

Trigeminal and cervical radiculitis after tozinameran vaccination against COVID-19

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SUMMARY

In this report, we describe a patient who developed an acute trigeminal neuritis and cervical radiculitis after receiving a Pfizer-BioNtech vaccination (tozinameran) against SARS-CoV-2.

BACKGROUND

At present, there are ongoing mass vaccination programmes globally for the prevention of SARS-CoV-2 infection. These vaccination programmes often use mRNA vaccines such as those developed by Pfizer-BioNtech and Moderna,^{1,2} which have not shown serious adverse effects in ongoing phase III clinical trials. There have been case reports of anaphylaxis in patients receiving the Pfizer-BioNtech vaccination against SARS-CoV-2, which has prompted a recommendation to exclude any person with a history of a severe or immediate allergic reaction to any of the vaccine components.³ However, no neurological complications have been described thus far.

CASE PRESENTATION

A 52-year-old female healthcare worker with a medical history of diabetes mellitus, hypertension, hyperlipidaemia and scoliosis presented with numbness, swelling and pain over the left face and neck. Her symptoms started 3 hours after receiving the first dose of the tozinameran vaccine on the left deltoid. She had no prior drug allergy or adverse reactions to previous vaccinations. She described pain and numbness that progressed from her left suboccipital region to the left shoulder, periauricular region and jaw, eventually involving the left face over the span of hours. The symptoms peaked approximately 16 hours post-injection, and at the peak, she reported numbness involving the entire left face, left buccal mucosa and neck, particularly in the C2 and C3 distribution. There was swelling and redness in the same distribution.

The patient was admitted on the third day of symptoms. She was afebrile and haemodynamically stable. There was hypoesthesia throughout the left face, to a greater degree over the mandibular (V3) division than the maxillary (V2) or ophthalmic (V1) divisions. The patient also had hypoesthesia over the left C2 and C3 dermatomes. There were no other neurological deficits. There was point tenderness at the left suboccipital region and soft tissue swelling with erythema in the left neck and periauricular region. There was no evidence of meningism. There were no other systemic symptoms.

INVESTIGATIONS

The blood count and serum electrolytes were normal. Glycated haemoglobin levels were 7.1%. Pre and post gadolinium contrast-enhanced MRI of the brain with trigeminal nerve protocol and pre and post gadolinium contrast-enhanced MRI of the cervical spine were performed. MRI of trigeminal nerve revealed an abnormal asymmetric thickening and robust perineural sheath enhancement of the V3 segment of the left trigeminal nerve (figures 1–3) as it enters the left foramen ovale (skull base). MRI of the brain revealed no other abnormalities save for mild changes of small vessel disease in the cerebral white matter. The MRI of the cervical spine revealed significant levo-scoliosis and mild changes of cervical spondylosis with multilevel degenerative disc disease, but no cervical spinal cord lesion, significant ipsilateral neural foramen stenosis, nor ipsilateral nerve root thickening or post-contrast enhancement.

TREATMENT

We diagnosed a sensory radiculitis over the left C2/3, as well as a left trigeminal neuritis after tozinameran vaccination. The patient was treated with pregabalin for analgesia. The left facial numbness, erythema and swelling resolved by day 7 of symptoms. However, there was persistent numbness around the auricular region at the time of discharge. At outpatient review 6 weeks after onset, she had persistent neuropathic pain and numbness despite treatment with pregabalin. As such, she was started on a tapering course of oral prednisolone.

OUTCOME AND FOLLOW-UP

The patient underwent nerve conduction studies, including the facial and blink reflex, on day 16 of symptoms, which were within normal limits. Her symptoms improved gradually after discharge, but improved the most after oral prednisolone. However, she has residual numbness over the left V3 distribution and persistent numbness and ache over the left deltoid region. She was advised against proceeding with her second dose of the vaccination.

DISCUSSION

While neurological complications of vaccinations have been observed,^{4–8} the exact mechanism behind the development of complication is not clear. Molecular mimicry has been postulated as a possible mechanism in patients who present with neurological complications⁹ post vaccination, but molecular mimicry often requires the development



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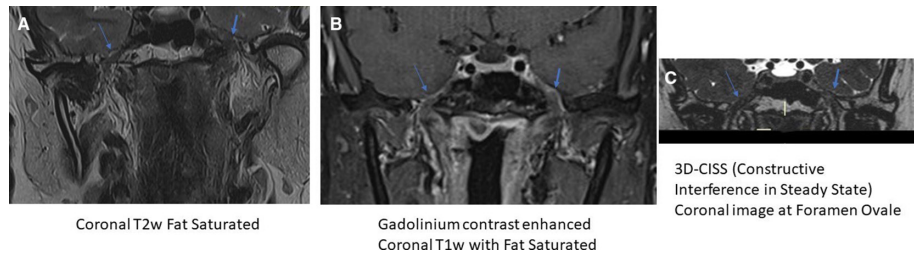


Figure 1 (A–C) Coronal T2w with fat-saturated and gadolinium-enhanced coronal T1w with fat-saturated images depict abnormal asymmetric thickening and robust perineural sheath enhancement of the V3 (mandibular) segment of the left trigeminal nerve (short arrow) as it enters the foramen ovale. Normal V3 segment of right trigeminal nerve (long arrow) is shown on coronal images for comparison.

of a humeral response, which is traditionally thought to require at least 10–14 days to develop. Immune-mediated inflammatory response is another postulated mechanism, which may require less time to develop¹⁰ than molecular mimicry.

