



## Case Report

## Acute Disseminated Encephalomyelitis: A rare form of COVID-19's neurotropism

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## ABSTRACT

**Introduction:** the COVID-19 pandemic still accounts for thousands of cases every day. It's neurological involvement has been well documented most likely due to auto-immune mechanisms than the virus itself.

**Case report:** we report the case of a 38 years old women who developed an Acute Disseminated Encephalomyelitis following a COVID-19 infection, with a favorable outcome after immunosuppressive therapy.

**Discussion:** In this chapter, we discuss ADEM's pathogenesis as well as its clinical and radiological features before detailing its relationship with infectious and vaccination episodes. We also discuss how our patient disease evolved.

**Conclusion:** Acute Disseminated Encephalomyelitis is an immune-mediated disorder in which the widespread inflammation of the brain and spinal cord is responsible for a variety of symptoms. The novel COVID-19 virus and its vaccine are both a newly incriminated etiologies of this demyelinating disorder.

### 1. Introduction

The novel SARS-Cov-2 virus responsible of the current COVID-19 pandemic still raises a sustained interest fueling more studies every day.

The neurotropism of the SARS-Cov-2 has been well documented in the literature and a wide range of neurological disorders are being reported every day.

We report the case of a 38 years old women hospitalized in our unit for the management of a monophasic Acute Disseminated Encephalomyelitis (ADEM) following a recent COVID-19 infection.

### 2. Case report

A 38 years old women, without any prior medical history first developed a cough and a fever 10 days prior to her admission for which she received a symptomatic treatment by a local physician without any improvement. 3 days later the patient developed a headache and an

incoherent speech associated to behavioral changes (aggressiveness), adding to that visual and auditory hallucinations as well as a rapidly progressive motor deficit of the lower limbs.

In light of the patient's neurological symptoms and the persistence of her respiratory signs, she was admitted to the ER. Initial physical examination revealed an agitated and confused patient with a GCS of 13/15, afebrile (36.9 °C), with an oxygen saturation of 88% on ambient air and 95% under High Flow Therapy (70% FiO<sub>2</sub> at a 60L/min flow rate). Neurological examination revealed a lower limb flaccid paraparesis, a paresthesia with an umbilicus sensory level, as well as a urinary retention.

Laboratory findings showed an elevated WBC (22 × 10<sup>3</sup>/μL), predominantly neutrophils (93%), a low lymphocytes count (750/μL), a CRP level of 152,61 mg/L, with a hemoglobin at 11 g/dl, serum ferritin level of 1050,32 ng/mL, and an IL-6 level of 70pg/mL. normal electrolyte levels, as well as normal liver and kidney function tests. Arterial blood gas tests revealed a pH of 7.34, a PaCO<sub>2</sub> of 34.4 mmHg and a PaO<sub>2</sub>

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of 68 mmHg, a nasal swap was performed and the SARS-Cov-2 RT-PCR came back positive, CSF study following a lumbar punctation revealed a high WCC ( $17 \text{ cell/mm}^3$ ), positive oligoclonal band test (OCB+) and IgG index (1.2).

Chest CT showed abnormalities consistent with a COVID-19 pneumonia involving overall around 25–50% of the lungs. (Fig. 1). MRI of the brain (Fig. 2) revealed FLAIR and DWI nodular hyperintensities in the juxtacortical frontal and temporal white matter, as well as the subcortical grey matter, specifically the left thalamus and the brainstem. While the spine MRI (Fig. 3) showed discrete T2 hyperintensities with contrast enhancement along the posterior column of the cervical spinal cord, suggestive of myelitis.

Given the clinical, biological and radiological features of the disease, and after concertation, we retained the diagnosis of Acute Disseminated Encephalomyelitis (ADEM).

The patient was treated with Ceftriaxone, Ciprofloxacin and Acyclovir 3 days prior to an intravenous injection of 400mg of Tocilizumab, and high doses of methylprednisolone.

The patient's neurological symptoms slowly regressed within 5 days, and a progressive withdrawal from oxygen was performed simultaneously.

Follow-up laboratory tests showed an improvement of the inflammatory markers.

The patient was discharged within 11 days after admission.

### 3. Discussion

Neurological features related to SARS-Cov-2 have been widely reported [1] and the neurotropism of the SARS-Cov-2 virus much as the other coronaviruses has been firmly established [2,3].

We report the case of a patient who developed an Acute Disseminated Encephalomyelitis (ADEM) following a SARS-Cov-2 infection.

