Neuralgic amyotrophy following COVID-19 mRNA vaccination

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Learning points for clinicians

Neuralgic amyotrophy is commonly preceded by an antecedent event such as infection, surgery and less commonly vaccinations. COVID-19 mRNA vaccines (BNT162b2 and mRNA-1273) may be, albeit rare, a trigger of neuralgic amyotrophy. All patients recovered considerably, further reiterating that the benefits of mRNA vaccines outweigh adverse events.

Words: 47

Case description

Patient 1

A 50-year-old male presented with acute onset right upper limb pain followed by weakness and numbness of the arm and lateral forearm 25 days after first dose of BNT162b2 vaccine (ipsilateral to injection site). Clinical examination, corroborated by MRI (Figure 1A-B), indicated predominant upper and middle trunk involvement of the brachial plexus. Nerve conduction study (NCS) and electromyography (EMG) performed 10 and 31 days from symptom onset were normal. He improved with corticosteroid upon review at 7 weeks.

Patient 2

A 44-year-old male developed acute onset neck and posterior shoulder pain, followed by right medial forearm and hand numbness, as well as hand weakness, 4 days after second dose of BNT162b2 vaccine (32 days after first dose, contralateral to injection site). Clinical examination, corroborated by NCS and EMG performed 15 and 42 days from onset, showed predominant lower trunk involvement of the brachial plexus. MRI brachial plexus findings are shown in Figure 1C-D. He did not receive corticosteroid and made significant improvement upon review at 8 weeks.

Patient 3

A 58-year-old male developed acute onset shoulder and left upper limb pain, followed by predominantly distal hand weakness and numbness 7 days after second dose of mRNA-1273 vaccine (35 days after first dose, ipsilateral to injection site). Clinical examination, corroborated by NCS and EMG performed 35 days from onset, as well as MRI, showed predominant lower

trunk involvement of the brachial plexus. He improved with corticosteroid when reviewed at 5 weeks.

Patient 1 and 3 had negative SARS-CoV-2 polymerase chain reaction (PCR) tests, while this was not done for Patient 2. None had clinical or laboratory evidence of antecedent infections (e.g., respiratory, hepatitis), other triggers of neuralgic amyotrophy (NA) or family history suggestive of hereditary NA. MRI cervical spine were either normal (Patient 1) or showed multi-level spondylosis with mild nerve impingement (Patient 1 and 2) which did not account for their clinical presentations.

Discussion

Neuralgic amyotrophy (also known as brachial neuritis or Parsonage-Turner syndrome) is commonly preceded by an antecedent event such as infection (including SARS-CoV-2 and hepatitis E), surgery and less commonly vaccinations[1, 2]. Two cases have been reported after BNT162b2 and none after mRNA-1273 vaccines [3, 4]. We expand on this and report the first associated with mRNA-1273 vaccine. All patients fulfilled commonly adopted criteria[5] for NA (excluding family history). Despite the close temporal relationship to vaccines, we cannot be certain of causality from our small observational series. However, a possible association between NA and mRNA vaccines may be extrapolated by:

1. Biological plausibility. Although rare, vaccination is a well-characterized trigger for NA. Van Alfen et. al reported only five out of 246 cases linked to vaccines[1]. Our patients had no other triggers.

2. Latency. In a series of 246 cases, the majority occurred 1-7 days after the antecedent event; specifically, 65.3% of cases that followed infection occurred in this time interval and 10.2% after 2 weeks[1]. Two of our patients developed NA within a week of second dose while the other occurred 25 days after first dose. The timing of neurological symptoms post-vaccination possibly correlates with temporal development of neutralizing antibodies after mRNA vaccination, and may account for inflammation of the brachial plexus.

Considering an incidence of 2-3/100,000/year[1], 3 cases of NA after vaccinating approximately 3.9 million persons in Singapore from 30 December 2020 to 9 July 2021, suggest a rare occurrence as with other vaccines[1]. Data from United States Vaccine Adverse Event Reporting System corroborate our observation[6]. It is noteworthy that all our patients recovered considerably, further reiterating that the benefits of mRNA vaccines outweigh adverse events.

Words: 595

Funding source: None

Conflicts of Interest: None

Ethics approval: The study was approved by the Singapore Health Services institutional review board (CIRB 2020/2410). Waiver of consent was granted.

Author contribution:

Study concept and design: JSK, YG, BYQT, TU

Acquisition and analysis of data: JSK, YG, BYQT, ACFH, RHMH, AM, PLK, JV, KWPN

Drafting of manuscript: JSK, YG, BYQT

Critical revision of manuscript for important intellectual content: All

Study supervision: AMLQ, TU

All authors approved the final manuscript.

