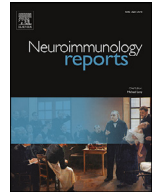




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Transverse myelitis 48 hours after the administration of an mRNA COVID 19 vaccine

Patrick McLean*, Lori Trefts, MD

Medical College of Georgia, Augusta, GA, United States



ARTICLE INFO

Keywords:

Coronavirus
mRNA vaccine
Transverse myelitis

ABSTRACT

Background Vaccinations against SARS-CoV-2 have been a topic of political, social, and medical intrigue since the declaration of the COVID-19 pandemic in early 2020. The vaccine side effects have been relatively mild to date, with few observed systemic effects.

Case presentation A 69-year-old previously healthy female presented with symptoms of asymmetric bilateral lower and upper extremity weakness 2 days after vaccination with the Pfizer-BioNTech mRNA vaccine. MRI of the cervical spine revealed a non-compressive myelitis extending from C3-4 to T2-3. Common known causes of transverse myelitis were ruled out by diagnostic techniques.

Conclusions Transverse myelitis is a rare autoimmune disorder that has been shown to have a temporal association with vaccination in the past. With a progressively partisan societal view on vaccinations, it is important for clinicians to remain vigilant on documenting potential associations without encouraging fear of causation.

1. Introduction

Due to the 2019 Novel Coronavirus pandemic, a new class of vaccines has become a household name. The introduction of mRNA vaccines comes with the concept of an exceptionally safe vaccination method, as well as one that can be manufactured at a rapid pace (Pascolo, 2008). One vaccine, produced by Pfizer-BioNTech works by shuttling an mRNA molecule into cells which instructs the cells to create a spike protein present on the outside of the virus. The immune system then forms a response to the protein, leading to immunity (Pfizer, 2021). The Pfizer-BioNTech mRNA COVID-19 vaccine was shown to be 95% effective in preventing infection. In the safety report, the most common symptoms were localized arm soreness at the site of vaccination, fatigue and headache. To date there have been no reported significant neurological side effects (Polack et al., 2020). We present the first documented case of transverse myelitis temporally associated with an mRNA vaccine. Transverse myelitis is a rare immune mediated disorder of the spinal cord often causing autonomic, motor, and sensory deficits below the level of the spinal cord lesion. It is frequently associated with autoimmune disorders (Frohman and Wingerchuk, 2010), however there is an observed temporal association between vaccinations and transverse myelitis (Agmon-Levin et al., 2009).

2. Case report

Three days prior to admission, the patient, a 69-year-old Caucasian female, had received her first dose of the Pfizer-BioNTech CoVID-19

mRNA vaccine. Day 1 post-vaccination, the patient experienced mild aching at the site of the vaccination but had no difficulties with her typical exercise routine of a 2-mile walk. On the morning of day 2 post-vaccination, the patient began to experience nausea and one episode of vomiting. Later that day she experienced lower extremity weakness and incoordination, worse on the right side than the left. Day 3 post-vaccination, patient reported to the hospital after the sensation of weakness and paresthesia extended to her hands bilaterally. At the time of presentation, she was no longer ambulatory.

Patient's prior medical history was remarkable for surgically treated cervical cancer, hypothyroidism, hyperlipidemia, restless leg syndrome, and right leg sciatica. Home medications include carbidopa-levodopa, fenofibrate, fluoxetine, and levothyroxine. Patient is a never-smoker and denies alcohol use. She had no known autoimmune diagnoses in herself or in her family. She had received no other vaccinations within the last month and denied any recent viral illnesses including COVID-19.

Patient was afebrile on admission. Clinical examination revealed bilaterally weakened grip strength and finger extension, as well as diffusely weakened lower extremities. Reflexes were noted to be slightly exaggerated, raising clinical suspicion for an upper motor lesion. The remainder of the neurological and general exam was normal.

An MRI of the brain and cervical spine was ordered on hospital day 1. The brain MRI revealed no acute intracranial process and no T2 hyperintensities.

