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Small-Fiber Neuropathy After Vaccination With mRNA-1273 SARS-CoV-2 Vaccine

To the Editor:

We report a 43-year-old woman who developed painful tingling in her right foot 3–4 weeks after her second mRNA-1273 severe

acute respiratory syndrome coronavirus 2 (SARS CoV-2) vaccination dose. Over 2 months, this spread to involve her right thigh, both upper extremities, and her left foot. Examination was normal, including preserved pinprick and proprioceptive sensation and normal reflexes. Electromyography and nerve conduction studies (EMG/NCS) were normal. Skin biopsy revealed reduced intraepidermal nerve fiber density (4 fibers/mm) in the distal right lower extremity, consistent with small-fiber neuropathy (SFN) (See **Photomicrograph, Supplemental Digital Content 1**, <http://links.lww.com/JCND/A53>, which demonstrates reduced nerve fiber density distally). Staining for amyloid was negative. Her glycosylated hemoglobin was 5.6%, erythrocyte sedimentation rate was 32 mm/h, thyroid testing was normal, vitamin B12 level was 619 pg/mL, and angiotensin converting enzyme level was 26 U/L. Anti-nuclear antibodies, hepatitis C antibodies, Lyme antibodies, Sjogren's antibodies, paraneoplastic antibodies (anti-Hu, anti-Ri, and anti-Yo), and contactin-associated protein 2 (CASPR2) antibodies were negative. Cryoglobulins were not detected. Serum protein electrophoresis did not demonstrate monoclonal gammopathy. She had no history of previous exposure to SARS-CoV-2.

DISCUSSION

SFN is defined as a sensory neuropathy affecting predominantly the small caliber myelinated and unmyelinated nerve fibers.¹ Symptoms include tingling, burning, or shooting pain and cutaneous allodynia.¹ Pinprick and temperature sensation may be diminished, but proprioception and deep tendon reflexes are typically spared and nerve conduction studies may be normal.¹ Diabetes and heavy alcohol use are the most common identifiable causes of SFN, but it is commonly idiopathic and some cases may be autoimmune.¹

There is a growing body of evidence suggesting a relationship between SFN and SARS-CoV-2 infection.² SFN has been reported after other vaccines,³ but little is

known about the relationship between SFN and SARS-CoV-2 vaccination.

Our patient had characteristic features of SFN after vaccination with the mRNA-1273 SARS CoV-2 vaccine. She had preserved reflexes on examination and normal nerve conduction studies, consistent with a lack of large fiber involvement. The presence of SFN was confirmed by skin biopsy. Her symptoms began just a few weeks after receiving her second vaccine dose and no other cause for SFN was identified.

Small-fiber neuropathy has also been previously reported after vaccination with BNT162b2 SARS-CoV-2 vaccine (manufactured by Pfizer), and cases reported as sensory Guillain-Barré syndrome after ChAdOx1 nCoV-19 vaccine (manufactured by AstraZeneca) actually had clinical and skin biopsy features of SFN.^{4,5} These case reports, reports of SFN with other vaccines, and reports of SFN after SARS-CoV-2 infection suggest that SFN may be a potential complication of SARS-CoV-2 vaccination.

Clinicians should remain aware of this potential complication of SARS-CoV-2 vaccination to facilitate appropriate diagnosis and management, but its incidence is rare. Over 220 million Americans have been fully vaccinated with either Pfizer's BNT162b2 SARS-CoV-2 vaccine, Moderna's mRNA-1273 SARS-CoV-2, or Janssen's Ad26.COV2.S vaccine.⁶ However, there have only been 338 incidents reported as "peripheral neuropathy" or "paresthesia" with the Pfizer vaccine in the Vaccine Adverse Event Reporting System, 257 with the Moderna vaccine, and 34 with the Janssen vaccine.⁷ Furthermore, the broader symptomatic categories in the database likely overestimate the incidence of skin biopsy confirmed SFN. Therefore, the rare incidence of this potential complication should not discourage vaccination to prevent the higher risks of morbidity and mortality with SARS-CoV-2 infection.

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