ISSN: 2754-4516

Journal of Medicine and Healthcare

SCIENTIFIC Research and Community

Mini Review

Open Access

Relation of Covid-19 Vaccines with Inflammatory Neuropathies: Mini-Review

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Received: May 28, 2022; **Accepted:** June 02, 2022; **Published:** June 09, 2022

Introduction

Numerous vaccines have been associated with various neurological adverse effects. Guillain-Barré syndrome [GBS], transverse myelitis, encephalitis, and optic neuritis have been reported following vaccination with human papillomavirus, yellow fever, measles, tetanus, rabies, rubella, and hepatitis A or B [1]. COVID-19 vaccines are not exempted from such adverse effects. Moderna (mRNA-1273), Pfizer-BioNTech (BNT162b2), and Johnson & Johnson's Janssen (Ad26.COV 2.S) are the COVID-19 vaccines in use in the United States of America [USA]. These vaccines are generally well-tolerated. Common side effects are pain at injection site, fever, redness, headache, or myalgias. Neurological adverse events associated with COVID-19 vaccines are rare [2].

We will specifically look at inflammatory neuropathies in the context of COVID-19 vaccines in this article. Inflammatory neuropathy after vaccination first came to headlines in 1976, when an increased incidence of GBS was reported after swine influenza vaccine [3]. However, subsequent studies provided a clearer picture, showing that cumulative GBS risk from influenza was significantly higher than that from influenza vaccines [4].

Discussion

Inflammatory neuropathies are autoimmune-mediated inflammatory disorders resulting in demyelination of peripheral nervous system. The exact pathogenic mechanism is unclear but molecular mimicry has been proposed. mRNA of the vaccines enters the human cell and starts making spike protein found on the virus's surface. Antibodies are produced against the spike protein. A vaccine consists of an antigen, an adjuvant, and a delivery system. Adverse reactions after vaccination can result from any of these components. The antibodies against spike proteins produced by COVID-19 vaccines bind to sialic acid-containing glycoproteins and gangliosides on cell surfaces [5]. These antibodies cross-react with myelin protein of peripheral nerves or nerve roots leading to activation of complement system. Inflammatory neuropathies are divided into acute and chronic, namely Acute Inflammatory Demyelinating Polyneuropathy [AIDP] and Chronic Inflammatory Demyelinating Polyneuropathy [CIDP] respectively. AIDP is the most common form of GBS. AIDP has a more rapid course. Symptoms typically reach a nadir in 4 weeks or less. Back pain and autonomic symptoms are common in AIDP, along with bulbar involvement or respiratory compromise. CIDP has a more indolent course. As per established criteria, it takes more than 8 weeks to develop the greatest weakness in CIDP. Patients typically present with weakness in both proximal and distal muscle groups, sensory loss, and paresthesias which could be slowly progressive or they present with a more relapsing/remitting course. Unlike AIDP, autonomic symptoms and back pain are less common in CIDP. Also, respiratory compromise or bulbar involvement is rare in CIDP patients.

Garg and Paliwal conducted a review of published studies on COVID-19 vaccines associated with neurological complications. The review looked at published reports of several neuroinflammatory, peripheral nerve, neurovascular, and neuromuscular complications associated with COVID-19 vaccines [6]. Fernandes et al published a case series of 4 patients. 2 of the patients developed new-onset seizures and transverse myelitis following Pfizer-BioNtech vaccine. And other 2 patients developed meningitis-retention syndrome and GBS following AstraZeneca COVID-19 vaccine [7]. Jee-Eun Kim et al. reported a case series of 13 patients which resulted in GBS and variants after COVID-19 vaccination in South Korea [8]. Out of 13 patients, 5 received Pfizer-BioNtech and 8 received AstraZeneca vaccine. GBS is more commonly related to adenovirus vaccines, but it also has been reported in relation to mRNA vaccines on several occasions [9-11]. Documented inflammatory demyelinating polyneuropathy post ChAdOx1 nCoV-19 vaccine in 4 patients. 1 patient had GBS

symptoms flareup, whereas 3 patients had new onset GBS [12]. Bagella reported a case of GBS after ChAdOx1 nCoV-19 which later developed into CIDP [13]. Taga and Lauria, in their review article published in February 2022, did comprehensive research of available data on peripheral nervous system disorders in relation to COVID-19. They did not find any report associating CIDP with COVID-19. Some cited literature mentioned exacerbation of CIDP symptoms after COVID-19 infection in existing CIDP patients [14]. Published a case report on CIDP after Moderna vaccination [15]. Abo-Zed and Pinevich published a case of post-Moderna COVID-19 vaccine new-onset GBS development which later evolved into CIDP [16]. Remarkably, the patient had a previous history of GBS/AIDP 4 years ago after receiving the influenza vaccine. Published a case series of 4 patients which developed CIDP after AstraZeneca vaccine [17]. As of May 2022, there are 61 reported events in Vaccine Adverse Event Reporting System [VAERS] in the USA when searched under CIDP and COVID-19 vaccine. Most of these reported events are self-reported by patients or family members. Overall, there is convincing data available for the occurrence of inflammatory neuropathies in the context of COVID-19 and COVID-19 vaccines, more so for AIDP with rare reports of CIDP.

Conclusion

Inflammatory neuropathies do exist in the population in the background independent of relation with vaccines. This means that some of these adverse events will be noticed in the postvaccination window by chance. This is important to understand as fear of adverse reactions from vaccines is reportedly the leading cause of vaccine hesitancy. It requires large observational studies to establish a causal relationship between inflammatory neuropathies and COVID-19 vaccines.

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