MRI of the cervical spine revealed extensive T2 signal abnormalities seen particularly in the anterior aspect, as well as the mid-cord extending from C3-4 down to T2-3, consistent with acute transverse myelitis.

* Corresponding author.

E-mail address: pmclean@augusta.edu (P. McLean).

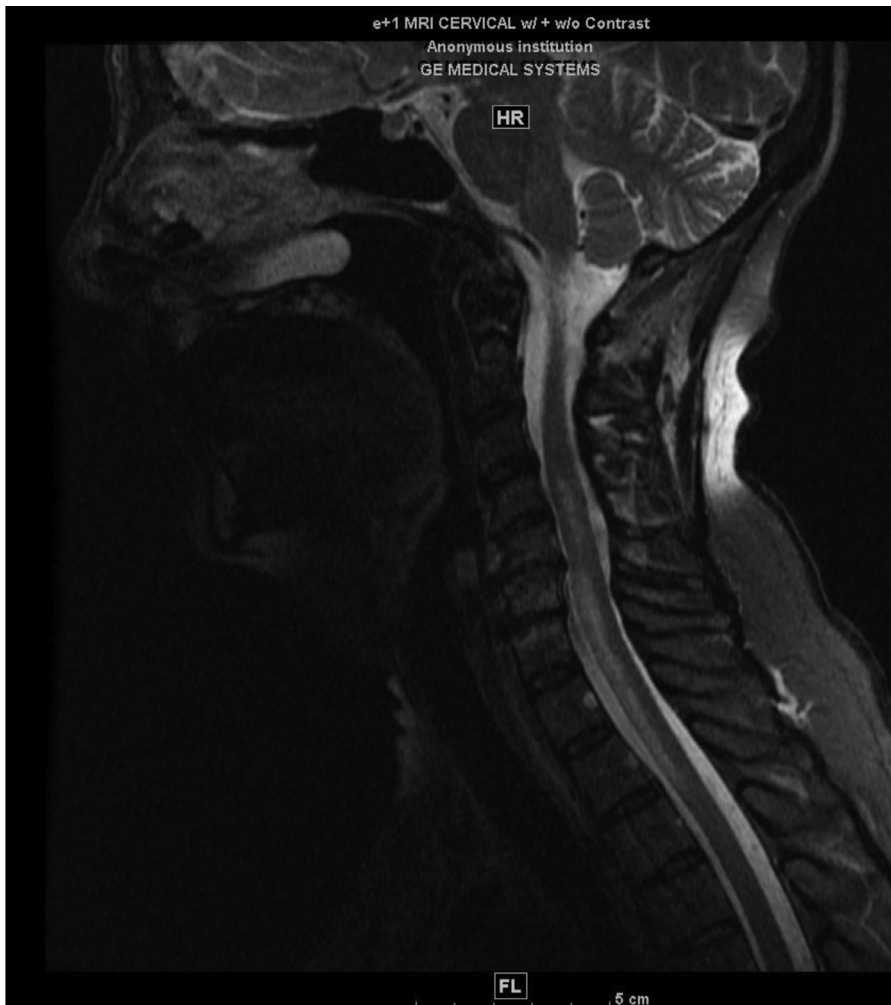


Fig. 1. MRI of cervical spine revealing extensive T2 hyperintensities extending from C3-4 to T2-3.

Disc disease was noted, however there was no evidence of spinal cord compression (**Figure 1**).

CSF studies revealed a normal nucleated cell count, protein, and glucose. MS profile revealed 2 oligoclonal bands in the CSF with 2 matching bands in the serum. Screening the CSF for VDRL, HSV, and Lyme yielded no results. Neuromyelitis optica and myelin oligodendrocyte glycoprotein IgG by cell-based assay were negative.

The following labs were also negative or normal: TSH, folate, SPEP, UPEP, ESR, ANA, HIV, rheumatoid factor, RPR, hepatitis screening, adenovirus antibody, ACE, dsDNA, ANCA, CMV, copper, EBV, zoster, West-Nile virus, enterovirus, HTLV, Sjogren's, vitamin E, anti Hu, anti CV2, anti amphiphysin.

