J Korean Med Sci. 2022 Nov 3;37(43):e322
https://doi.org/10.3346/jkms.2022.37.e322
eISSN 1598-6357·pISSN 1011-8934

JKMS

Correspondence

Check for updates

Letter to the Editor: Rule Out Alternative Mechanisms Before Attributing Elevated Hemidiaphragm to Parsonage Turner Syndrome and SARS-CoV-2 Vaccination

Josef Finsterer [1] **and Fulvio A Scorza** [2]

[1]Neurology & Neurophysiology Center, Vienna, Austria
[2]Disciplina de Neurociência, Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM), São Paulo, Brasil

OPEN ACCESS

▸ See the article "Diaphragmatic Dysfunction due to Neuralgic Amyotrophy After SARS-CoV-2 Vaccination: A Case Report" in volume 37, number 38, e283.

Received: Oct 5, 2022
Accepted: Oct 13, 2022
Published online: Nov 3, 2022

Address for Correspondence:
Josef Finsterer, MD, PhD
Neurology & Neurophysiology Center, Postfach 20, 1180 Vienna, Austria.
Email: fipaps@yahoo.defifigs1@yahoo.de

© 2022 The Korean Academy of Medical Sciences.
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs
Josef Finsterer
https://orcid.org/0000-0003-2839-7305
Fulvio A Scorza
https://orcid.org/0000-0002-0694-8674

Disclosure
The authors have no potential conflicts of interest to disclose.

Dear Editor,

We read with interest the article by Kang et al.[1] about a 63-year-old male with a history of arterial hypertension and hyperlipidemia who developed SARS-CoV-2 vaccination associated plexopathy of the right upper limb (Parsonage Turner syndrome [PTS]), clinically exclusively involving the right phrenic nerve. Treatment with analgesics reduced pain, but right diaphragmatic weakness persisted until the last follow up, 8 months after onset.[1] The study is stimulating but raises concerns that should be discussed.

We disagree with the diagnosis of PTS. Because the phrenic nerve originates from the cervical roots C3-5 without merging with other nerve branches of the brachial plexus, paralysis of the right diaphragm may result from radiculopathy or radiculitis of the C3-5 roots rather than plexitis. Another argument against the plexopathy is that there was no muscle weakness in the muscles innervated by nerves emanating from the right brachial plexus. A reduction in the compound muscle action potential (CMAP) when the axial nerve or the musculocutaneous nerve is stimulated could also be due to radiculopathy. There was also no sensory deficit in a distribution suggestive of plexopathy.

We also disagree with the statement that differential diagnoses of a SARS-CoV-2 vaccination associated PTS are sufficiently excluded. MRI of the cervical spine to rule out vertebral stenosis, spinal infarction, spondylosis, spondylarthritis, or herniated disc is missing. It is not mentioned whether F-wave studies of the ulnar, radial, median, and axillar nerves were performed. Needle electromyography (EMG) of muscles innervated by plexus branches is absent. Since plexitis has also been reported in connection with SARS-CoV- infection,[2] it is crucial to be informed about the result of the PCR test. We should also know the results of the virus panel and the results of cerebro-spinal fluid (CSF) tests to rule out polyradiculitis (Guillain Barre syndrome). Polyradiculitis is a known complication of SARS-CoV-2 vaccinations.[3]

Generated by xmlinkpress

Confirmation of the phrenic nerve lesion by nerve conduction studies (NCSs) of the right phrenic nerve is lacking. Compound muscle action potential (CMAP) latency and amplitude upon phrenic nerve stimulation at the collum and recoding from the diaphragm may show prolonged distal latency and reduced CMAP.[4] We should know if needle EMG of the diaphragm was done, which can show chronic denervation in case of a phrenic nerve lesion. A radiculopathy of the phrenic nerve fibers was not excluded.

A limitation of the study is that electrophysiological studies only concerned the right side and not the contralateral side. This is crucial to document any side differences in exams and to confirm the right-sided lesion.

Another limitation is that pulmonary embolism (PE) was not ruled out.[1] PE must be ruled out because it can be associated with unilateral elevation of the diaphragm[5] and because thrombosis is a common complication of SARS-CoV-2 vaccinations.[6] Elevated hemidiaphragm was reported in 14% of patients with PE.[5] PE may even manifest with shoulder pain.[7]

An explanation for dyspnoea after the first vaccine dose was not given.[1] There was no pneumonia and no elevation of the diaphragm on the X-ray shown in **Fig. 1**.[1] We should know if Bickerstaff encephalitis (BBE), a subtype of Guillain Barre syndrome has been ruled out.

We disagree with the notion that PST is an idiopathic condition in every case. Most commonly, PTS is due to diabetes. Other causes of PTS include hereditary neuralgic amyotrophy due to a point mutation or duplication in the *SEPT9* gene, viral infection, parasitic infection, surgery, or anesthesia.

