Acute Thalamic Ischemic Stroke in an Older Patient Newly Vaccinated with COVID-19 Vaccine Based on Adenoviral Vectors

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ABSTRACT

Introduction. Recent reports have shown several cases of cerebrovascular events after vaccination against COVID-19. The effects have been described mainly in women within the first two weeks of receiving the vaccine. **Clinical Case.** We describe here the first Colombian case of a cerebrovascular event after vaccination against COVID-19 in a 67-year-old woman with a vascular history. Four days after application of the messenger ribonucleic acid (mRNA) vaccine, she exhibited deviation of the labial commissure, ipsilateral ptosis, and limitation of march with lateralization. The event was associated with a subacute ischemic event in the right thalamus in parasagittal situation, changes in chronic ischemic microangiopathy of small vessels, and vascular crossing in the right cerebellar angle, without other alternative causes. **Conclusion.** The development and rapid use of vaccines has allowed the hospitalization and mortality statistics associated with COVID-19 to be reduced, but at the same time, it has generated concern about the potential side effects, generating controversy among the general population, especially in individuals with cardiovascular diseases. In our case, we provided evidence for the discussion of potential cerebrovascular events related to the application of vaccines in older people with a history of cerebrovascular diseases. This was done in order to analyze and control in subsequent studies the modulation of medical history on the likely effects of vaccination. However, despite the unavoidable side effects, the benefits of vaccination are superior.

KEYWORDS: Ischemic stoke, COVID-19, vaccinated

Vaccination against COVID-19 aims to reduce admission to intensive care units (ICUs) and minimize fatal outcomes by generating a protective immune response. Therefore, after the emergency approval of several vaccines, mass vaccination campaigns were initiated. The rapid approval of the COVID-19 vaccines brought relief and reduced morbidity and death. However, several thrombotic events related to the AZD1222 (AstraZeneca) vaccine were reported at the beginning of March 2021, which generated concern in the medical community and the public sector. Although rare, the European Medical Association (EMA) identified 202 thrombotic events among the 5.5 million people who had been inoculated,[1] of which 45 were fatal. The affected individuals were primarily women under the age of 60 years. There was a chronological pattern noted in which the first reaction occurred within a few days after inoculation and was followed, after a healthy interval, by a period of deterioration within 6 to 12 days postvaccination.[2]

The two vaccines most often implicated in associated thrombotic episodes have come from recombinant, nonreplicating chimpanzee adenovirus Type 26 viral platforms developed by the AstraZeneca and Janssen Laboratories.[1,3] In this single case report, we describe a 67-year-old woman with a pre-existing history of vascular disease who experienced a vascular brain event within four days of receiving the BNT162b2 (Pfizer-BioNTech) messenger ribonucleic acid (mRNA) vaccine.

CLINICAL CASE

A 67-year-old female patient with a history of previous cerebrovascular event five years prior, immunoglobulin A (IgA) nephritis, and hypothyroidism presented at the emergency department, referred by a home doctor, due to a 12-hour evolution of a neurological disorder. It consisted of dysarthria, drowsiness, and exacerbated dizziness with walking, and attenuated with rest. She was administered the BNT162b2 vaccine against COVID-19 four days prior. On physical examination, the patient was drowsy, dysarthric with a slight deviation of the labial commissure to the right, ipsilateral ptosis, and walking limitation with lateralization to the left.

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The case was addressed as a possible case of acute cerebrovascular disease. Control paraclinical examinations were requested, which included a simple cranial computed tomography (CT) scan, and the situation was reassessed considering these results.

On the CT images, no hemorrhagic or space-occupying lesions were seen. An ischemic event was found in the right thalamic location, with subacute characteristics. Due to the persistence of symptoms and the limitation of the CT scan to evaluate certain areas of the brain, a posterior fossa disease was considered. For this reason, a brain magnetic resonance imaging (MRI) scan was requested, among other studies, to assess a possible cardioembolic origin for the condition. The echocardiogram reported a normal-sized left ventricle with preserved global and segmental systolic function. The ejection fraction was 72 percent, with good ventricular function. Due to the clinical improvement of the patient, she was discharged 24 hours after admission to finish the studies on an outpatient basis. Pharmacological management was reserved for secondary prevention.