ADEM is an acute inflammatory demyelinating disorder of the central nervous system (CNS) most commonly affecting children [4,5], typically triggered by a viral or bacterial infection (often of the upper respiratory tract) or post vaccination [6]. Relatively rare [5], it's diagnosis often raises the issue of differential diagnosis with other causes of

acquired CNS demyelinating syndromes [4,7], to that end, consensus clinical diagnostical criteria have been proposed [8] easing the process of a positive diagnosis.

ADEM's pathogenesis isn't fully understood, the leading theory suggests an antigenic analogy between myelin antigens and the pathogen responsible for ADEM [9], which explains why cases of ADEM have been reported both in patients with COVID-19 and subjects vaccinated with the AZD1222 COVID-19 vaccine [10,11]. In fact, a literature review by Sriwastava et Al [12] identified a total of 43 cases of COVID-19-related myelitis 10 of which being ADEM cases.

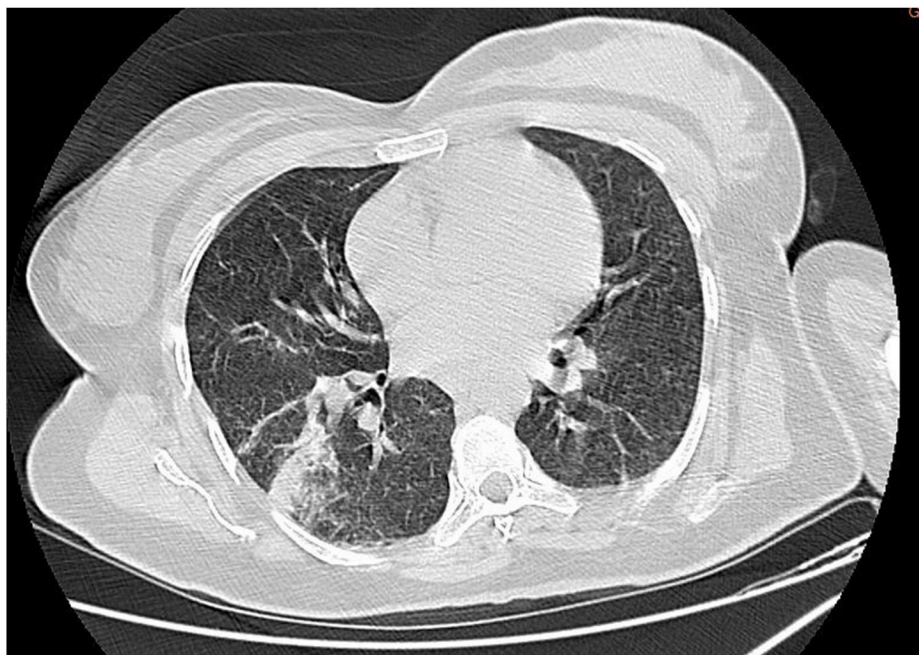
Typically, ADEM is preceded (days and up to few weeks prior), by an infectious episode or a vaccination [13]. Clinically, ADEM usually causes a monophasic demyelinating episode responsible of an acute onset of neurological symptoms depending on which region of SNC is affected, accompanied with encephalopathy, often rapidly deteriorating [13].

ADEM's radiological features may vary from punctate to sizable lesions, affecting the periventricular and subcortical white matter, as well as the grey matter, including the cortex, basal ganglia, and thalamus, also, infratentorial involvement of the brainstem, the cerebellum, and/or the spinal cord is also possible [7,14–16]. Keeping in mind that new lesions and/or enlargement of existing MRI lesions is possible throughout ADEM's evolution [15,17].

The patient was treated with immunosuppressive therapy using an IL-6 inhibitor (Tocilizumab) and high doses of methylprednisolone after an antibiotic coverage. The patient showed clinical and biological improvement within days. She was discharged with minimal residual symptoms (weakness of the lower limb) and put under gradually lower doses of oral prednisolone. No follow-up MRI was performed per patient's choice.

