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Clinical Research

Pituitary apoplexy following adenoviral vector-based COVID-19 vaccination

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ABSTRACT

Pituitary apoplexy (PA) may complicate the course of coronavirus disease 2019 (COVID-19), posing a potential threat to life. Among vaccines designed to prevent COVID-19, there are those adenoviral vector-based, such as Vaxzevria® (formerly COVID-19 Vaccine AstraZeneca). The product insert states that it can cause very rare coagulation disorders, in particular thrombosis with thrombocytopenia syndrome in some cases accompanied by bleeding, cerebrovascular venous or sinus thrombosis, and thrombocytopenia, including immune thrombocytopenia, also associated with bleeding. Here, we report the onset of PA after Vaxzevria® in a 28-year-old healthy Caucasian female, who experienced long-lasting tension-type headache, hyperprolactinemia and menstrual changes, without thrombocytopenia or thrombosis.
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Pituitary apoplexy (PA) has been recently described as a possible complication of coronavirus disease 2019 (COVID-19).[1,2] PA represents a potentially life-threatening condition due to impaired blood supply of the pituitary gland from either hemorrhage or infarction.[1] Both bleeding and thrombotic events have been reported following Vaxzevria® (formerly COVID-19 Vaccine AstraZeneca), even in unusual sites such as cerebral venous sinuses, with or without thrombocytopenia.[3] A 28-year-old healthy Caucasian female suffered of 38 °C fever for 24 h and tension-type headache for a full month after the first dose of Vaxzevria®. The post-vaccinal laboratory tests did not reveal thrombocythemia (platelets: 239.00 x10^3/μL), neither thrombosis (D-dimer: < 270.00 ηg/mL). At a time distance of two months from the first inoculation, the patient underwent the second dose, and headache came back even more intense without fever or visual changes. Because of the persistence of headache accompanied by amenorrhea and hyperprolactinemia (Table 1), most likely from prolactin-inhibiting factor impairment, the patient was submitted to magnetic resonance imaging (MRI) without contrast 69 days after the second dose: a signal alteration possibly related to a hemorrhagic event was detected in the right half of the sella turcica (Fig. 1A). The gadolinium contrast-enhanced MRI performed 35 days later confirmed the PA presence (Fig. 1B); the control MRI at a time distance of 101 days showed an improving picture, in conjunction with menstrual recovery. The present case is quite similar to that reported by Piñar-Gutiérrez et al.[4] and call attention to the possible PA onset in course of COVID-19 and post-COVID-19 vaccination by means of viral vector-based vaccines. In women of childbearing age, PA can lead to menstrual changes, a side effect not to be overlooked given that more than 36,000 reports of menstrual changes or unexpected vaginal bleeding following COVID-19 vaccination have so far reached the United Kingdom "Yellow Card" surveillance system alone.[5]

Abbreviations: COVID-19, Coronavirus disease 2019; MRI, Magnetic resonance imaging; PA, Pituitary apoplexy; VITT, Vaccine-induced immune thrombotic thrombocytopenia.

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Table 1
Post-vaccinal laboratory tests showing only isolated hyperprolactinemia (basal concentration: 47.98 ηg/mL), with no further alteration of pituitary values, neither sign of vaccine-induced immune thrombotic thrombocytopenia (VITT).[6]

LAB TESTS	PATIENT RESULTS	NORMAL RANGES
LEUKOCYTES	5.59 × 10^3/μL	4.00–10.00 × 10^3/μL
ERYTHROCYTES	4.58 × 10^6/μL	4.00–5.50 × 10^6/μL
ERYTHROCYTES SEDIMENTATION RATE	9.00 mm/h	<15.00 mm/h
HEMOGLOBIN	13.00 g/dL	12.00–16.00 g/dL
HEMATOCRIT	40.50 %	36.00–48.00 %
PLATELETS	239.00 × 10^3/μL	150.00–450.00 × 10^3/μL
D-DIMER	<270.00 ηg/mL	<500.00 ηg/mL
ALANINE TRANSAMINASE	19.00 U/L	≤55.00 U/L
ASPARTATE TRANSAMINASE	20.00 U/L	≤34.00 U/L
CREATININE	0.66 mg/dL	0.57–1.11 mg/dL
GLUCOSE	88.00 mg/dL	70.00–100.00 mg/dL
HUMAN GROWTH HORMONE	1.10 ηg/mL	0.20–7.00 ηg/mL
THYROID STIMULATING HORMONE	1.65 μU/mL	0.35–4.50 μU/mL
FOLLICLE STIMULATING HORMONE	5.10 mU/mL	<25.00 mU/mL
LUTEINIZING HORMONE	4.00 mU/mL	<15.00 mU/mL
PROLACTIN	47.98 ηg/mL	2.70–26.70 ηg/mL

