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CASE REPORT OPEN ACCESS

# A CASE OF COMBINED CENTRAL AND PERIPHERAL DEMYELINATION IN A PATIENT WITH PEDIATRIC MULTIPLE SCLEROSIS AFTER SARS-COV-2 VACCINATION

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**ABSTRACT**

We present a case of combined central and peripheral demyelination in a patient with pediatric multiple sclerosis after the first dose of ChAdOx1-S (Chimpanzee Adenovirus Oxford 1) vaccination. The patient presented with ascending flaccid quadriparesis with respiratory failure that required mechanical ventilation. The lumbar puncture revealed albuminocytological dissociation, was negative for presence of JCV (John Cunningham Virus) in the CSF (Cerebrospinal Fluid) and ruled out other infections. A few days later he developed anisocoria and multiple new enlarging acute demyelinating lesions in the brain MRI (Magnetic Resonance Imaging). He was treated with intravenous immunoglobulin, corticosteroids and plasma exchange with gradual improvement. All other diseases were excluded via MR Spectroscopy, MR Angiography and serum and CSF laboratory investigations. Seven months later, the patient is under intense physiotherapy and is improving every day.

**Keywords:** Combined Central and Peripheral Demyelination, Multiple Sclerosis, Sars-Cov-2 Vaccination, ADEM

## Introduction

Combined central and peripheral demyelination (CCPD) is a rather new and uncommon neurological entity that only recently started being recognized and studied. Usually, inflammatory demyelinating diseases affect either the central (CNS) or the peripheral (PNS) nervous system due to the fact that most autoimmune cells target and react to specific antigens of the CNS or the PNS respectively. Lately, cases of demyelination in both CNS and PNS are being described under various names, such as multiple sclerosis (MS) associated with chronic inflammatory demyelinating polyneuropathy (CIDP). The term combined central and peripheral demyelination unifies all these heterogeneous phenotypes.[1]

In most case series the patients develop clinical features of both central and peripheral nervous system disease either simultaneously, or with temporally separated onset of CNS or PNS involvement.[2] Demyelinating lesions are found in the brain and/or spinal MRI and nerve conduction studies show features of demyelinating polyneuropathy. In a large case series in Japan, 67.5% of patients fulfilled the McDonald criteria for MS and 87.5% fulfilled the EFNS/PNS (European Federation of Neurological Societies/Peripheral Nervous Systam) criteria for CIDP.[1] Disease course is progressive in two third of patients - presenting as new relapse or ongoing progression of symptoms - or monophasic, usually with better prognosis.[3]

We present a case of acute concurrent demyelination in both central and peripheral nervous system in a patient with pediatric MS after vaccination with ChAdOx1-S.

## Case Report

A 42 years old male presented in the emergency department with a three days complaint of general weakness, malaise and difficulty in swallowing. The symptoms started around two weeks after he was vaccinated with the first dose of ChAdOx1-S vaccine against Sars-Cov-2. At first, he felt numbness, paraisthesias and weakness in the legs which rapidly progressed to the arms, combined with difficulty in speaking and swallowing. Three days later he referred to the hospital due to the fact that he could not walk and eat. He was examined in the E.R. by an internist. His brain CT was unremarkable, his arterial blood gases showed mild hypoxemia and hypercapnia and his chest CT revealed signs of aspiration pneumonia. Since his PCR Sars-Cov-2 test

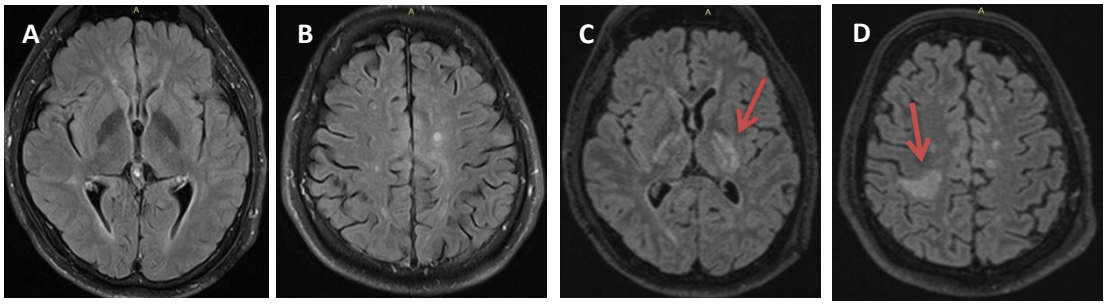


**Figure 1. A, B:** Baseline demyelinating lesions in brain MRI in February 2021. **C, D:** Brain MRI in May 2021 after intubation. New demyelinating lesions in the corticospinal tracts bilaterally and in the white matter of the right parietal lobe (red arrows).