Overall, the interesting study has limitations that challenge the results and their interpretation. Clarifying these weaknesses would strengthen the conclusions and could improve the study. Before attributing elevated hemidiaphragm to PTS and SARS-CoV-2 vaccination alternative mechanism need to be ruled out.

REFERENCES

1. Kang J, Cho JY. Diaphragmatic dysfunction due to neuralgic amyotrophy after SARS-CoV-2 vaccination: a case report. *J Korean Med Sci* 2022;37(38):e283.
PUBMED | CROSSREF
2. Salomon M, Marruganti S, Cucinotta A, Lorusso M, Bortolotti P, Brindisino F. Parsonage-Turner Syndrome mimicking musculoskeletal shoulder pain: a case report during the SARS-CoV-2 pandemic era. *J Telemed Telecare* Forthcoming 2022. DOI: 10.1177/1357633X221100059.
PUBMED | CROSSREF
3. Finsterer J, Scorza CA, Scorza FA. Guillain-Barre syndrome related to SARS-CoV-2 vaccinations. *Clínics (Sao Paulo)* 2022. DOI: 10.1016/j.clinsp.2022.100113.
PUBMED | CROSSREF
4. Vincent M, Court-Fortune I, Costes F, Antoine JC, Camdessanché JP. Phrenic nerve conduction in healthy subjects. *Muscle Nerve* 2019;59(4):451-6.
PUBMED | CROSSREF
5. Zubairi AB, Husain SJ, Irfan M, Fatima K, Zubairi MA, Islam M. Chest radiographs in acute pulmonary embolism. *J Ayub Med Coll Abbottabad* 2007;19(1):29-31.
PUBMED

6. Cheong KI, Chen CF, Chen JS, Wu YW, Chiu KM, Tu CM. Acute pulmonary embolism following Moderna mRNA-1273 SARS-CoV-2 vaccination - a case report and literature review. *Acta Cardiol Sin* 2022;38(4):539-41.
PUBMED
7. Lee DG, Chang MC. Neck-to-shoulder pain as an unusual presentation of pulmonary embolism in a patient with cervical spinal cord injury: a case report. *Medicine (Baltimore)* 2017;96(42):e8288.
PUBMED | CROSSREF

The Author's Response: Letter to the Editor in Response to Professor Josef Finsterer

Jieun Kang [1] **and Joong-Yang Cho** [2]

[1]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Inje University Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea
[2]Department of Neurology, Inje University Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea

OPEN ACCESS

Received: Oct 26, 2022
Accepted: Oct 27, 2022
Published online: Nov 3, 2022

Address for Correspondence:
Jieun Kang, MD, PhD
Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Inje University Ilsan Paik Hospital, Inje University College of Medicine, 170 Juhwa-ro, Ilsanseo-gu, Goyang 10380, Republic of Korea.
Email: realodette@gmail.com

© 2022 The Korean Academy of Medical Sciences.
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs
Jieun Kang
https://orcid.org/0000-0003-2342-0676
Joong-Yang Cho
https://orcid.org/0000-0002-5916-3846

Disclosure
The authors have no potential conflicts of interest to disclose.

We thank Professor Josef Finsterer for his concerns and comments expressed in his letter to the editor on our case report of diaphragmatic dysfunction associated with SARS-COV-2 vaccination.[1] The concerns raised are valid and we agree with his opinion that the diagnosis of neuralgic amyotrophy should be made after excluding all other possibilities. Here, we would like to further discuss the details of the diagnostic work-up that was not explained in our brief case report.

In upper brachial plexopathy, findings of the sensory studies are abnormalities in the lateral antebrachial cutaneous, median sensory (particularly to the thumb), and radial sensory (particularly to the thumb) nerves.[2] Studies of the supracapsular, axillary, and musculocutaneous nerves may appear abnormal.[2] Findings of needle electromyography (EMG) include abnormalities in the supraspinatus, infraspinatus, deltoid, biceps brachii, and brachioradialis muscles. In our case, sensory nerve conduction studies (NCS) showed a decreased amplitude of sensory nerve action potentials in the right lateral antebrachial cutaneous than in the left (right = 9.2 microV; left = 30.9 microV). Further, motor NCS showed the compound muscle action potential amplitudes in the right axillary and musculocutaneous nerves were approximately 30% lower than those in the left nerves. These study results supported the diagnosis of right upper brachial plexopathy.

Due to the patient's shoulder pain, we also considered the possibility of radiculopathy, and needle EMG was performed. The study was compatible with right cervical radiculopathy in the C7-T1.

