Autoimmune encephalitis mediated by postvaccination and infection of SARS-CoV-2 in a patient with a narcolepsy type 1

Rosa Peraita-Adrados, Natalia Bravo-Quelle

Introduction. We present a narcolepsy type 1 patient that develop an autoimmune encephalitis post vaccine and/or a SARS-CoV-2 infection.

Case report. At 23 years old, the patient was referred to the emergency room with difficult speaking, headache and tremor followed by changes in behavior, autonomic dysfunction, right focal motor seizure and lethargy. He has received seven weeks before mRNA-1273 (Moderna) vaccine followed by a SARS-CoV-2 infection four weeks after vaccination (positive antigen test).

Results. The neurological examination was normal (visual fields, cranial nerves, motor, sensory and reflexes). Nasopharyngeal swab polymerase chain reaction (PCR) testing for COVID-19 was negative. Cerebrospinalfluid (CSF) had highly elevated protein and lymphocytic pleocytosis. CSF bacterial and fungal cultures for viral infections were negative. Brain magnetic resonance imaging (MRI) showed no abnormality on the non-enhanced sequences but the diffusion weighted imaging showed restricted diffusion with high signal on the left hemisphere mainly in the cerebral cortex with a gyro morphology, patched distribution with involvement of the temporal and frontal lobes. Chest, abdomen and pelvis computed tomography; pelvic and scrotum ultrasound, showed no malignancy. Onconeural antibodies were negative. The patient was treated with plasmapheresis and corticosteroids with a good clinical outcome and near complete resolution of the MRI abnormalities.

Conclusion. The patient fulfilled the diagnostic criteria for autoimmune encephalitis with subacute onset. COVID-19 infection and vaccination could constitute a risk in a patient with narcolepsy as in this case and, could help to provide better understanding of the implication of immune-mediated processes in the pathophysiology of the diseases.

Key words. Autoimmune encephalitis. Comorbidity. MRI. mRNA-1273 vaccine (Moderna). Narcolepsy type 1. SARS-CoV-2 infection.

Introduction

Narcolepsy type 1 is caused by a deficiency in hypothalamic neurotransmission through a selective loss of hypocretin-producing neurons [1]. This mechanism of neural destruction potentially indicates an autoimmune pathogenesis although the existence of autoantibodies has been reported but their relevance is unclear and recent studies suggest that narcolepsy type 1 is a T-cell-mediated disease [2]. T-cell have been found; they target hypocretin neurons, but also other molecules. The role of environmental factors as a trigger in genetically predisposed subjects has also been suspected. H1N1 influenza and H1N1 vaccinations have also been related to narcolepsy onset [3]. Recently a comorbidity analysis using data from FinnGen, suggests shared effects between narcolepsy type 1 and other autoimmune diseases. Narcolepsy type 1 genetic variants shape autoimmunity and response to environmental triggers, including influenza A infection and immunization with Pandemrix® [4].

We present a narcolepsy type 1 patient that develop an autoimmune encephalitis post vaccine and a SARS-CoV-2 infection.

Case report

A caucasian male patient was diagnosed at the age of 19 with narcolepsy with cataplexy (narcolepsy type 1) after a two year history of irresistible sleep episodes and subsequent sudden muscle weakness caused by laughter. In addition, he presented sleep paralysis and a disturbed nocturnal sleep. The Epworth sleepiness scale score was 15/21 and the body mass index of 22.7 kg/m^2. The video-polysomnography showed fragmented nocturnal sleep,

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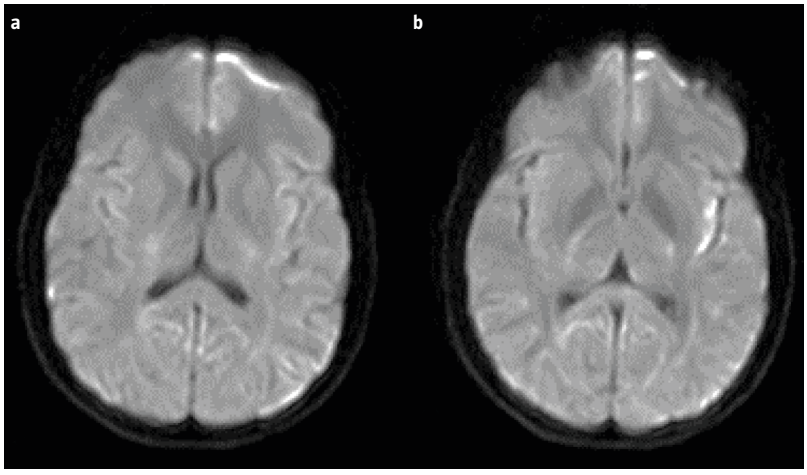
Figure 1. Magnetic resonance imaging of the brain performed as an emergency. The diffusion sequence shows cortical involvement and gyral morphology in the left cerebral hemisphere, with patchy distribution affecting the posteroinferior insular portion, and the superior and medial margin of the superior temporal gyrus; inferior frontal gyrus with involvement of the anterior pole, paramedian region and convexity. Artifactual image due to the patient's poor cooperation in the emergency department.



