

Parsonage-Turner syndrome following COVID-19 vaccination

INTRODUCTION

Parsonage-Turner syndrome (PTS), also known as neuralgic amyotrophy, is an acute idiopathic brachial neuritis, typically characterised by acute onset of excruciating pain followed by weakness and wasting in the upper limb.¹ Antecedent events such as infection, exercise, trauma, surgery and vaccination are reported in approximately 50% of affected individuals.¹ PTS has been reported following COVID-19 vaccination, but the current literature is limited to several case reports and a passive reporting system.^{2,3} Herein, we report on the clinical, radiological and laboratory features of 12 cases with PTS post COVID-19 vaccination.

METHODS

We reviewed medical records of the patients who were diagnosed with PTS following COVID-19 vaccination in three

referral hospitals (Seoul, South Korea) between June and October 2021. We collected and analysed the detailed clinical information as follows: the type and order (in case of different types) of COVID-19 vaccine, laterality of symptom presentation, timeline regarding the vaccination, symptom onset and nadir, clinical presentation, motor grade at nadir, the results of electrodiagnosis, brachial plexus MRI, cerebrospinal fluid (CSF) analysis, treatment regimen and the outcomes.

RESULTS

We identified 12 patients (7 men and 5 women) who developed PTS after a receipt of COVID-19 vaccine. Clinical features of the patients are summarised in table 1 (and online supplemental figure). Age ranged between 23 and 81 (average 51). Vaccination was the only possible trigger in all cases. Six patients had received adenoviral vector-based vaccines (four received AstraZeneca and two received Janssen), and the others had mRNA-based vaccines (five had Pfizer and one had Moderna).

All but two developed PTS after receipt of the first dose of COVID-19 vaccine. The interval from the vaccination to symptom onset and nadir ranged between 2 days and 16 days (median 6.5) and between 5 days and 55 days (median 20.5), respectively. Disease severity at nadir varied across patients, with Medical Research Council grade of the weakest muscles ranging from 2 to 5. Electrodiagnostic studies revealed abnormalities consistent with brachial neuritis in most patients.

Intriguingly, PTS occurred at the same side of vaccine injection in all but two cases (contralateral in patient 8 and bilateral in patient 12). Notably, MRI or sonographic evaluations revealed prominent ipsilateral axillary and/or cervical lymph nodes in seven of eight patients (87.5%) (online supplemental figure). CSF analysis showed albuminocytological dissociation in all three tested patients (patients 1, 3 and 12). We administered oral or intravenous corticosteroid in all patients but three: two patients showed rapid clinical improvement (patients 5 and 7), and one patient refused to receive the treatment

Table 1 Summary of clinical characteristics

No	Sex/age (years)	Vaccine (dose)	Laterality	Days from vaccination to symptom onset/nadir	Weakest muscle strength at nadir (MRC)	MRI	CSF analysis*	Treatment	Outcome
1	M/31	Janssen	Ipsilateral	6/7	III	Prominent ipsilateral axillary and cervical lymph nodes	WBC 0, protein 70	None	Full recovery by week 1
2	M/37	Janssen	Ipsilateral	14/14	IV+	Normal	ND	Oral prednisolone, gabapentin	Near-full recovery by week 10
3	M/71	AstraZeneca (first dose)	Ipsilateral	16/35	III	Signal changes and enlargement from the C8 root to the inferior trunk, prominent ipsilateral cervical and axillary lymph nodes	WBC 2, protein 57	Oral prednisolone, gabapentin	Poor recovery by week 15
4	M/63	AstraZeneca (first dose)	Ipsilateral	14/14	III	ND	ND	None	Poor recovery by week 4, lost to follow-up thereafter
5	F/65	AstraZeneca (first dose)	Ipsilateral	5/6	III	Prominent ipsilateral axillary lymph nodes	ND	None	Full recovery within 2 months
6	M/61	AstraZeneca (second dose)	Ipsilateral	2/3	II	Signal changes and enlargement from the C8 root to the inferior trunk and medial cord, prominent cervical and axillary lymph nodes	ND	Oral prednisolone	Partial recovery by month 5
7	F/31	Cross-vaccination (AstraZeneca and then Pfizer)†	Ipsilateral	2/10	IV	Prominent ipsilateral axillary and cervical lymph nodes	ND	None	Full recovery by week 3
8	F/50	Pfizer (first dose)	Contralateral	4/16	III	Normal	ND	NSAIDs, fentanyl patch, IVMP	Good response to IVMP
9	M/58	Pfizer (first dose)	Ipsilateral	5/30	II	ND	ND	Oral prednisolone, pregabalin	Poor recovery by week 8
10	F/23	Pfizer (first dose)	Ipsilateral	10/11	V	ND (ipsilateral axillary lymphadenopathy in ultrasonography)	ND	Oral prednisolone, pregabalin	Partial recovery within week 6
11	F/81	Pfizer (first dose)	Bilateral	15 NA	IV	Normal	ND	Pregabalin, nortriptyline, NSAIDs	Poor recovery by month 6
12	M/39	Moderna (first dose)	Ipsilateral	7/14	IV	Prominent ipsilateral axillary lymph nodes	WBC 1, protein 76	IVMP followed by oral prednisolone, gabapentin	Poor recovery by week 8

*Values were expressed as cells/ μ L (WBC) and mg/dL (protein).

†Parsonage-Turner syndrome occurred 2 days after Pfizer vaccination following initial AstraZeneca vaccination.

CSF, cerebrospinal fluid; F, female; IVMP, intravenous methylprednisolone; M, male; MRC, Medical Research Council; ND, not done; NSAIDs, non-steroidal anti-inflammatory drugs; WBC, white blood cell.

