Research Article ISSN 2768-6647

Medical and Clinical Case Reports

Neurological Complications Following mRNA COVID-19 Vaccination: Peripheral Axonal Neuropathy and Transverse Myelitis

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Received: 03 Apr 2024; **Accepted:** 08 May 2024; **Published:** 16 May 2024

Citation: Lopez-Carriches C, Leco-Berrocal MI, Ricardo Taheri, et al. CREB and AKT Levels Higher in Attention Deficit Disorder (ADD) Individuals. Med Clin Case Rep. 2024; 4(2): 1-4.

ABSTRACT

Vaccines used in the coronavirus pandemic have reported some minor side effects such as pain at the injection site, headache, myalgia and fever. Also major neurological side effects have been experienced by some patients. Cases of complications have been found in the peripheral nervous system, especially Guillen Barre Syndrome, subacute axonal sensorimotor polyneuropathy, brachial plexopathy, chronic inflammatory demyelinating polyneuropathy. Also in the Central Nervous System, especially transverse myelitis, which responds well to treatment with corticosteroids.

We reviewed the literature to assess the frequency of this type of complication.

Keywords

COVID-19, SARS-CoV-2, Vaccine, Peripheral axonal neuropathy, Transverse myelitis.

Introduction

The number of patients diagnosed with COVID-19 is still increasing with over 10% ending in death [1]. Many of these have been related to increased age. Therefore massive vaccination of this population has had a vital importance to prevent this outcome.

The main mechanism of action of the FDA approved COVID-19 vaccines is messenger RNA (mRNA) vaccines (Comirnaty from Pfizer/BioNTech and Spikevax from Moderna). The mRNA encoding protein S is encapsulated in lipid nanoparticles. The nucleic acid vaccines introduce mRNA or DNA coding for SARS-CoV-2 spike protein into the cells, to induce cells to produce antibodies. These vaccines have reported an efficacy of up to 95% and are currently used in several countries [2].

Also, viral vector vaccines are used. These vaccines use a chemically weakened virus (e.g. adenovirus) to insert the code for SARS-CoV-2 antigens into the cells. Jcovden manufactured by Johnson and Johnson is produced with human adenovirus that carries protein S. Also, Vaxzevria, manufactured by Astrazeneca, includes non-replicative chimpanzee adenovirus which carries protein S [3]. Vaccines against COVID-19 have caused minor side effects such as pain and swelling at the injection site, headache, fever, or muscle aches. More important complications are also being reported, including neurological complications such as Bell's Palsy condition, Guillain-Barre syndrome, transverse myelitis, cerebral venous sinus thrombosis, acute disseminated encephalomyelitis, acute demyelinating polyneuropathy and reactivation of herpes zoster in many people [4,5].

Materials and Method

We searched PubMed database using the keywords "COVID-19" or "SARS-CoV-2" and "vaccine," "peripheral axonal neuropathy"

and "transverse myelitis" to identify all published papers on neurological complications of COVID-19 vaccines. The search was conducted on December 30th, 2023.

Results

In the analyzed literature, cases of complications have been found in the peripheral nervous system, especially Guillen Barre Syndrome, subacute axonal sensorimotor polyneuropathy, brachial plexopathy, chronic inflammatory demyelinating polyneuropathy (CIDP) [6-9] table 1.

Also in the Central Nervous System, especially transverse myelitis, which responds well to treatment with corticosteroids [10-27] table 2.

Table 1: Complications in the peripheral nervous system.

Author	Symptoms	Vaccine	Begining of symptoms	Age/ Sex	Treatment	Evolution
Roncati [6]	Left cubital tunnel syndrome	Spikevax®	7th day	28/F	Surgery	+
Leemans [7]	Upper and lower extremity weakness	Comirnaty®	7th day	79/M	IGs iv	+
Leemans [7]	Motor weakness and paresthesia	Comirnaty®	4th week	57/M	MT	+
Leemans [7]	Hypoaesthesia in lower extremities	Comirnaty®	2nd week	80/M	None	+
Leemans [7]	Hypoexthesia in lower extremities, mouth and genitalia	Vaxzevria®	4th week	62/M	None	+
Leemans [7]	Hypoaesthesia feet and hands, facial paralysis	Comirnaty®	2nd week	61/F	IGs	+
Leemans [7]	Muscle pain, facial paralysis	Comirnaty®	11th day	62/M	MT	+
Leemans [7]	Leg weakness, hypoesthesia and pain	Vaxzevria®	1st week	63/M	IG	+
Leemans [7]	Hypoaesthesia and paresthesia in the legs and hands	Comirnaty®	2nd week	81/F	IG	+
Wen [8]	Limb weakness and hypoaesthesia, diplopia, dyspnea and CIDP	Inactivated COVID-19 vaccine	1st day	23/M	Rituximab (RTX)	+
Safavi [9] 23 cases	Distal predominant paresthesias and burning sensations in both their upper and lower limb, face, mouth, and scalp.	1 Vaxzevria® 1 Jcovden® 9 Spikevax® 12 Comirnaty®	1st month	40/ 92% female	Corticosteroid or IGs iv	+

Recovery (+); Worsening (-).

