Combined central and peripheral demyelination (CCPD) is a rare demyelinating process that involves both the central and peripheral nervous system and can occur after infection or vaccination. Here we describe the case of a patient that developed CCPD after having received the first dose of ChAdOx1 nCoV-19 vaccine.

A 52-year-old man with no significant comorbidities presented to the ER reporting sudden-onset tingling paresthesia in his fingers and toes, and reduced hand dexterity. Three weeks earlier, a COVID-19 outbreak had occurred in the penitentiary where he worked. Eleven days before admission, he was vaccinated with ChAdOx1 nCoV-19. At admission, the neurological examination showed VII cranial nerve deficit, dysthria, and bilateral hand intrinsic muscles deficit (MRC = 4/5), normal deep tendon reflexes, and a slightly ataxic gait. Head and chest CT scan and blood exams were unremarkable. He was admitted to the Neurology Unit (Day 0). On Day 2, sensory disturbances worsened, reflexes became diffusely weak, and cranial nerves involvement became prominent with diplopia, perioral paresthesia, bilateral facial diplegia, dysphagia, hypophonia, and severe dysarthria. Three days later, he noted hypophonia and fatigability during speech. An ophthalmoscopic exam revealed bilateral optic papillitis; visual acuity was 8/10 right and 9/10 left. Visual evoked potentials showed bilateral slow conduction with right mild amplitude reduction. A second IVIg cycle did not provide substantial benefit. On day 28, brain MRI revealed contrast-enhancing multifocal bilateral demyelinating lesions (Figure 1B–G). After 5 days of high-dose intravenous corticosteroids (1g die, Days 30–34), the patient completely recovered, and he was discharged with oral prednisone. After 2 months, he is clinically stable.

CSF examination on day 1 showed normal proteins and white blood cell count; cytometric dissociation emerged on days 7 and 19.

Electromyography on day 1 showed severe, distally predominant, demyelinating symmetric polyradiculoneuropathy (DADS) with prolonged distal motor latency at lower limbs, diffuse reduction in nerve conduction velocity, absent F-waves in most of the explored nerves and increased temporal dispersion at lower limbs. On day 13 neurophysiological studies showed a slight worsening. Serum and CSF IL-6 and IL-8 cytokines peaked during the first disease stage, decreasing thereafter (Figure 2). Anti-spike antibodies progressively raised over time. Serum samples tested positive for anti-NF155 IgG autoantibodies and negative for anti-contactin-1, and anti-CNTN-1/CASPR-1 complex. IgG isotype determination is ongoing.

**Keywords:** COVID-19; Demyelination; CNS inflammation; Neuroimmunology; Peripheral neuropathy
Infectious and other autoimmune screening was negative (see Supplementary Material Table 1 for full lab diagnostics).

The rise of the anti-spike protein titre demonstrates a mounting immune response against SARS-CoV-2, which might have triggered an autoimmune process. Such finding seems to replicate the mechanisms of autoimmune-mediated complications of vaccination and is in accordance with data from a large CCPD case series, where recent vaccination/infection triggered two-thirds of cases.1
Peripheral nervous system (PNS) involvement can happen before, hand-in-hand with, or after central nervous system (CNS) involvement\textsuperscript{1,3,4} and influences the first treatment choice, as those with early PNS involvement might receive IVIg/plasmapheresis rather than steroids.\textsuperscript{1,4} CCPD has also been reported with anti-NF155 autoantibodies.\textsuperscript{3,4} This case exhibits some of the characteristic features of CCPD with anti-NF155 antibodies: the MS-like CNS involvement, with perivenular inflammation at periventricular sites (Figure 1D); absence of oligoclonal bands in CSF; damage in nerve roots and DADS.\textsuperscript{4}

An attempt to better characterize the patient’s immune response has been made by measuring cytokines levels both on serum and on CSF across the stay. The rise in IL-8 CSF levels (several times higher than serum) could point to an intrathecal autoimmune process, diverging from the pathogenesis of Guillain-Barré syndrome related to antiparanodal antibodies, with no oligoclonal bands and normal IgG indices.\textsuperscript{5}

The worldwide rollout of COVID-19 vaccines is eventually leading to the emergence of very rare syndromes after vaccination. Very rare events with unknown epidemiology are hardly interpretable in their relationship with vaccination. Here, although the temporal association of CCPD and vaccination does not prove any causal link, a connection with vaccine exposure must be considered, given the very rare nature of the syndrome and the negative findings emerging from all investigations.

**Supplementary material.** To view supplementary material for this article, please visit https://doi.org/10.1017/cjn.2021.256.

**Conflict of Interest.** None.

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