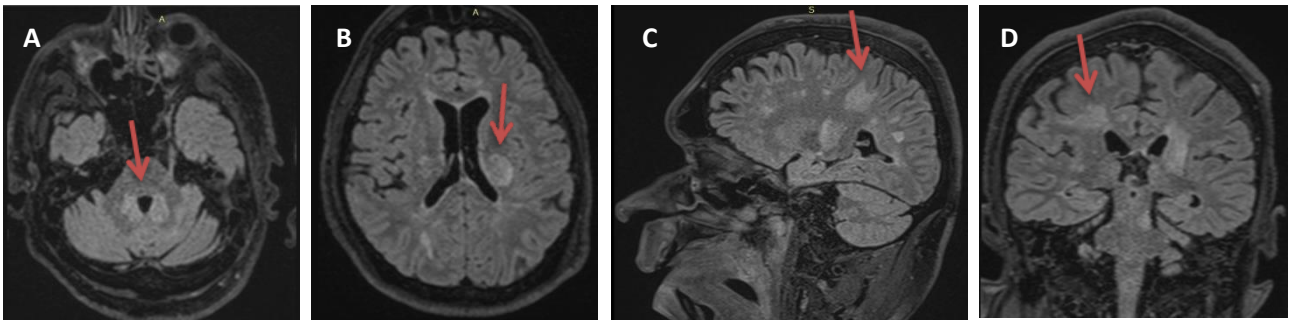


**Figure 2**. Brain MRI in May 2021 after intubation. **A:** New demyelinating lesions (red arrow) in the cerebral peduncles bilaterally. **B:** New demyelinating lesion in the periventricular white matter bilaterally, the largest one on the left (red arrow) **C:** New large demyelinating lesion (red arrow) in the white matter of the right parietal lobe. **D:** Large demyelinating lesions in the corticospinal tracts bilaterally and in the white matter of the right parietal lobe (red arrow).

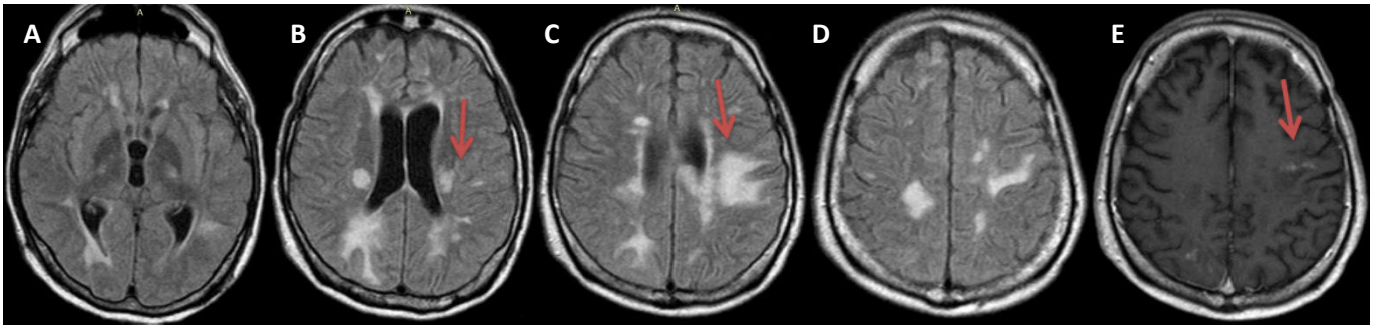


**Figure 3.** Brain MRI in June 2021. **A-D:** The demyelinating lesions on the left periventricular white matter and on the left parietal lobe (red arrows) are smaller in size and less diffuse. **E:** Patsy gadolinium enhancement in the demyelinating lesions in the white matter bilaterally and in the left frontal juxtacortical white matter (red arrow).

came back negative he was admitted to the internal medicine ward and a neurological consult was performed.

The neurological exam showed that the patient was lethargic, with dysarthria, dysphagia, bilateral peripheral facial nerve palsy and severe flaccid quadriparesis worst on the legs. He was intubated a few hours later due to respiratory failure which led to severe hypercapnia (pCO2=84mmHg).

In order to investigate the symptoms, once the patient was stable, a lumbar puncture (LP) was performed which showed mild cerebrospinal fluid (CSF) pleocytosis (30 white blood cells, mostly lymphocytes) and elevated CSF protein (146mg/dl). He was started on 30g intravenous immunoglobulin (IVIG) a day for five days and was transferred to an intensive care unit (ICU).

