Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

ción, la respuesta precoz al tratamiento esteroideo y la estabilidad plaquetar previa nos hacen creer en una relación causal. Según el algoritmo descrito por Naranjo et al., existe una relación probable de causalidad[5]. Por lo tanto, en los pacientes con PTI preexistente, sería prudente obtener un recuento de plaquetas antes y después de la vacunación para evitar eventos hemorrágicos fatales.

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Case report: Pituitary apoplexy after COVID-19 vaccination

Caso clínico: Apoplejía hipofisaria tras vacunación frente a la COVID-19

Dear Editor,

The discovery and widespread use of different SARS-CoV-2 vaccines has made it possible to combat the COVID-19 disease in an effective and safe way. Among the adverse effects that have been observed during the implementation of the vaccination campaign is the appearance of thrombosis and bleedings associated with a syndrome known as Vaccine-Induced Thrombotic Thrombocytopenia (VITT), related only to viral vector vaccines. VITT is more frequent in young women and appears to be a phenomenon similar to heparin-induced thrombocytopenia and have an autoimmune source.[1,2]

Pituitary apoplexy, described as an infarction or hemorrhage of the pituitary gland, is a rare entity generally associated with pituitary adenomas and constitutes, in most cases, an endocrine emergency that may require decompressive surgery and specific treatment. Currently, in the context of SARS-CoV-2 infection, rare and specific cases of pituitary apoplexy have been described both associated and not associated with pituitary adenomas. However, to date, there have been no reported cases of vaccine-associated pituitary apoplexy.[3]

We present the case of a 37-year-old woman who, 5 days after vaccination with ChAdOx1-S, developed a high-intensity frontal headache with partial relief with habitual analgesia. A complete physical examination was performed, which did not demonstrate the presence of neurological focality, cranial nerve involvement, or campimetric involvement. Despite this, due to the intensity of the headache, a brain MRI was performed (Fig. 1). It showed signs concordant with adenohypophysis hemorrhagic bleeding in association with a possible 10 mm intraglandular adenoma without chiasmatic involvement. The patient did not present syndromic signs consistent with Cushing's disease or acromegaly, nor did she present symptoms or signs of pituitary hormonal deficits prior to the event. A campimetry and a pituitary hormonal analysis were performed, both yielding normal results. Symptoms were resolved within 2–3 weeks with no complementary treatment and without associated hormonal deficits in that period.

To our knowledge, this is the first case of pituitary hemorrhage described after SARS-CoV-2 vaccination. The possible presence of a previous undiagnosed adenoma could have influenced the appearance of a hemorrhagic phenomenon at this level. Unfortunately, a hemogram was not performed at the time of the event, so we could not confirm the presence of thrombocytopenia that would reinforce the association between pituitary bleeding and vaccination in

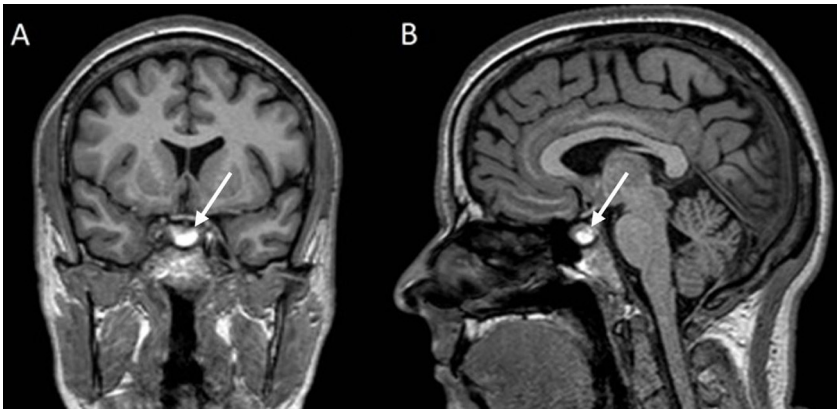

Fig. 1. Coronal (A) and sagittal (B) slices of the skull MRI. Adenohypophysis hemorrhagic bleeding in association with a possible 10 mm intraglandular adenoma without chiasmatic involvement.

the context of VITT. At the time of our evaluation, two months later, the patient had a normal blood count without observing this abnormality. In this context, we cannot affirm the correlation between both phenomena, although the temporal evolution of the clinical picture and the radiological findings in which evidence of acute bleeding was denoted does make us consider this case as probably associated with vaccination.[4] Generally, the evaluation of headache after SARS-CoV-2 vaccination in the context of screening for cerebral sinus thrombosis is carried out through a cranial CT scan. In this type of examination, the pituitary area is difficult to evaluate, especially when small bleeds occur without hormonal and/or campimetric repercussions, such as in the case presented. Therefore, these types of entities may be underdiagnosed.