the multiple sleep latency test revealed a mean sleep latency of 1,3 minute and two sleep onset rapid eye movement periods. The HLA-DQB1*06:02 typing was positive. Physical and neurological examinations were normal.

Past medical history revealed gastroesophageal reflux, cannabis use and periodically oppressive frontal headaches accompanied by photophobia controlled with paracetamol. An acute episode of rhabdomyolysis of the right lower extremity was related to prolonged exercise at 18 years old. He was treated with sodium oxybate 4.5 g /24 hours, venlafaxine 37.5 mg/24 hours, modafinil 100mg/24 hours and esomeprazole 20 mg/24 hours.

At 23-year-old, the patient was referred to the emergency room with 24 hours progressively history of difficulty speaking, headache and tremor followed by changes in behavior, autonomic dysfunction (bradycardia and profuse sweating), one right focal motor seizure and lethargy. He has received seven weeks before the first dose of the Modern (mRNA) vaccine and three weeks later he was diagnosed with SARS-CoV-2 infection with a positive antigen test.

Neurological exam revealed visual fields, cranial nerves, motor, sensory explorations and reflexes normal and symmetrical. A mixed aphasia with motor predominance, behavioral disinhibition and unmotivated laughter were observed. An intentional tremor –appeared a few days before– was related to the increase of the dose of venlafaxine. The hours-long headache subsided during admission. The behavioral disorder consisted of unmotivated laughter and a tendency to disinhibition.

Nasopharyngeal swab polymerase chain reaction testing for COVID-19 was negative.

A standard electroencephalogram showed slow background activity. Cerebrospinal fluid had highly elevated protein and lymphocytic pleocytosis. Cerebrospinal fluid bacterial and fungal cultures for viral infections (including herpes simplex virus 1/2 and varicella-zoster virus) were negative. Onconeuronal antibodies in cerebrospinal fluid and serum were normal.

The patient was treated with six consecutive cycles of plasmapheresis and corticosteroids 1 g/24 hours followed by six weeks of gradually lower doses with a good clinical outcome. Repeat magnetic resonance imaging two months later showed near complete resolution of the imaging abnormalities. The patient was discharged after three weeks with a normal neurological examination including language, behavior and autonomic functions.

Narcolepsy type 1 symptoms remained unmodified in relation to symptoms prior to encephalitis.

The local clinical and research ethics ommittee approved the study. The patient signed an informed consent form.

Image analysis

An urgent brain magnetic resonance imaging showed no abnormality on the non-enhanced sequences, including diffusion, susceptibility weighted imaging T_1, T_2 and weighted FLAIR, but the diffusion weighted imaging showed restricted diffusion with high signal on the left hemisphere mainly in the cerebral cortex with a gyro morphology, patched distribution with involvement of the temporal and frontal lobes (Fig. 1).

Chest, abdomen and pelvis computed tomography, pelvic and scrotum ultrasound, showed no malignancy.

A control brain magnetic resonance imaging (DWI sequence) two months later demonstrated a significant improvement of the abnormalities observed in the left cerebral cortex (Fig. 2).

Discussion

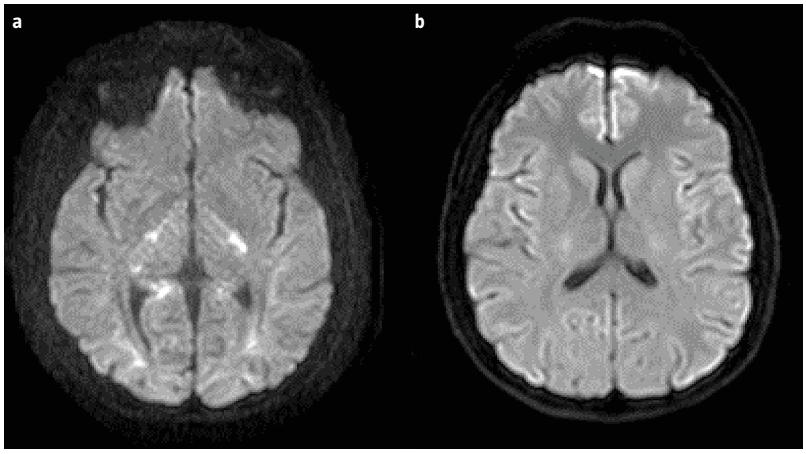
The patient fulfilled the diagnostic criteria for autoimmune encephalitis with subacute onset, focal