Serum was positive for Coxsackie B5 with titers of 1:8, and Coxsackie B6 with titers of 1:16. Patient reported no history of rash or viral prodrome. These results were discussed with infectious disease and the low titers were deemed to be clinically insignificant.

Patient was treated with 5 days of 1 gram per day of IV methylprednisolone and aggressive physical and occupational therapy. She was discharged home with outpatient physical and occupational therapy. After leaving the hospital she had slow continuous improvement in function. At two-week follow-up outpatient, patient still had residual weakness worse on right side, as well as increased tone in her lower extremities. She required the use of a walker and stated she had been experiencing some urinary urgency and incontinence. She attests to gradual daily improvement. After thoughtful discussion with her treating physicians, the patient decided to forgo her second dose of the COVID 19 mRNA vaccine.

3. Discussion

There has been a recent spotlight on transverse myelitis. An association with a post-inflammatory state of CoVID-19 pneumonia has been noted in recent literature ([Chow et al., 2020](#); [Munz et al., 2020](#)). Three reported cases of transverse myelitis were noted in trials for AstraZeneca's ChAdOx1 nCoV-19 vaccine, with two being ruled unrelated, and one being considered a possible relationship by an independent panel of neurological experts ([Voysey et al., 2021](#)). The presented case in which the only remarkable factor is recent vaccination could be accounted for by the background rate of idiopathic transverse myelitis, which has been shown to have an incidence rate between one and four new cases per million people per year ([Bhat et al., 2010](#)). However, one proposed mechanism of autoimmunity in relation to mRNA vaccines could be molecular mimicry, where cross reactivity with a structurally similar host protein could cause an acute autoimmune reaction ([Agmon-Levin et al., 2009](#); [Rojas et al., 2018](#)). mRNA vaccines are a novel approach to vaccinations and have shown to be efficacious and safe ([Baden et al., 2021](#); [Polack et al., 2020](#)). Pfizer-BioNTech's vaccine safety report showed no suspected cases of transverse myelitis in 43,252 participants ([Polack et al., 2020](#)). At the time of writing this report, there have been 277,196,174 doses of mRNA vaccinations in the US (155,394,989 Pfizer-BioNTech and 121,801,185 Moderna) ([The University of Alabama at Birmingham, 2021](#)), and there are presently no documented cases of transverse myelitis or other autoimmune disorders in relation to the vaccine.

We have presented what we believe to be the first case of transverse myelitis following administration of the Pfizer-BioNTech mRNA vaccine. Common causes of transverse myelitis including multiple sclerosis, NMO, MOG, enteroviruses, and a variety of systemic inflammatory diseases were ruled out by various laboratory tests. The case should be interpreted as an association, rather than a causation, but the temporal relationship should inspire vigilance in reporting future cases.

Neither author has any conflict of interest or funding to report.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.nerep.2021.100019](https://doi.org/10.1016/j.nerep.2021.100019).