Data availability statement

All data relevant to the study are included in the article

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Figure legend

Figure 1A-D: Radiological features of neuralgic amyotrophy

MRI brachial plexus (Patient 1) shows patchy oedema and enhancement of the right brachial plexus (trunks and divisions) (**A, arrows**). Patchy oedema and enhancement of the right scalene muscles (**B, arrow**) suggestive of subacute denervation is seen; MRI brachial plexus (Patient 2) shows mild oedema (**C, arrow**) and enhancement (**D, arrow**) of the right posterior scalene muscle, suggestive of subacute denervation. No mass is seen.

A: Coronal short tau inversion recovery (STIR), **B**: Coronal post-contrast T1-weighted **C**: Coronal T2-weighted Turbo Inversion Recovery Magnitude (TIRM) with fat saturation, **D**: Coronal post-contrast T1-weighted with fat saturation.

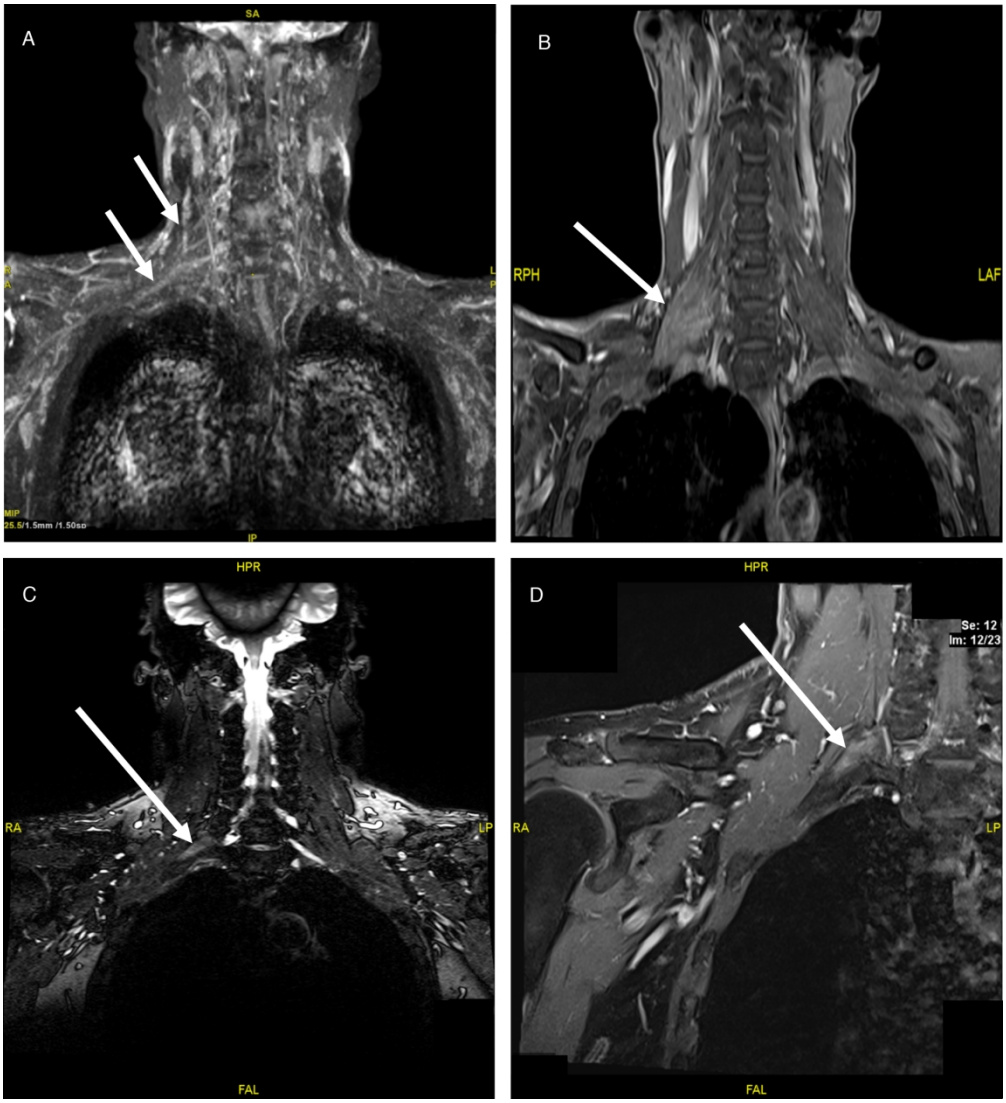

Figure 1A-D: Radiological features of neuralgic amyotrophy
MRI brachial plexus (Patient 1) shows patchy oedema and enhancement of the right brachial plexus (trunks and divisions) (A, arrows). Patchy oedema and enhancement of the right scalene muscles (B, arrow) suggestive of subacute denervation is seen; MRI brachial plexus (Patient 2) shows mild oedema (C, arrow) and enhancement (D, arrow) of the right posterior scalene muscle, suggestive of subacute denervation. No mass is seen.
A: Coronal short tau inversion recovery (STIR), B: Coronal post-contrast T1-weighted C: Coronal T2-weighted Turbo Inversion Recovery Magnitude (TIRM) with fat saturation, D: Coronal post-contrast T1-weighted with fat saturation.