesia described as sharp, stabbing or lancinating • Other features similar to classic SFN	• Diabetes mellitus • Amyloidosis • HIV • Sarcoidosis • Alcohol toxicity • Neurotoxic medication

HIV, human immunodeficiency virus; SFN, small fibre neuropathy.

Table 2. Initial investigations for small fibre neuropathy[2]

Blood tests	
• Full blood count	• Sodium
• CRP	• Potassium
• Vitamin B12/B6	• Liver function tests
• Folate	• Thyroid function tests
• HbA1c	• Serum protein electrophoresis
• Creatinine	

CRP, C-reactive protein; HbA1c, haemoglobin A1C.

Box 1. Therapeutic Guidelines Australia vitamin B6 regulations[10]

Updated March 2023

- Products containing >10 mg/daily dose of vitamin B6 must have a label warning about peripheral neuropathy
- Products must not contain more than 100 mg/daily dose of vitamin B6

Key points

- The diagnosis of a sensory neuropathy is typically based on history and examination, and this can give clues regarding the possible aetiology.
- Initial investigation of a small fibre neuropathy should include blood tests to help identify the most common treatable aetiologies.
- A comprehensive medication history including both prescribed medications and over-the-counter medications (eg vitamins and supplements) is important.

Authors

Finn O'Sullivan BAdvSc, Medical Student, Macquarie University, Sydney, NSW

Jason Yu MBBS, BSci, FRACGP, DCH, Allergist and General Practitioner, MyHealth South Eveleigh, Sydney, NSW

Bosco Wu MBBS, BMedSci (Hons), FRACGP, General Practitioner, MQ Health General Practice, Discipline of Primary Care, Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, NSW

Tim Tse BMed, MD, MMed, FRACGP, General Practitioner, MQ Health General Practice, Discipline of Primary Care, Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, NSW

Jessica Qiu BMed, MD (Dist), BSc (Med) (Hons), FRACP, Neurologist, Neurology Department, Nepean Hospital, Sydney, NSW; Clinical Associate Lecturer, Faculty of Medicine and Health, University of Sydney, Sydney, NSW

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Correspondence to:
finn.osullivan1@students.mq.edu.au

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correspondence **ajgp@racgp.org.au**