Phrenic nerve EMG was not conducted in our case. We diagnosed the diaphragmatic dysfunction based on the elevated hemidiaphgram on chest radiographs and abnormal ultrasound findings of the elevated diaphragm. Ultrasound is noninvasive and has both high sensitivity and specificity for detection of diaphragmatic dysfunction.[3] As we have

described in the report, the diaphragmatic excursion and diaphragm thickening fraction were significantly reduced in the case patient, fulfilling the ultrasonographic criteria of diaphragmatic dysfunction.[4,5] Needle EMG can detect evidence of denervation and is the best method to differentiate between neuropathic and myopathic causes of diaphragm weakness.[6] However, it is uncomfortable, and can be technically challenging to perform and interpret. Pneumothorax may occur as a complication due to the proximity of vital structures and the depth of the diaphragm.[4,5] C3-5 roots radiculopathy or radiculitis, the potential differential diagnosis that Professor Finsterer pointed out, might have occurred together with brachial plexopathy in our patient, but it is difficult to differentiate them and we determined the patient's symptoms were more consistent with brachial plexopathy correlating with the clinical features.

He was negative for SARS-CoV-2 infection confirmed by a real-time PCR test. The possibility of pulmonary embolism was excluded from chest CT with contrast enhancement. The chest CT images were reconstructed with 2-mm section thickness, which in general allows detection of pulmonary embolism.[7,8] Although very small subsegmental pulmonary embolism might have been missed, we believe it is unlikely that such a tiny embolism could have contributed to significant shoulder pain and diaphragmatic dysfunction.

Since Guillain-Barre syndrome is a known complication of SARS-CoV-2 vaccination,[9] it is reasonable to consider its possibility. Guillain-Barre syndrome has several forms and its initial signs and symptoms are variable among patients.[10] Phrenic nerve paralysis can develop in patients with Guillain-Barre syndrome. However, we thought unilateral involvement of limb and diaphragm in Guillain-Barre syndrome was not typical, thus, a cerebrospinal fluid study was not conducted. Further, the patient did not have signs or symptoms suggestive of Bickerstaff brainstem encephalitis, such as ataxia, ophthalmoplegia, change in consciousness, or dysarthria.[11]

We appreciate your feedback that every neuralgic amyotrophy is not idiopathic. As you mentioned, infectious or immune triggers, and/or individual (genetic) susceptibility are assumed to be the cause of neuralgic amyotrophy. More importantly, we agree that efforts should be made to rule out all other possibilities before making the diagnosis of neuralgic amyotrophy.

REFERENCES

1. Kang J, Cho JY. Diaphragmatic dysfunction due to neuralgic amyotrophy after SARS-CoV-2 vaccination: a case report. *J Korean Med Sci* 2022;37(38):e283.
PUBMED | CROSSREF
2. Simmons Z. Electrodiagnosis of brachial plexopathies and proximal upper extremity neuropathies. *Phys Med Rehabil Clin N Am* 2013;24(1):13-32.
PUBMED | CROSSREF
3. Boon AJ, Sekiguchi H, Harper CJ, Strommen JA, Ghahfarokhi LS, Watson JC, et al. Sensitivity and specificity of diagnostic ultrasound in the diagnosis of phrenic neuropathy. *Neurology* 2014;83(14):1264-70.
PUBMED | CROSSREF
4. Kokatnur L, Rudrappa M. Diaphragmatic palsy. *Diseases* 2018;6(1):16.
PUBMED | CROSSREF
5. Dubé BP, Dres M. Diaphragm dysfunction: diagnostic approaches and management strategies. *J Clin Med* 2016;5(12):113.
PUBMED | CROSSREF

6. Sarwal A, Walker FO, Cartwright MS. Neuromuscular ultrasound for evaluation of the diaphragm. *Muscle Nerve* 2013;47(3):319-29.
PUBMED | CROSSREF
7. Jeong YJ, Lee KS, Yoon YC, Kim TS, Chung MJ, Kim S. Evaluation of small pulmonary arteries by 16-slice multidetector computed tomography: optimum slab thickness in condensing transaxial images converted into maximum intensity projection images. *J Comput Assist Tomogr* 2004;28(2):195-203.
PUBMED | CROSSREF
8. Heuschmid M, Mann C, Luz O, Mahnken AH, Reimann A, Claussen CD, et al. Detection of pulmonary embolism using 16-slice multidetector-row computed tomography: evaluation of different image reconstruction parameters. *J Comput Assist Tomogr* 2006;30(1):77-82.
PUBMED | CROSSREF
9. Finsterer J, Scorza FA, Scorza CA. Post SARS-CoV-2 vaccination Guillain-Barre syndrome in 19 patients. *Clinics (Sao Paulo)* 2021;76:e3286.
PUBMED | CROSSREF
10. van den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, van Doorn PA. Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. *Nat Rev Neurol* 2014;10(8):469-82.
PUBMED | CROSSREF
11. Yuki N. Fisher syndrome and Bickerstaff brainstem encephalitis (Fisher-Bickerstaff syndrome). *J Neuroimmunol* 2009;215(1-2):1-9.
PUBMED | CROSSREF