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Letter to the Editor

Neurological side effects to SARS-CoV-2 vaccinations are common and reported since introduction of the vaccines

[1] Fulvio A Scorza, [2] Josef Finsterer

[1] Disciplina de Neurociência. Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM). São Paulo, Brasil

[2] Neurology & Neurophysiology Center, Vienna, Austria

Corresponding Author: **Josef Finsterer**

We read with interest the article by Leemans *et al*. about a case series of eight patients with neurological complications of a SARS-CoV-2 vaccination [1] Two patients were diagnosed with chronic inflammatory demyelinating polyneuropathy (CIDP), one with Parsonage-Turner syndrome (PTS), one with axonal polyneuropathy, and four with Guillain-Barre syndrome (GBS) [1]. It was concluded that further epidemiological studies are warranted to elucidate the relation between SARS-CoV-2 vaccinations and consecutively occurring peripheral nervous system (PNS) disease [1]. The study is appealing but raises concerns that should be discussed.

We disagree with the statement that the patient with plexopathy (patent number 2) is the first ever described with SARS-CoV-2 vaccination associated plexitis [1]. In a recent case report about a patient with plexopathy of the cervico-brachial plexus (Parsonage Turner syndrome (PTS)) following a SARS-CoV-2 vaccination, 13 patients with PTS were reviewed [2].

Description of patient 2 lacks a specification which differentials have been ruled out by which means. Differential diagnoses that need to be excluded include bursitis, rotator cuff injury, calcific tendonitis, impingement syndromes, Guillain-Barre syndrome (GBS), chronic inflammatory demyelinating polyneuropathy, cervical disc prolapse, cervical radiculopathy, mononeuritis monoplex. amyotrophic lateral sclerosis, quadrilateral space syndrome, tumours of the spinal cord, multifocal motor neuropathy (MMN), neuronitis multiplex, polymyalgia rheumatica, thoracic outlet syndrome (TOS), cervical artery dissection, and arthritis.

Missing is the discussion of a genetic cause of PTS. Since hereditary plexopathy is a well-known entity, we should be informed about the family history with particular regard to shoulder pain and upper limb sensory disturbances. Mutated genes associated with hereditary plexopathy include *SEP9* and the chromosome 17p11.2 deletion, commonly associated with hereditary neuropathy and liability to pressure palsies (HNPP) [3].

Concerning patient 8, the diagnosis GBS is not convincing as paraneoplastic neuropathy can manifest with similar features on nerve conduction studies (NCS) and cerebrospinal fluid (CSF) investigations as in the index case, and as paraneoplastic neuropathy can also respond favourably to IVIG. Absence of specific paraneoplastic antibodies does not exclude a paraneoplastic PNP. It should be also considered that the patient had toxic neuropathy due to application of oxaliplatin.

A cause of CIDP not considered in the two included patients is autoimmune nodopathy due to antibodies against neurofascin, contactin-1, or contactin-related protein-1 [4]. We should be told if these differential diagnoses were excluded in the two patients with CIDP, particularly if their family history was positive or negative for CIDP.

We disagree with the statement that today no data about the frequency of neuromuscular complications following a SARS-CoV-2 vaccinations have been published [1]. In a recent review about the neurological complications of anti-SARS-CoV-2 vaccinations, it was found that the most frequent complications of anti-SARS-CoV-2 vaccination are headache, followed by GBS and venous sinus thrombosis (VST) [5].

Concerning patient 3, who developed axonal polyneuropathy after vaccination, we should know if there was pre-existing polyneuropathy, which became symptomatic due to the vaccination. Missing in this respect is an explanation of the pathogenesis of polyneuropathy.

Missing is also the exclusion of an acute SARS-CoV-2 infection in all eight patients. Since the described neurological diagnoses can be also triggered by a SARS-CoV-2 infection and since vaccination does not always prevent from getting infected, it is crucial that an infection is excluded by a negative PCR test in all eight patients.

Overall, the interesting review has some limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could enhance the study. Alternative etiologies should be excluded before diagnosing SARS-CoV-2 vaccination associated PNS disease.

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