One previous study that performed nerve biopsies on three individuals who had neuropathies after vaccination confirmed the presence of inflammatory deposits in the endoneurium.¹¹ While associations have been made about vaccinations and autoimmunity, the mechanisms behind these are yet to be clearly understood.¹² A recent review¹³ of potential neurological effects of SARS-CoV-2 vaccinations summarised the current reported neurological adverse events in patients who have received the different types of vaccination and found that only one case of transverse myelitis was deemed to have been associated with SARS-CoV-2 vaccination. In that particular case, the patient was injected with a non-replicating viral vector-based vaccine (ADZ1222).¹⁴

In our patient, we postulate that immune-mediated inflammation rather than molecular mimicry is a more likely mechanism due to the fairly rapid onset of the symptoms (3 hours post vaccination) and the response to corticosteroids. The use of an mRNA-based vaccine in our patient introduces a few additional considerations about the possible mechanisms of the trigeminal and cervical radiculitis. mRNA-based vaccines require modifications to the mRNA to ensure stability while avoiding pathogen-associated molecular patterns that may trigger an excessive inflammatory response.¹⁵ Furthermore, mRNA-based vaccines require the use of lipid nanoparticle encapsulation (a combination of ionisable cationic lipids, cholesterol, phospholipid and polyethylene glycols (PEGs)) in order to reach the intracellular machinery required to translate the transcripts into proteins.¹⁶ The mRNA modifications used (the m¹ψ mRNA modification¹⁷) and the components of the lipid nanoparticle encapsulation, particularly the PEG,¹⁸ which has been implicated as a possible cause of anaphylaxis in patients receiving the Pfizer-BioNTech vaccination, are two potential agents that could have provoked inflammation in our patient. We theorise that the latter is a more likely the culprit, given the rapid onset of symptoms that would

suggest the delivery agent rather than the mRNA construct is more likely culpable.

While the temporal association of the development of the radiculitis in close proximity to the vaccination is suggestive that they may be associated, it remains possible that the development of the trigeminal and cervical radiculitis is not related to the vaccination. Hence, caution must be used to interpret this case report in the context of the ongoing vaccination efforts against SARS-CoV-2.

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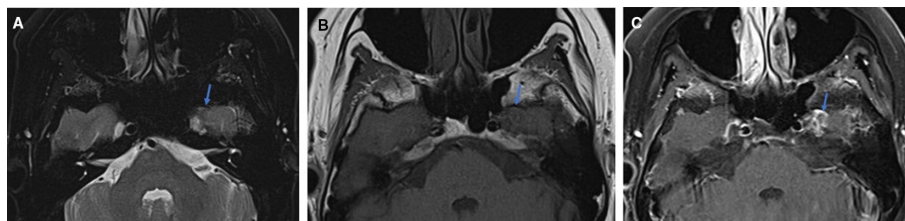


Figure 2 (A–C) Axial images confirm thickening of endocranial V3 segment of the left trigeminal nerve as it enters the left foramen ovale (skull base).

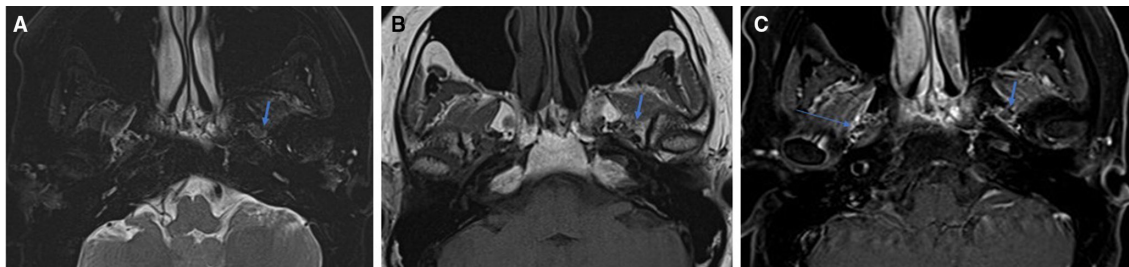


Figure 3 (A–C) Axial images at the foramen ovale (skull base) showing subtle thickening of the V3 segment of the left trigeminal nerve.

Learning points

- ▶ Neurological complications can occur post vaccination for SARS-CoV-2, and clinicians will need to monitor for these complications.
- ▶ Cranial neuropathies are rare but important complications of vaccinations.
- ▶ Diagnosis is made by a combination of clinical, imaging and nerve conduction studies, but will also likely require exclusion of other differentials or causes.
- ▶ The pathophysiology of post vaccination neurological complications is poorly understood.
- ▶ Treatment appears to be supportive, with neuropathic pain agents being the mainstay of treatment.
- ▶ Corticosteroids can be considered for patients with no contraindications.

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