After a few hours in the ICU he developed anisocoria, so a brain MRI was performed. It revealed multiple new large and diffuse demyelinating lesions in the left cerebellar peduncle and in the parieto-occipital white matter bilaterally with restricted diffusion and gadolinium enhancement (Figure 1-2). Also, there was gadolinium enhancement in the trigeminal and facial nerves bilaterally. Due to these finding he received 1g of methylprednisolone intravenously for five days together with the IVIG and anisocoria was reversed. The brain MRI which was performed two days after was worse. The demyelinating lesions were even larger in size and more diffuse. When the treatment was concluded, an MR Spectroscopy (MRS) was performed which showed high lactic acid and choline levels and low NAA levels in all the lesions.

A new LP was performed 15 days later which revealed albuminocytological dissociation. CSF was negative for EBV (Epstein-Barr Virus), CMV (Cytomegalovirus), VZV (Varicella-Zoster Virus), HSV1 (Herpes Simplex Virus 1), HSV2 (Herpes Simplex Virus 2), HHV-6 (Human Herpesvirus 6) and enterorivus. A CSF sample was sent for detection of JCV via Real Time PCR which came back negative. He also tested negative for HIV.

The patient was in a stable condition but he could not be weaned from the ventilator so it was decided to undergo five sessions of plasma exchange.

Around a month since he was intubated, he started to show signs of clinical improvement. He began to open his eyes and breathe on his own with gradually less ventilatory support. A third brain MRI was performed which showed considerable size reduction of the demyelinating lesions (Figure 3). They were much less diffuse this time and there was only mild patchy gadolinium enhancement.

He was discharged from the ICU to our neurological clinic with a tracheostomy, fully conscious with quadriplegia. A week later we performed a brain MR Angiography (MRA) which was normal and the fourth brain MRI with unremarkable changes from the last one. We also performed a full panel of serum autoantibodies and plasma protein immunoelectrophoresis which were normal. The patient was discharged to a rehabilitation facility and is undergoing intense physiotherapy. Nowadays he is able to sit on a chair and stand with bilateral support.

## Discussion

Our patient is a 42 years old male with a history of pediatric MS since age 14. The diagnosis of MS was made in 1995 after an episode of left limb numbness. The brain and cervical spine MRI revealed multiple demyelinating lesions, the visual evoked potentials had a prolonged latency bilaterally and oligoclonal bands were present in the CSF. At age 19 he was started on interferon beta-1α. He had relapses with motor and sensory symptoms and at the age of 23 he presented with left sided optic neuritis which was treated successfully with corticosteroids. His neurological status has been somewhat stable since 2018 with a baseline EDSS (Expanded Disability Status Scale) 3.5-4 (left hemiparesis-hemihypesthesia, bilateral pyramidal reflexes and ataxia of gait). In 2020, one year before this episode, he was started on siponimod with a diagnosis of active progressive MS and remained clinically stable with no relapses since.

At first, considering his symptoms of rapidly progressive ascending flaccid quadriparesis with respiratory failure soon after vaccination, together with albuminocytological dissociation in the CSF, a clinical hypothesis of possible acute inflammatory demyelinating polyradiculoneuropathy (AIDP) was made. Hence, the treatment with IVIG was started.

A day after he was put on mechanical ventilation, he developed anisocoria, a sign of increased intracranial pressure. Since his initial brain CT was unremarkable, we performed an urgent brain MRI which revealed multiple large and diffuse demyelinating supra and infratentorial lesions [the radiologist described them as ADEM (Acute disseminated encephalomyelitis)-like] with contrast enhancement. Despite the addition of intravenous methylprednisolone in his treatment, these lesions were increasing rapidly, taking into account that they were much larger in size in the brain MRI performed just two days after. Even though he showed a mild clinical improvement with the reversal of anisocoria, his condition was very serious.

In view of the fact that his clinical data changed, we reconsidered the diagnosis of AIDP and tried to shed some light into the situation taking into account the new developments. We had a patient who at first showed clinical signs of peripheral nervous system disease after vaccination, with the addition of new acute demyelinating lesions in the brain MRI together with clinical signs of central nervous system involvement. Our differential diagnosis consisted of acute MS relapse together with AIDP (a form of CCPD), acute disseminating encephalomyelitis (ADEM), progressive multifocal leukoencephalopathy (PML), CNS tumor and vasculitis of the CNS.

In order to investigate these possibilities a MRS was performed which showed increased choline to creatine ratio and decreased NAA to creatine ratio, together with high levels of lactic acid, a sign of anaerobic metabolism and necrosis. The metabolic profile of the MRS was compatible with PML, so we immediately performed a second LP in order to rule out infectious diseases and test the CSF for JCV with the method of Real Time PCR. The results were negative, so the diagnosis of PML was dismissed. Furthermore, there was albuminocytological dissociation in the CSF and the patient could not be weaned off the ventilator due to paralysis of the respiratory muscles, so with the aim of treating the possible AIDP together with the MS relapse we decided that the patient should undergo plasma exchange. After the sessions the patient started showing signs of improvement for the first time and soon after he could breathe on his own. The patient's family refused brain biopsy in order to further investigate the nature of the lesions.