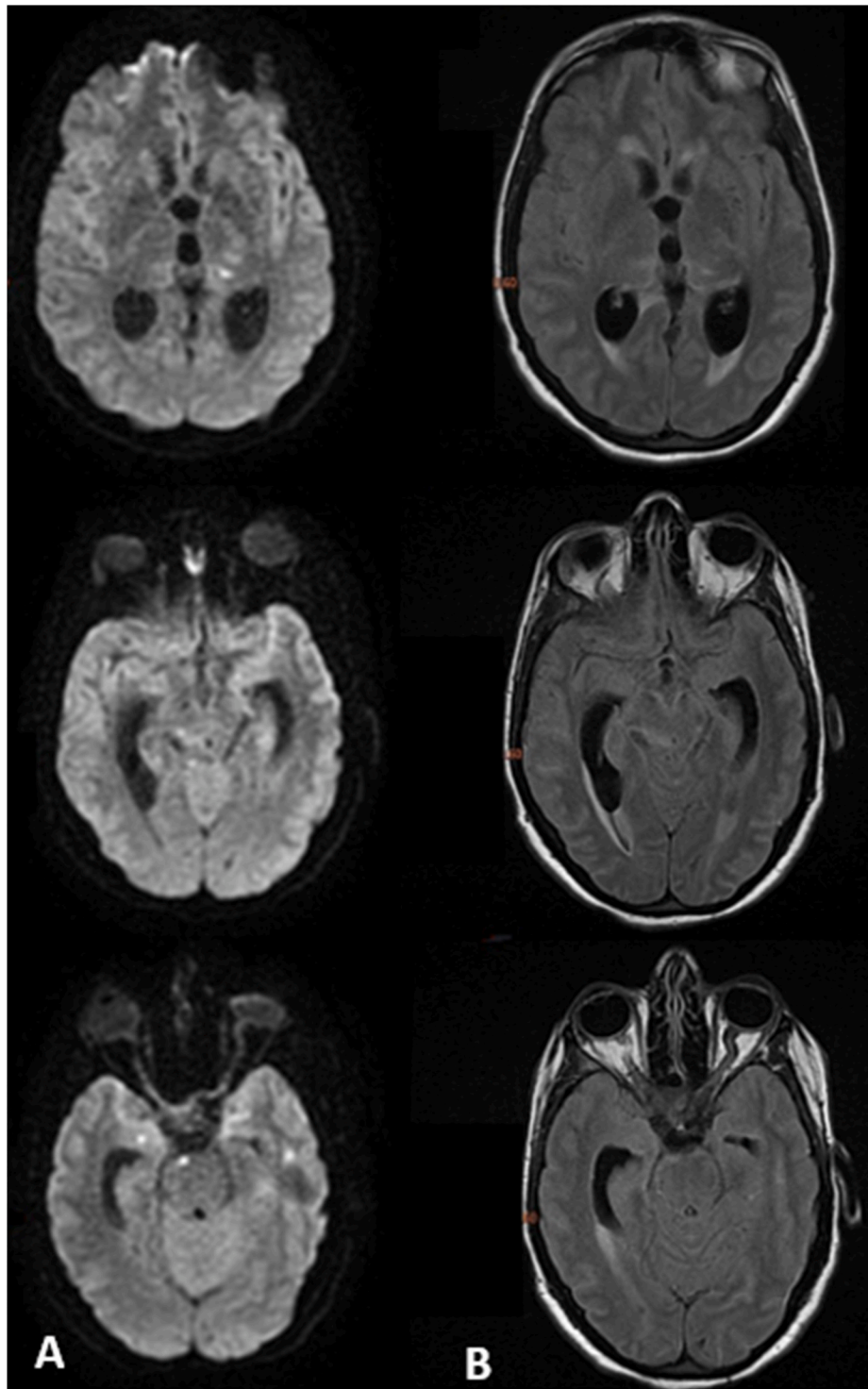
Our case report joins only a dozen cases of COVID-19 induced ADEM [12,18] that have been documented in the literature so far. In fact among the 525443 confirmed cases in Morocco registered to this day [19], to the best of our knowledge no other cases of ADEM have been reported.

Although irrelevant to the subject at hand our case also shines light on a crucial key point in the management of COVID which is the importance of preventing any delay in the diagnosis of COVID-19 thus



**Fig. 1.** Axial lung window showing ground-glass opacities with interlobular septal thickening realizing a crazy paving pattern, as well as right lung peripheral pulmonary consolidation.

SARS-Cov-2 RT-PCR positive, CT findings consistent with COVID-19 pneumonia CO-RADS 6.



**Fig. 2.** Axial Fluid-attenuated inversion recovery (B) and Diffusion-weighted imaging (A) sequence images showing multiple nodular hyperintensities, varying in size, located in the juxtacortical white matter, the left thalamus, and the brainstem.

testing for the virus early-on which wasn't the case here as the patient only received a symptomatic treatment initially.

#### 4. Conclusion

COVID-19 neurotropism is now well established, and more and more cases of COVID-19's neurological involvement are being reported every day.