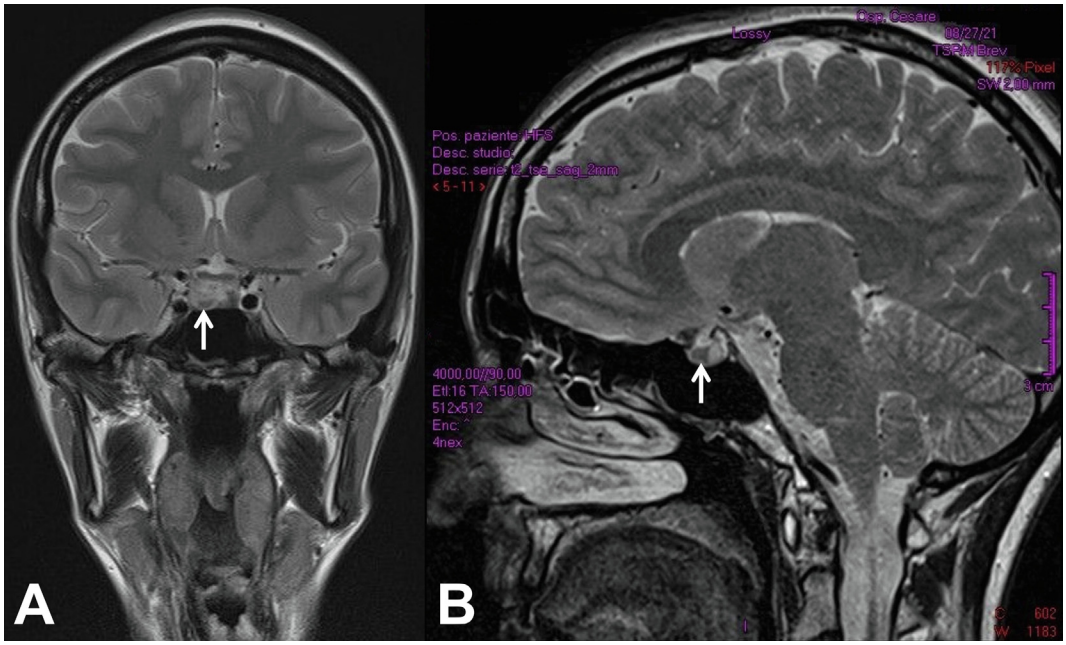

Fig. 1. MRI images proving PA and excluding lesions in the cortex, cerebellum, brain stem, pituitary stalk, and posterior lobe. A) Unenhanced T2-weighted coronal section performed 69 days after the second vaccination dose: in the right part of the anterior hypophysis lobe, an oval area about 10x5 mm in size is well noticeable (arrow). B) Enhanced T2-weighted sagittal section performed 35 days later: the same area is not contrast-enhanced (arrow) and corresponds to a small convexity in the superior rim of the pituitary capsule, while the hypophysis stalk and posterior lobe show an early and marked contrast enhancement.

Statement of ethics

The research was approved by the ethics committee of University of Modena and Reggio Emilia. This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki of 1975, as revised in 2008.

Informed consent

Informed consent was obtained from the patient for publication of the anonymized details concerning with her medical case and any accompanying images.

Data availability statement

All relevant data generated or analyzed during this research were included in the article; further enquiries can be directed to the corresponding author upon reasonable request.

Author contributions

LR: study concept and design, drafting of the manuscript, and study supervision. AM: interpretation of imaging data, and critical revision. All authors approved the final version of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Martinez-Perez R, Kortz MW, Carroll BW, et al. Coronavirus disease 2019 and pituitary apoplexy: a single-center case series and review of the literature. *World Neurosurg*. 2021;152:e678–e687.

2. Frara S, Allora A, Castellino L, di Filippo L, Loli P, Giustina A. COVID-19 and the pituitary. *Pituitary*. 2021;24(3):465–481.
3. European Medicines Agency. Vaxzevria (previously COVID-19 Vaccine AstraZeneca): EPAR – product information. Annex I – summary of product characteristics. Available online at: https://www.ema.europa.eu/en/documents/product-information/vaxzevria-previously-covid-19-vaccine-astrazeneca-epar-product-information_en.pdf [last accessed April 6, 2022].
4. Piñar-Gutiérrez A, Remón-Ruiz P, Soto-Moreno A. Case report: pituitary apoplexy after COVID-19 vaccination. *Med Clin (Barc)*. 2021. https://doi.org/10.1016/j.medcli.2021.09.028.
5. Male V. Menstruation and Covid-19 vaccination. *BMJ*. 2022;376 o142.
6. Greinacher A, Langer F, Makris M, et al. Vaccine-induced immune thrombotic thrombocytopenia (VITT): update on diagnosis and management considering different resources. *J Thromb Haemost*. 2022;20(1):149–156.