A third brain MRI was performed a little over a month since the first one so as to evaluate the course of his CNS lesions. There was radiological improvement as well with considerable reduction in the size of the lesions. They were less diffuse, with well-marginated borders and only patchy gadolinium enhancement. The patient returned to our clinic fully conscious, but with quadriplegia. In order to rule out vasculitis of the CNS we tested the serum for autoimmune antibodies which were negative. We also performed a brain MRA which was normal together with a fourth brain MRI which was mostly unchanged from the last one but with mild improvement in the size of the lesions. The patient was discharged to a rehabilitation center where he is to this day with considerable and constant improvement in his motor skills.

This case presented a diagnostic challenge for us because of its complexity, the involvement of both the central and peripheral nervous system with temporal dispersion between the symptoms and the fact that the patient was already diagnosed with a chronic demyelinating CNS disease. Since the patient was in a stable neurologic condition the last year, we evaluated all his symptoms as acute and new. The basic differential diagnosis was MS relapse with AIDP, PLM and ADEM. In the bibliography we did not find any case of ADEM in a patient with MS. We also excluded the diagnosis of ADEM due to the involvement of the peripheral nervous system. The second most probable diagnosis was PML. Even though the MRS findings were compatible with PML, the fact that the CSF PCR for JCV was negative, together with the gadolinium enhancing lesions in the brain MRI and the clinical and radiological improvement of the patient ruled out this diagnosis. The fact that he improved and is still getting better excludes the diagnosis of brain tumor. The possibility of an autoimmune or infectious vasculitis was

ruled out by the negative laboratory investigations along with the normal MRA.

So, we concluded on the rare, yet most possible, clinical scenario of a form of CCPD that presented as an MS relapse concurrently with AIDP. In favor of this hypothesis are the findings and the evolution of the lesions in the brain MRI which are consistent with acute demyelination due to MS relapse and the results of both lumbar punctures that showed high protein with a few cells, a sign of peripheral nervous system involvement, since all alternative diagnosis were excluded. The patient responded to standard treatment given in these conditions with IVIG, corticosteroids and PLEX. The facts that this condition was triggered by vaccination and that he keeps getting better to this day, supports our diagnosis. This is the first reported case of CCPD that was triggered by a vaccine against Sars-Cov-2. Unfortunately, due to faculty restrictions we were not able to perform nerve conduction studies in the acute phase in order to evaluate the peripheral nervous system involvement this way. We also could not test for the anti-neurofascin 155 autoantibodies in the serum which is positive in some forms of CCPD.[4] Overall, we think that the clinical, laboratory and radiological data support our diagnosis.

## Conclusion

CCPD is an emerging neurological entity that is being increasingly recognized and studied nowadays. It is very heterogeneous and quite rare. Due to the COVID-19 pandemic a large amount of the population with central nervous system demyelinating diseases, such as MS, was vaccinated, so we have to be alert to these possible side effects. This case highlights how difficult and complex the diagnosis can be.

## Acknowledgement

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## Conflict of Interest

We have no conflicts of interest to disclose. All authors declare that they have no conflicts of interest.

## References

1. Hidenori Ogata, Dai Matsuse, Ryo Yamasaki, Nobutoshi Kawamura, Takuya Matsushita, Tomomi Yonekawa, Makoto Hirotani, Hiroyuki Murai, Jun-ichi Kira. A nationwide survey of combined central and peripheral demyelination in Japan. Journal of Neurology Neurosurgery and Psychiatry; 2016. p. 29-36. DOI: 10.1136/jnnp-2014-309831
2. R. Cuenca Hernández, R. Gordo Mañasa, J. Gredilla Molinero. Combined central and peripheral demyelination: A case description. Neurologia; 2017. Oct: p. 547- 550. DOI: 10.1016/j.nrl.2015.12.017
3. A Cortese, D Franciotta, E Alfonsi, N Visigalli, E Zardini, L Diamanti, P Prunetti, C Osera, M Gastaldi, G Berzero, A Pichiecchio, G Piccolo, A Lozza, G Piscosquito, E Salsano, M Ceroni, A Moglia, G Bono, D Pareyson, E Marchioni. Combined central and peripheral demyelination: Clinical features, diagnostic findings, and treatment. Journal of Neurological Sciences; 2016. April: p. 182-187. DOI: 10.1016/j.jns.2016.02.022
4. Kira Ji. Anti-neurofascin 155 antibody-positive chronic inflammatory demyelinating polyneuropathy/combined central and peripheral demyelination: Strategies for diagnosis and treatment based on the disease mechanism. Frontiers in Neurology; 2021. June. DOI: 10.3389/fneur.2021.66