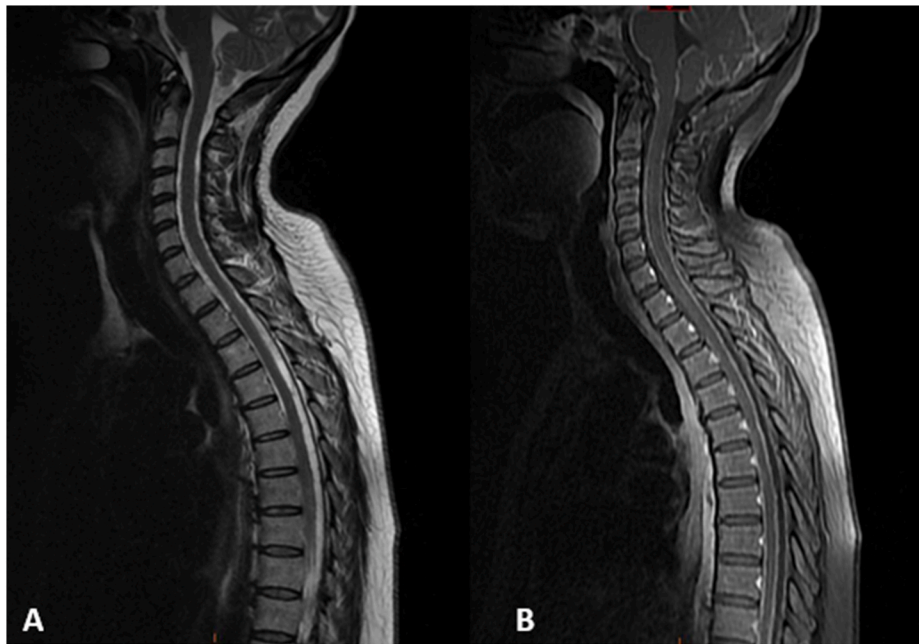
Demyelinating disorders related to COVID-19 infections or vaccines

constitute a rare neurological entity. The most common cases being of Acute Transverse Myelitis (ATM), ADEM cases constitute even a rarer entity.

This work has been reported in line with the SCARE 2020 Guidelines [20].

#### Provenance and peer review

Not commissioned, externally peer-reviewed.



**Fig. 3.** Sagittal T2 (A) and T1 C+ (B) spine MRI showing discrete T2 hyperintensities with contrast enhancement along the posterior column of the cervical spinal cord.

#### Ethical approval

This is a case report, therefore Ethics committee/IRB approval is not required.

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#### Author contribution

SAMIA BERRICHI: Study conception, Data collection; data analysis; writing & editing.

ZAKARIA BOUAYED: Data collection; data analysis; writing & editing.

SARA BERRAJAA: Contributor.

CHOUKRI BAHOUH: Contributor.

AMINE MOHAMMED OULALITE: Contributor.

BADIE DOUQCHI: Contributor.

ISLAM BELLA: Contributor.

HOUSSAM BKIYAR: Supervision and review data validation.

HOUSNI BRAHIM: Supervision and review data validation.

#### Registration of research studies

Name of the registry:

Unique Identifying number or registration ID:

Hyperlink to your specific registration (must be publicly accessible and will be checked):

#### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Guarantor

SAMIA BERRICHI.

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#### Declaration of competing interest

There are no conflicts of interest.