References

- Agmon-Levin, N., Kivity, S., Szyper-Kravitz, M., Shoenfeld, Y., 2009. Transverse myelitis and vaccines: a multi-analysis. *Lupus* 18 (13), 1198–1204.
- Baden, L.R., El Sahly, H.M., Essink, B., Kotloff, K., Frey, S., Novak, R., Diemert, D., Spector, S.A., Roupael, N., Creech, C.B., McGettigan, J., Khetan, S., Segall, N., Solis, J., Brosz, A., Fierro, C., Schwartz, H., Neuzil, K., Corey, L., Gilbert, P., Janes, H., Follmann, D., Marovich, M., Mascola, J., Polakowski, L., Ledgerwood, J., Graham, B.S., Bennett, H., Pajon, R., Knightly, C., Leav, B., Deng, W., Zhou, H., Han, S., Ivarsson, M., Miller, J., Zaks, T., Group, C.S., 2021. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N. Engl. J. Med.* 384 (5), 403–416.
- Bhat, A., Naguwa, S., Cheema, G., Gershwin, M.E., 2010. The epidemiology of transverse myelitis. *Autoimmun. Rev.* 9 (5), A395–A399.
- Chow, C.C.N., Magnussen, J., Ip, J., Su, Y., 2020. Acute transverse myelitis in COVID-19 infection. *BMJ Case Rep.* 13 (8).
- Frohman, E.M., Wingerchuk, D.M., 2010. Clinical practice. Transverse myelitis. *N. Engl. J. Med.* 363 (6), 564–572.
- Munz, M., Wessendorf, S., Koretsis, G., Tewald, F., Baegi, R., Kramer, S., Geissler, M., Reinhard, M., 2020. Acute transverse myelitis after COVID-19 pneumonia. *J. Neurol.* 267 (8), 2196–2197.
- Pascolo, S., 2008. Vaccination with messenger RNA (mRNA). *Handb. Exp. Pharmacol.* (183) 221–235.
- Pfizer, 2021. The Facts About The Pfizer-BioNTech COVID-19 Vaccine https://www.pfizer.com/news/hot-topics/the_facts_about_pfizer_and_biontech_covid_19_vaccine.
- Polack, F.P., Thomas, S.J., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., Perez, J.L., Perez Marc, G., Moreira, E.D., Zerbini, C., Bailey, R., Swanson, K.A., Roychoudhury, S., Koury, K., Li, P., Kalina, W.V., Cooper, D., Frenck Jr., R.W., Hammitt, L.L., Tureci, O., Nell, H., Schaefer, A., Unal, S., Tresnan, D.B., Mather, S., Dormitzer, P.R., Sahin, U., Jansen, K.U., Gruber, W.C., Group, C.C.T., 2020. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N. Engl. J. Med.* 383 (27), 2603–2615.
- Rojas, M., Restrepo-Jimenez, P., Monsalve, D.M., Pacheco, Y., Acosta-Ampudia, Y., Ramirez-Santana, C., Leung, P.S.C., Ansari, A.A., Gershwin, M.E., Anaya, J.M., 2018. Molecular mimicry and autoimmunity. *J. Autoimmun.* 95, 100–123.
- The University of Alabama at Birmingham, 2021. COVID-19 Vaccination Dashboard. UAB <https://vax.uab.edu/>.
- Voysey, M., Clemens, S.A.C., Madhi, S.A., Weckx, L.Y., Folegatti, P.M., Aley, P.K., Angus, B., Baillie, V.L., Barnabas, S.L., Bhorat, Q.E., Bibi, S., Briner, C., Cicconi, P., Collins, A.M., Colin-Jones, R., Cutland, C.L., Darton, T.C., Dheda, K., Duncan, C.J.A., Emary, K.R.W., Ewer, K.J., Fairlie, L., Faust, S.N., Feng, S., Ferreira, D.M., Finn, A., Goodman, A.L., Green, C.M., Green, C.A., Heath, P.T., Hill, C., Hill, H., Hirsch, I., Hodgson, S.H.C., Izu, A., Jackson, S., Jenkin, D., Joe, C.C.D., Kerridge, S., Koen, A., Kwatra, G., Lazarus, R., Lawrie, A.M., Lelliott, A., Libri, V., Lillie, P.J., Mallory, R., Mendes, A.V.A., Milan, E.P., Minassian, A.M., McGregor, A., Morrison, H., Mujadidi, Y.F., Nana, A., O'Reilly, P.J., Padayachee, S.D., Pittella, A., Plested, E., Pollock, K.M., Ramasamy, M.N., Rhead, S., Schwarzbold, A.V., Singh, N., Smith, A., Song, R., Snape, M.D., Sprinz, E., Sutherland, R.K., Tarrant, R., Thomson, E.C., Torok, M.E., Toshner, M., Turner, D.P.J., Vekemans, J., Villafana, T.L., Watson, M.E.E., Williams, C.J., Douglas, A.D., Hill, A.V.S., Lambe, T., Gilbert, S.C., Pollard, A.J., Oxford, C.V.T.G., 2021. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 397 (10269), 99–111.