Letter to the Editor, BMJ (2021)
Rapid repose to: https://www.bmj.com/content/374/bmj.n1786/rr-0

Autoimmune damage to the nerves following Covid vaccines: EMA issued warning to patients and healthcare professionals

Hamid A. Merchant[1]

EMA recently investigated the cases of Guillain-Barre syndrome (GBS) following Covid vaccine AstraZeneca (AZ) and have issued a warning to raise awareness of healthcare professionals and the public about GBS cases following Covid vaccinations and recommended revising the product information for Covid vaccine AZ [1]. MHRA later also concluded that as a precautionary measure they will also be adding a warning for GBS in the product information [2]. A similar warning has been issued by the United States FDA for the GBS followed by Janssen (J&J) Covid vaccine [3]. GBS is a rare but serious condition in which the immune system starts attacking the body's healthy nerve cells in the peripheral nervous system that can result in pain, numbness, muscle weakness usually in the feet, hands and limbs) that can also spread to the chest and the face. EMA has advised people to seek immediate medical attention if they develop weakness and paralysis in the extremities progressing to the chest or face following the Covid vaccine.

The EMA could not find enough evidence to confirm the association of GBS with the vaccine, however, this may be explained by the vaccine biodistribution to the nerves following intramuscular injection. The vaccine transfection and translation in the nerves may spur an immune response against nerve cells potentially resulting in autoimmune nerve damage. The preclinical evaluation of Covid vaccine AZ (study 514559) evidenced vaccine distribution) to various body tissues beyond injection site including sciatic nerves [4].

Study 514559 showed that the Covid vaccine AZ was distributed to sciatic nerves in almost all animals and the distributed fractions did not clear throughout the study. The last sample was taken on 29 days post-administration and sciatic nerves of 70% of animals were still tested positive at the end of the study. The vaccine distribution to the sciatic nerves may lead to conditions like sciatica that has been previously linked to the viral infection of the sciatic nerve, such as herpes. The MHRA pharmacovigilance database reported ~187 cases of sciatica post-Covid vaccine AZ as of 28th July 2021. There were at least 127 other instances of nerve injury and 301 cases of various forms of neuropathies (including 207 cases of peripheral neuropathy) listed in the MHRA database [2].

The biodistribution of the vaccine to other nerves is not known as the study 514559 checked for sciatic nerves only being anatomically closer to the injection site (hind limb) in mice. The facial (cranial) nerves, on the contrary, are anatomically closer to the vaccine injection site in humans (deltoid muscle). The MHRA database listed ~1031 cases of facial cranial nerve disorders (527 cases of Bell's palsy and 457 cases of facial paresis/paralysis), 20 cases of Miller

[1] School of Applied Sciences, University of Huddersfield, Huddersfield, West Yorkshire, United Kingdom HD1 3DH. Tel: +44 1484 472387, Email: hamid.merchant@hud.ac.uk

Fisher syndrome and additional 372 cases of Guillain-Barre syndrome (2 fatal) following AZ vaccine up until 28th July 2021.

It is worth noting that the Covid vaccine AZ clinical trials were paused twice and, on both occasions, the trial subjects developed a neurological condition, transverse myelitis. One of the subjects was later diagnosed with multiple sclerosis [5], declared unrelated to the vaccine. Surprisingly, as of 28th July 2021, there are 77 cases of transverse myelitis, 16 cases of myelitis and another 13 cases of encephalomyelitis following Covid vaccine AZ in the MHRA database. Moreover, there are additional 56 cases of multiple sclerosis and another 49 cases reporting a relapse of multiple sclerosis within the MHRA database. The vaccine-induced multiple sclerosis (if proven) may also be an autoimmune response to the vaccine distribution and transfection to the nerves.

The biodistribution (study 514559) also evidenced the vaccine distribution via blood circulation to other tissues notably bone marrow, liver, mammary glands and spleen. The vaccine encoded gene transfection to distant tissues is likely to attract an immune response against various body tissues that can manifest into various autoimmune conditions. Recently, vaccine distribution to the vasculature and interaction with circulatory platelets have been proposed as a likely mechanism for thrombosis with thrombocytopenia syndrome (TTS) [6]. These autoimmune responses may well be transient in many healthy subjects, and the immune response is likely to be very selective towards vaccine transfected cells only, however, the possibility of developing a chronic autoimmune condition in some individuals cannot be overruled. The regulatory authorities are, therefore, requested to review the cases of GBS in association with various other neuropathies and vaccine biodistribution data from preclinical trials. This will not only help in explaining a causal link but will also help take necessary precautionary measures in time for public safety. A similar issue has been reported with Janssen (J&J) Covid vaccine [7], and we anticipate other viral-vector Covid vaccines such as CanSinoBIO (China) and Sputnik V (Russia) are likely to pose a similar risk. The detailed tissue-specific distribution of mRNA vaccines encoding SARS-CoV-2 spike proteins (Pfizer or Moderna) is not fully known that could offer invaluable insights into the long-term safety of mRNA vaccines. However, the surrogate studies using similar formulations by Pfizer [8] and Moderna [9] did confirm a biodistribution of mRNA vaccines beyond the injection site. We urge regulatory authorities to mandate manufacturers to perform adequate biodistribution studies on vaccine formulations and request further data to better understand the implications of vaccine transfection in distant tissues before mass vaccine rollout in children or recommending additional adult booster doses.

MHRA is requested to investigate the cases of post-vaccine GBS and related signals of nerve damages in association with wider signals of auto-immune reactions in their database. Most of the adults in UK are already vaccinated, therefore, early recognition of post-vaccine autoimmune conditions like GBS may help in offering early therapeutic interventions to those who are potentially affected with the condition that can help to prevent disease progression and chronic illness. GBS case reports following Covid vaccines [10, 11] also emphasise the importance of early therapeutic intervention. Novel Covid vaccines work on the premise of gene delivery and their long-term safety must be assessed if genetic vaccines were to be sustained beyond the CoViD-19 pandemic.

Click here to access the published version of this article for FREE at the BMJ website.

References

[1] https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-5-august-2021

[2] https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting

[3] https://www.fda.gov/media/150723/download

[4] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1003840/CMA_UKPAR_COVID_19_Vaccine_AstraZeneca_PAR_16.07.2021.pdf

[5] https://www.statnews.com/2020/09/09/astrazeneca-covid19-vaccine-trial-hold-patient-report/

[6] https://doi.org/10.1101/2021.06.29.450356

[7] https://www.medpagetoday.com/infectiousdisease/covid19vaccine/93537

[8] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/944544/COVID-19_mRNA_Vaccine_BNT162b2__UKPAR___PFIZER_BIONTECH__15Dec2020.pdf

[9] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/977367/UKPAR_COVID_19_Vaccine_Moderna_07.04.2021_CMA_Reliance_PAR__-__final.pdf

[10] https://casereports.bmj.com/content/bmjcr/14/4/e242956.full.pdf

[11] https://onlinelibrary.wiley.com/doi/10.1111/ncn3.12537