central nervous system symptoms, cerebrospinal fluid elevated protein and lymphocytic pleocytosis, and magnetic resonance imaging suggestive findings [5]. The comorbidity of narcolepsy type 1, considered as an autoimmune disease, and autoimmune encephalitis after receiving Moderna vaccine has not been reported to date to the best of our knowledge.

Reversible neurological and MRI changes following SARS-CoV-2 vaccination have been published [6,7] and the absolute risk, assuming a causal effect attributable to vaccination, was low. In addition, a narcolepsy type 1 had begun in a patient after recovery following a COVID-19 infection [8]. In our case an autoimmune encephalitis following vaccination and infection appeared in a patient with a typical narcolepsy type 1 diagnosed five years before. Pfizer and Moderna vaccines, constructed as messenger RNA vaccines, may trigger an autoimmune response, leading to the construction of antibodies against neuronal cell-surface [5,9].

The occurrence of an autoimmune disease can in turn influence the development of others in genetically predisposed individuals, which explains the increased associations observed in a previous long-term study providing a better understanding of the implication of immune-mediated processes in the pathophysiology of the diseases [10].

Figure 2. A control brain magnetic resonance imaging, imaging two months later demonstrated a significant improvement of the abnormalities observed in the left cerebral hemisphere.



Conclusion

We think the important clinical message would be of continuing to monitor adults with narcolepsy type 1, because infection by SARS-CoV-2 and vaccination or both- could constitute a risk of developing one more additional autoimmune disease with age.

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Encefalitis autoinmune tras vacunación e infección por el SARS-COV-2 en un paciente con narcolepsia de tipo 1

Introducción. Presentamos un paciente diagnosticado de narcolepsia de tipo 1 que desarrolló una encefalitis autoinmune posvacunal y/o tras una infección por el SARS-CoV-2.

Caso clínico. Paciente de 23 años que es remitido a urgencias por trastorno del lenguaje y temblor, acompañados de cefalea, trastorno del comportamiento, disfunción autonómica, crisis focal motora derecha y letargo. El paciente había sido vacunado siete semanas antes con la primera dosis de la vacuna Moderna (ARN mensajero) y, cuatro semanas después de la vacunación, presentó una infección por el SARS-CoV-2 con test de antígenos positivo.

Resultados. La exploración neurológica mostró un nivel de conciencia normal y una afasia mixta de predominio motor (campimetría, pares craneales, reflejos y sensibilidad normales). El test de reacción en cadena de la polimerasa para la COVID-19 fue negativo. En el líquido cefalorraquídeo se apreció una linfocitosis y proteínas elevadas. Los cultivos para hongos y bacterias fueron negativos. Los anticuerpos onconeuronales fueron normales. La resonancia magnética cerebral mostró en la secuencia de difusión una restricción con afectación cortical y morfología giral en el hemisferio cerebral izquierdo, y distribución parcheada con afectación de lóbulo frontal y temporal izquierdos. Una tomografía axial computarizada de tórax-abdomen-pelvis fue normal, al igual que las ecografías pélvica y escrotal. Al paciente se le trató con plasmaféresis y corticoides, con buena evolución clínica y resolución casi completa de las anomalías en la neuroimagen.

Conclusión. Se trata de un paciente con narcolepsia de tipo 1 con criterios de encefalitis autoinmune de comienzo subagudo. La infección por el SARS-CoV-2 o la vacunación, o ambas, constituyen un riesgo para desarrollar una o más enfermedades autoinmunes con la edad –como sucede en este caso–, lo que permite comprender la implicación de procesos inmunomediados en la fisiopatología de estas enfermedades.

Palabras clave. Comorbilidad. Encefalitis autoinmune. Infección por el SARS-CoV-2. Narcolepsia de tipo 1. Resonancia magnética cerebral. Vacuna Moderna (ARNm).