#### References

- [1] J. Helms, S. Kremer, H. Merdji, et al., Neurologic features in severe SARS-CoV-2 infection, *N. Engl. J. Med.* 382 (23) (2020) 2268–2270, <https://doi.org/10.1056/NEJMc2008597>.
- [2] R.R. Reichard, K.B. Kashani, N.A. Boire, E. Constantopoulos, Y. Guo, C. F. Lucchinetti, Neuropathology of COVID-19: a spectrum of vascular and acute disseminated encephalomyelitis (ADEM)-like pathology, *Acta Neuropathol.* 140 (1) (2020) 1–6, <https://doi.org/10.1007/s00401-020-02166-2>.
- [3] E. Song, C. Zhang, B. Israelow, et al., Neuroinvasion of SARS-CoV-2 in human and mouse brain, *J. Exp. Med.* 218 (3) (2021), <https://doi.org/10.1084/jem.20202135>.
- [4] B.M. Greenberg, Transverse myelitis and acute disseminated encephalomyelitis, *Mult. Scler. CNS. Inflamm Disord.* (2014) 144–152, <https://doi.org/10.1002/9781118298633.ch14>. Published online July 22.
- [5] H. Torisu, Chapter 19 - epidemiology of acute disseminated encephalomyelitis, in: H. Yamanouchi, S.L. Moshé (Eds.), *Okumura ABT-AE and E in I and IRD*, Elsevier, 2018, pp. 143–149, <https://doi.org/10.1016/B978-0-323-53088-0.00019-1>.
- [6] M. Filippi, M.A. Rocca, Acute disseminated encephalomyelitis, *White Matter Dis An Updat Neurol* 12 (2020) 109–125, [https://doi.org/10.1007/978-3-030-38621-4\\_5](https://doi.org/10.1007/978-3-030-38621-4_5). Published online February.
- [7] D.M. Wingerchuk, B.G. Weinshenker, Acute disseminated encephalomyelitis, transverse myelitis, and neuromyelitis optica, *Continuum* 19 (4 Multiple Sclerosis) (2013) 944–967, <https://doi.org/10.1212/01.CON.0000433289.38339.a2>.
- [8] L.B. Krupp, B. Banwell, S. Tenembaum, Consensus definitions proposed for pediatric multiple sclerosis and related disorders, *Neurology* 68 (16 suppl 2) (2007), <https://doi.org/10.1212/01.wnl.0000259422.44235.a8>. S7 LP-S12.
- [9] M.F. Cusick, J.E. Libbey, R.S. Fujinami, Molecular mimicry as a mechanism of autoimmune disease, *Clin. Rev. Allergy Immunol.* 42 (1) (2012) 102–111, <https://doi.org/10.1007/s12016-011-8294-7>.
- [10] T. Parsons, S. Banks, C. Bae, J. Gelber, H. Alahmadi, M. Tichauer, COVID-19-associated acute disseminated encephalomyelitis (ADEM), *J. Neurol.* 267 (10) (2020) 2799–2802, <https://doi.org/10.1007/s00415-020-09951-9>.
- [11] L. Cao, L. Ren, Acute disseminated encephalomyelitis after severe acute respiratory syndrome coronavirus 2 vaccination: a case report, *Acta Neurol Belg* 1 (2021) 1–3, <https://doi.org/10.1007/s13760-021-01608-2>. Published online February.
- [12] S. Sriwastava, M. Tandon, S. Podury, et al., COVID-19 and neuroinflammation: a literature review of relevant neuroimaging and CSF markers in central nervous

- system inflammatory disorders from SARS-COV2, *J Neurol* (2021), <https://doi.org/10.1007/s00415-021-10611-9>. Published online.
- [13] F. Noorbakhsh, R.T. Johnson, D. Emery, C. Power, Acute disseminated encephalomyelitis: clinical and pathogenesis features, *Neurol. Clin.* 26 (3) (2008) 759–ix, <https://doi.org/10.1016/j.ncl.2008.03.009>.
- [14] S.E. Marin, D.J.A. Callen, The magnetic resonance imaging appearance of monophasic acute disseminated encephalomyelitis: an update post application of the 2007 consensus criteria, *Neuroimaging Clin N Am* 23 (2) (2013) 245–266, <https://doi.org/10.1016/j.nic.2012.12.005>.
- [15] K.S. Balasubramanya, J.M.E. Kovoov, P.N. Jayakumar, et al., Diffusion-weighted imaging and proton MR spectroscopy in the characterization of acute disseminated encephalomyelitis, *Neuroradiology* 49 (2) (2007) 177–183, <https://doi.org/10.1007/s00234-006-0164-2>.
- [16] D.L.H. Koelman, S. Chahin, S.S. Mar, et al., Acute disseminated encephalomyelitis in 228 patients: a retrospective, multicenter US study, *Neurology* 86 (22) (2016) 2085–2093, <https://doi.org/10.1212/WNL.0000000000002723>.
- [17] Y.Y.M. Wong, E.D. van Pelt, I.A. Ketelslegers, C.E. Catsman-Berrevoets, R. Q. Hintzen, R.F. Neuteboom, Evolution of MRI abnormalities in paediatric acute disseminated encephalomyelitis, *Eur J Paediatr Neurol EJPJN Off J Eur Paediatr Neurol Soc* 21 (2) (2017) 300–304, <https://doi.org/10.1016/j.ejpn.2016.08.014>.
- [18] G.C. Román, F. Gracia, A. Torres, A. Palacios, K. Gracia, D. Harris, Acute transverse myelitis (ATM): Clinical review of 43 patients with COVID-19-associated ATM and 3 post-vaccination ATM serious adverse events with the ChAdOx1 nCoV-19 vaccine (AZD1222), *Front. Immunol.* 12 (2021) 879. <https://www.frontiersin.org/article/10.3389/fimmu.2021.653786>.
- [19] Portail Officiel du Coronavirus au Maroc. [Hhttp://www.covidmaroc.ma/pages/Accueilfr.aspx](http://www.covidmaroc.ma/pages/Accueilfr.aspx).
- [20] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) Guidelines, *Int. J. Surg.* 84 (2020) 226–230, <https://doi.org/10.1016/j.ijssu.2020.10.034>.