The patient consulted the neurology service 12 days later, where she commented that, in addition to the condition described above, she presented visual field alteration due to binocular diplopia lasting three days and frequent anterograde forgetfulness. In addition, she reported a history of mild stroke five years prior. The current report of magnetic-nuclear resonance (MNR) showed a subacute ischemic event in the right thalamus in parasagittal situation, changes of chronic ischemic microangiopathy of small vessels, and vascular crossing in the right cerebellar-cerebellar angle (Figure 1). On physical examination, slight hypoesthesia of the left paracervical region was observed up to the distal third of the ipsilateral lower limb. There was slight thrust to the left side when asked to close her eyes, with decreased base of support and star gait. Therefore, it was decided in this new consultation to request the pending complementary studies to rule out a cardioembolic cause. MNR of the cervical spine and complementary studies were also requested. A follow-up appointment with results was arranged.

DISCUSSION

Vaccine development for COVID-19 began as soon as the virus genome was published in early January 2020. Initially, four main mechanisms for its development were proposed: deoxyribonucleic acid (DNA)-based vaccines, mRNA-based vaccines, protein-based vaccines, and inactivated viruses. DNA-based vaccines introduce the DNA encoding severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) into cells using viral vectors, inducing cells to produce spike proteins. mRNA vaccines similarly introduce mRNA into cells, usually through a lipid nanoparticle. Protein-based vaccines are based on the spike protein or its fragments. Finally, several vaccines are based on the inactivated SARS-CoV-2 virus.[4] Vaccines based on SARS-CoV-2 mRNA or adenovirus vectorized DNA spike protein are not linked or are weakly associated with immunothrombosis. In these vaccines, RNA/DNA is present only to a limited degree in muscle tissue, so it would be insufficient to drive an immunothrombosis mechanism.[5]

Once the vaccines were developed, even without data from prospective studies evaluating efficacy and side effects, a massive application scheme began. This was done to control the morbidity and mortality rate generated by the virus and the effects on global health and macroeconomic systems. The approval of vaccines by the various national and international health systems, such as the United States (US) Food and Drug Administration (FDA) and the World Health Organization (WHO), took place in the context of a global crisis. It was preferred to prioritize the life of the population, while still considering the potential adverse events of vaccination. In this scenario, some recent studies have reported rare, and sometimes fatal, cases of thrombotic and ischemic events induced by COVID-19 vaccines in patients with or without a vascular and cerebrovascular history.[6–9]

The first case of vaccine thrombosis was reported in Austria at the end of February 2021, in a nurse who died of a splanchnic thrombosis within 48 hours.[10] Since then, there have been more than 100 cases described by the EMA, including in older adults with neurological complications and postvaccination cerebrovascular events.[1] Vaccine-induced immune thrombotic thrombocytopenia can