(patient 4). We noted a variable degree of recovery at the last follow-up: complete in three, partial in four and poor in five.

DISCUSSION

Vaccination is one of the known potential triggers of PTS, with case series and reports for tetanus, smallpox, human papillomavirus, influenza and, recently, COVID-19 vaccines.² To date, there have been seven publications reporting 10 cases of PTS following COVID-19 vaccination (online supplemental table). While most of the reported cases (8/10) received mRNA vaccines, our observations implicate the adenoviral vector-based vaccine as well in 6 of 12 cases. The time interval between vaccination and PTS onset ranged from 2 to 16 days, which is in line with previous reports and coincided with the expected time course of the immune response against COVID-19 vaccines. Similar to previous reports, we found that PTS post COVID-19 vaccination mostly takes the classic form, but also observed atypical phenotypes of pure sensory or painless motor-predominant form in two cases.⁴

Intriguingly, we found that PTS occurred on the same side of vaccination in all except two cases. Combined with all previously reported cases, the rate of ipsilateral PTS reaches 77.3% (17 of 22 cases). Meanwhile, we noted an unexpectedly high frequency of ipsilateral reactive lymphadenopathy in our cases (87.5%). Although it has not been addressed in the context of PTS, reactive lymphadenopathy is reportedly a frequent finding at imaging with an incidence of up to 53% with the COVID-19 mRNA vaccines in patients with breast cancer.⁵ Taken together, we proposed the need for further research to investigate whether these local immune reactions are involved in the pathogenesis of ipsilateral brachial neuritis or whether they are simply observed together by chance.^{2,4}

It should be emphasised that we cannot establish a robust causal relationship between PTS and COVID-19 vaccination with case series. It is also worth mentioning that the benefits of COVID-19 vaccination far outweigh the potential risks. Corroborating the findings of previous case reports, our observations suggest

that COVID-19 vaccines may be associated with PTS characterised by ipsilateral occurrence and possibly accompanied by reactive lymphadenopathy. Further studies are warranted to assess the causality and significance of the ipsilateral association.

Young Gi Min ^{1,2} Jee-Eun Kim ³
Ji Young Hwang⁴ Je-Young Shin,¹
Jung-Joon Sung,^{1,2} Yoon-Ho Hong ⁵

¹Neurology, Seoul National University Hospital, Seoul, South Korea

²Translational Medicine, Seoul National University College of Medicine, Seoul, South Korea

³Neurology, College of Medicine, Ewha Womans University, Seoul, South Korea

⁴Radiology, College of Medicine, Ewha Womans University, Seoul, South Korea

⁵Neurology, Neuroscience Research Institute, Medical Research Council, Seoul National University College of Medicine, Seoul Metropolitan Government Boramae Medical Center, Seoul, South Korea

Correspondence to Professor Yoon-Ho Hong, Neurology, Neuroscience Research Institute, Medical Research Council, Seoul National University College of Medicine, Seoul Metropolitan Government Boramae Medical Center, Seoul 07061, South Korea; nrhong@gmail.com

Twitter Yoon-Ho Hong @Yoonho

Contributors YGM, J-EK and Y-HH conceptualised, designed the study and wrote the manuscript. YGM, JYH and J-EK collected data. YGM and J-EK prepared the figure. J-YS and J-JS interpreted the data. Y-HH supervised the work.

Funding This work was supported by a focused clinical research grant-in-aid (03-2016-0300) from the Seoul National University Hospital Research Fund.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involves human participants and was approved by the institutional review boards (IRBs) of Seoul National University Hospital (IRB 2110-049-1261), Seoul Metropolitan Government Boramae Medical Center (IRB 30-2021-122) and Ewha Womans University Seoul Hospital (IRB 2021-09-021). The participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology,

drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.



OPEN ACCESS

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/jnnp-2021-328182>).

YGM and J-EK contributed equally.

YGM and J-EK are joint first authors.



To cite Min YG, Kim J-E, Hwang JY, *et al.* *J Neurol Neurosurg Psychiatry* Epub ahead of print: [please include Day Month Year]. doi:10.1136/jnnp-2021-328182

Received 13 October 2021

Accepted 23 February 2022

J Neurol Neurosurg Psychiatry 2022;0:1–2.
doi:10.1136/jnnp-2021-328182

ORCID iDs

Young Gi Min <http://orcid.org/0000-0002-8091-7585>
Jee-Eun Kim <http://orcid.org/0000-0002-3811-3479>
Yoon-Ho Hong <http://orcid.org/0000-0002-3325-6358>

REFERENCES

- van Alfen N, van Engelen BGM, Alfen Nvan. The clinical spectrum of neuralgic amyotrophy in 246 cases. *Brain* 2006;129:438–50.
- Queler SC, Towbin AJ, Milani C, *et al.* Parsonage-Turner syndrome following COVID-19 vaccination: Mr neurography. *Radiology* 2022;302:211374.
- Nosedà R, Ripellino P, Ghidossi S, *et al.* Reporting of acute inflammatory neuropathies with COVID-19 vaccines: subgroup Disproportionality analyses in VigiBase. *Vaccines* 2021;9:1022.
- Cacciavillani M, Salvalaggio A, Briani C. Pure sensory neuralgic amyotrophy in COVID-19 infection. *Muscle Nerve* 2021;63:E7–E8.
- Garreffa E, Hamad A, O'Sullivan CC, *et al.* Regional lymphadenopathy following COVID-19 vaccination: literature review and considerations for patient management in breast cancer care. *Eur J Cancer* 2021;159:38–51.