Table 2: Cases of transverse myelitis.

Author	Symptoms	Vaccine	Begining of symptoms	Age/Sex	Treatment	Evolution
Malhotra [10]	Paresthesia lower limbs	Vaxzevria®	8th day	36/M	MT	+
Fitzsimmon [11]	Backache, paresthesia on feet, difficulty walking urinary retention	Spikevax®	1st day	63/F	IG iv MT	+
Koorapatiahi [12]	Cervical transverse myelopathy	Jcovden®	10th day	44/F	Plasma exchange MT	+
Pagenkopf [13]	Posterior chest pain and urinary retention.	1º dose Vaxzevria®	11th day	45/F	Prednisone	+
Helmchen [14]	Blindness due to optic neuritis, difficulty walking and urinary incontinence	Vaxzevria®	2nd weeks	40/F	Corticosteroids. Plasmapheresis	+
Havla [15]	Multiple sclerosis	1stº dose Comirnaty®	6th day	28/F	MT Plasma exchange	+
Chen [16]	Dizziness and unsteady walking	Inactivated COVID-19 vaccine	3rd day	-/F	MT	+
Khan [17]	Weakness in upper and lower limbs and difficulty to walk	1st dose Spikevax®	1st day	67/F	MT Plasmapheresis	+

Gao [18]	Instability and paresthesia of upper and lower limbs.	Spikevax®	6th day	76/F		
Guarnaccia [19]	Lip and foot numbness. tired legs, slight urinary incontinence	Comirnaty®	2 hours	32/F	MT	+
Alabkal [20]	Paresthesia in the feet	Comirnaty®	3rd day	26/F	MT	+
Notghi [21]	Numbness lower limbs and urinary incontinence	Vaxzevria®	7th day	58/M		
Sepahvand [22]	Paresthesia in both hands Decreased muscle strength	1st dose Sinopharm®	5th day	71/M	MT	+
Hirose [23]	Sensorimotor dysfunction of both lower limbs	Spikevax®	17th days	70/M	MT	+
McLean [24]	Bilateral lower and upper extremity weakness	Comirnaty®	2nd day	697F	MT	+
Nakano [25]	Weakness and Hypoesthesia in the lower extremities bilaterally	Comirnaty®	15th day	85/M	MT	Exitum
Spataro [26]	Leg weakness urinary retention	Vaxzevria®	4th day	20/M		+
Coelho [27]	Anosmia Ageusia Weak lower limbs	Vaxzevria®	3rd week	48/M	MT	+

Recovery (+); Worsening (-)

Discussion

In acute transverse myelitis, common clinical presentations include paresthesia and sensory deficits of the lower limbs, urinary retention, paraplegia and hyperactive reflexes [7]. The pathogenesis of vaccine-induced myelitis is unclear. It can be due to an immune reaction to the vaccine or due to thrombosis in the spinal cord [5]. There is probably a susceptibility of the patients. Molecular mimicry represents one of the main immunopathogenic factors, where similarity between the proteins of the viruses used for the vaccination and self-antigens (e.g. myelin) triggers an undesired immune-response [28]. There is also an acceleration of an ongoing autoimmune process by local activation of antigen-presenting cells and over processing of antigens induced by foreign antigens [29]. Polyclonal activation of B lymphocytes or bystander activation which enhances cytokine production and further induces the expansion of autoreactive T-cells [30]. The m-RNA-based vaccines give more demyelinating syndromes [31].

In almost all the cases consulted, methylprednisolone (MT) is used as a treatment with good results. Also IGs iv and plasmapheresis are used [17]. The pathogenesis of vaccine-induced myelitis is unclear. It can be an immune reaction to the vaccine or small infarcts due to thrombosis in the spinal cord [5]. There is probably a susceptibility of the patients. Molecular mimicry represents one of the main immunopathogenic factors, where similarity between the proteins of the viruses used for the vaccination and self-antigens (e.g. myelin) triggers an undesired immune response [28].

The acceleration of an ongoing autoimmune process by local activation of antigen-presenting cells and over-processing of antigens induced by foreign antigens [29]. Polyclonal activation of B lymphocytes or bystander activation which enhances cytokine production and further induces the expansion of autoreactive T-cells [30]. The m RNA-based vaccines produce more demyelinating syndromes [31].

Conclusions

After the coronavirus vaccine, neurological complications can occur, both in the central and peripheral nervous systems, but these vaccines are essential in a pandemic like the one that has emerged, so the benefit outweighs the risk.

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