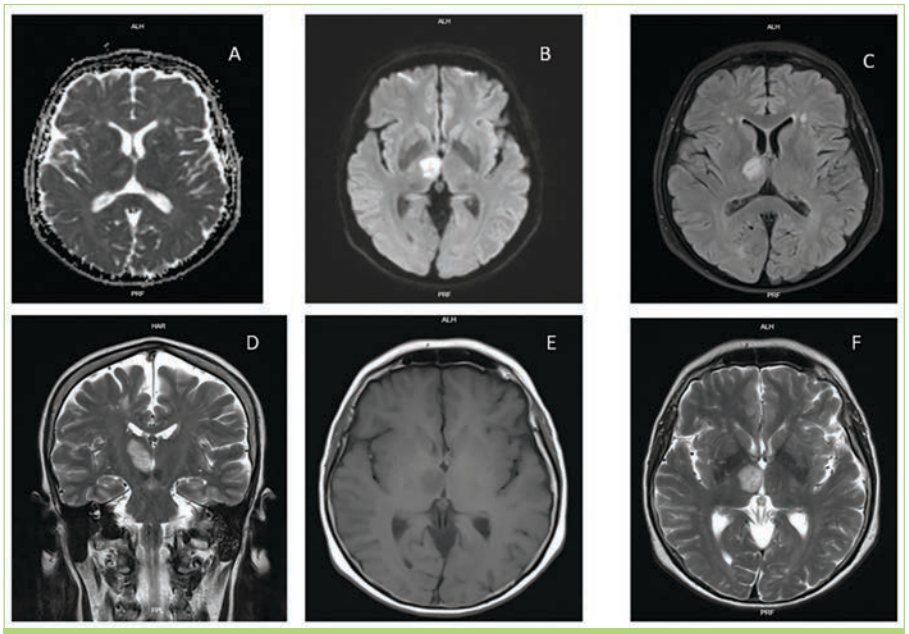

FIGURE 1. Brain magnetic resonance imaging (MRI) sequences
A: apparent diffusion coefficient (ADC)
B: trace diffusion
C: axial fluid-attenuated inversion recovery (FLAIR)
D: coronal FLAIR
E: T1 scan
F: T2 scan
At the level of the right thalamus in parasagittal situation, a hyperintense rounded area is observed in FLAIR and in T2, hypointense in T1, which restricts diffusion, presenting a diameter of 13×11mm without signs of perilesional oedema.

occur in common sites, such as the pulmonary venous beds and lower limbs.[11] However, a hallmark of this type of drug-induced thrombosis is its presentation at unusual sites, such as abdominal veins (splenic, portal, mesenteric), adrenal veins, cerebral veins, and ophthalmic veins. When there is development of arterial thrombosis events at the cerebral level (major cerebrovascular events), the middle cerebral artery can be affected. This often occurs in people with coexisting venous thrombosis.[7,12] Cases of thrombosis characteristically occur between four and 24 days after vaccination for COVID-19 and predominate in young, female patients without a history of thrombosis or thrombophilia.[10,12] In April 2021 in the US, six cases of thrombosis associated with the Janssen COVID-19 vaccine were reported. The characteristics were similar to those described in Europe with the Oxford vaccine. For this reason, on April 13, 2021, the US Centers for Disease Control and Prevention (CDC) and FDA quickly suspended the administration of the Janssen vaccine as a precaution until the risk was clarified.[13]

In our clinical case, the patient had a high cardiovascular risk and a history of previous cerebrovascular event five years prior. She was in the context of a new mild ischemic event that can develop five days after administration of the COVID-19 vaccine. From the semiological point of view, she was a patient who initially presented a picture of dysarthria, vertigo, and altered state of consciousness due to drowsiness, which were self-limited. The sequelae state consisted of hypoesthesia in the cervical region and left lower limb, gait alteration, and lateropulsion.

We considered that some patients vaccinated against COVID-19 with a vascular or cerebrovascular history might present with adverse events of thromboembolic origin. In our case, we suspected a cerebrovascular event of ischemic origin at the thalamic level, secondary to a first dose of the vaccine. The presumption is considered reasonable, even lacking the results of other studies that can be used to rule out possible alternative etiologies. In this way, it is considered a possible complication after the administration of immunization treatments. In clinical trials where the safety of mRNA vaccines was analyzed, the most serious adverse events of the nervous system, such as stroke, were related to significant medical history or an increased risk of developing stroke.[1,3] In other reported thrombotic events, the estimated incidence of this rare adverse event was around one in 100,000 people under the age of 60 years.[3] With the available evidence, it has not been possible to identify specific risk factors, nor has it been possible to demonstrate a causal link between the vaccine and stroke. For this reason, this situation warrants a more detailed analysis.

We believe that it is important to identify the risk of stroke recurrence in patients with a history of cerebrovascular disease who are to be inoculated against COVID-19. It is also important to recognize the signs of stroke after vaccination against COVID-19.[14] However, it is important to clarify that the risk of thromboembolic events associated with vaccination does not appear to be greater than the costs of the virus on people's health.

CONCLUSION

Vaccination has been shown to be the most effective way to immunize populations and provide protection against a wide range of diseases.[14] According to the University of Oxford, 53 percent of the world's population has received at least one dose of a COVID-19 vaccine.[15] In New York, the first study to quantify the population impact of the vaccination campaign was conducted.[16] Without vaccination, 893,539 infections, 90,836 hospitalizations, and 17,522 deaths were estimated between December 14, 2020, and July 15, 2021. Vaccination prevented 290,467 new cases, 48,076 hospitalizations, and 8,508 deaths.[16] Therefore, it is necessary to continue with the immunization of the population, as the most efficient option to contain the viral spread.

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