In conclusion, we suggest that this case should be taken into account for the evaluation of postvaccinal headache and the possibility of VITT, evaluating campimetric compromise and the possibility of hormonal deficits, both in patients with known pituitary adenomas and in cases without prior diagnosis. Despite not having occurred in our case, the development of an undiagnosed pituitary hormonal deficiency can lead to a torpid evolution.

Patient consent

Informed consent has been obtained from the patient for publication of the case report and accompanying images.

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Conflict of interest

The authors declare no conflict of interests.

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Cardiotoxicidad tardía por antraciclinas y alteración genética del metabolismo del hierro

Late anthracycline cardiotoxicity and genetic alteration of iron metabolism

Sr. Editor:

La leucemia linfoblástica aguda es la neoplasia más común en población infantil, siendo las antraciclinas el tratamiento que ha demostrado un mayor aumento en la supervivencia y tasas de curación. La cardiotoxicidad secundaria a estos fármacos, especialmente a largo plazo, ha ido adquiriendo importancia en los últimos años, debido al aumento de casos detectados como consecuencia de la mejoría del pronóstico y el desarrollo de alguna estrategia de prevención[1].

Presentamos el caso de una paciente de 42 años, fumadora, sin otros factores de riesgo cardiovascular ni tratamiento farmacológico. Fue diagnosticada de leucemia linfoblástica aguda T de mal pronóstico a los 2 años de edad, tratada con un esquema de quimioterapia que incluyó daunorrubicina a dosis acumulada de 440 mg/m^2, consiguiendo remisión completa. La función ventricular determinada por ecografía un año tras finalizar el tratamiento fue normal. Consultó por disnea de esfuerzo progresiva de 3 meses evolución, hasta ser de mínimos esfuerzos con ortopnea, disnea paroxística nocturna y edemas hasta rodilla. Sin dolor torácico. En la exploración se objetivaba taquicardia con tercer ruido, plétora yugular y hepatomegalia, y en la analítica destacaba un NT-ProBNP 17161 pg/ml además de una ferritina elevada (848 ng/ml) de años de evolución. El electrocardiograma mostraba ritmo sinusal con QRS estrecho y el ecocardiograma un ventrículo izquierdo no dilatado con hipoquinesia global y fracción de eyección del 20%. Se realizó una resonancia magnética nuclear cardíaca que confirmó esta disfunción grave del ventrículo izquierdo sin realce tardío de gadolinio, y una tomografía axial computarizada coronaria que descartó cardiopatía isquémica.

La paciente experimentó mejoría progresiva tras iniciar tratamiento con diuréticos, inhibidores de la enzima convertidora de la angiotensina, betabloqueadores y antialdosterónicos, llegando a recuperar la función ventricular varios meses después, aunque manteniendo cierta limitación al esfuerzo. El estudio del gen *HFE* identificó la mutación H63D en heterocigosis, y la paciente fue diagnosticada de miocardiopatía hipoquinética no dilatada en posible relación con toxicidad tardía por antraciclinas.

El mecanismo más aceptado de toxicidad es la generación de radicales libres de oxígeno durante el metabolismo intracelular del fármaco. Produce un daño en el ácido desoxirribonucleico y disfunción mitocondrial[2], que lleva a la apoptosis y fibrosis, siendo el miocardio un tejido especialmente sensible. Esto conduce a un fallo cardíaco que puede manifestarse desde el momento del tratamiento (toxicidad aguda) hasta varias décadas después (toxicidad tardía). El factor de riesgo más importante es la dosis acumulada total, siendo especialmente susceptibles aquellos pacientes que reciben más de 300 mg/m^2. Otros factores son: edad menor de 5 años, irradiación torácica concomitante, elevado riesgo cardiovascular, así como el tiempo transcurrido desde el tratamiento, con una incidencia del 7,5% a los 30 años[3]. Se cree que la lesión de los miocitos se produce en el momento de la exposición, seguido de un deterioro funcional progresivo que lo hace depender de mecanismos de compensación hasta llevar al fallo cardíaco clínico.

Es conocida la participación del hierro, como cofactor, en la generación de radicales libres de oxígeno por antraciclinas[4]. En este contexto, se ha demostrado que la existencia de una alteración