PITUITARY APOPLEXY AND COVID-19 INFECTION/VACCINATION

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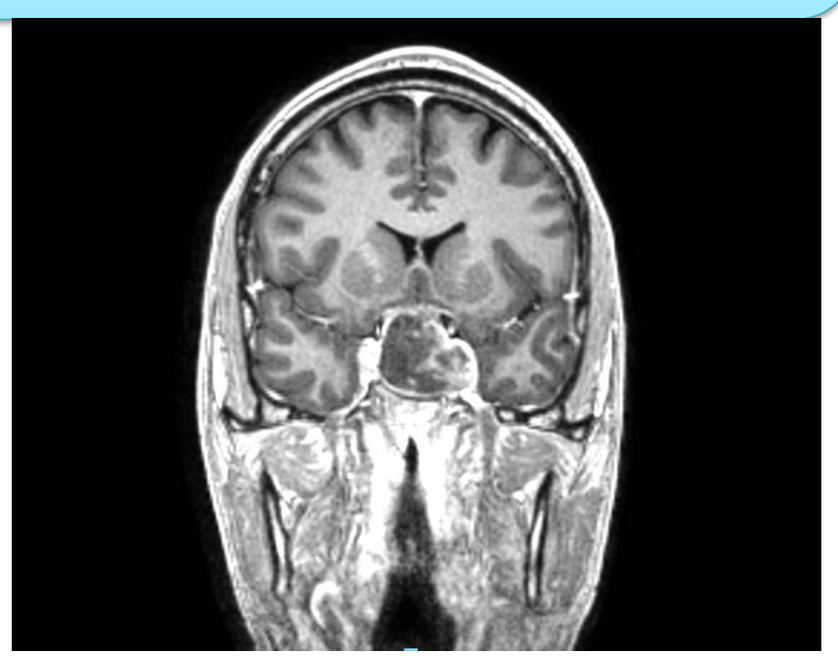
CASE REPORT

A 50-year-old man was admitted to our hospital for vomit, nausea, diplopia and headache resistant to analgesic drugs. Symptoms started the day after his third COVID-19 mRNA vaccine (Moderna) whereas SARS-CoV-2 nasal swab was negative. Pituitary MRI showed recent bleeding in macroadenoma (pituitary apoplexy). A stress dose dexamethasone was started due to the risk of adrenal insufficiency and to reduce oedema

1st day	2nd day	4th day	5th day	6th day
SARS-CoV-2 Vaccine (Moderna)	Nausea, Vomit, Severe Headache, Diplopia, Fever, Hypothension SARS-CoV-2 nasal swab negative	Persistence of headache (Pain VAS 8/10), diplopia and fever	Persistence of headache (Pain VAS 8/10) and diplopia; Increased fever (38.5 °C)	Persistence of headache (Pain VAS 6/10)



Biochemistry showed secondary hypogonadism; inflammatory markers were elevated as well as white blood cells count, fibrinogen and D-dimer; platelets were within the low normal reference range

Pituitary tumour transsphenoidal resection was performed and pathology report was consistent with pituitary adenoma with focal haemorrhage and necrosis; we found immunohistochemical evidence for **SARS-CoV-2 nearby pituitary vessels, in the presence of an evident lymphocyte infiltrate**

BIOCHEMISTRY	
TSH 0.41 µIU/mL (n.v. 0.25-4.5)	PRL 5.1 ng/mL (nv 5-20 ng/ml)
fT4 7.1 pg/mL (n.v. 5.5-12)	VES: 19 mm (nv 0-18 mm)
FSH 1.9 mIU/mL (n.v. 1.2- 8.6)	CRP: 1.93 mg/dl (n.v. < 0.5)
LH 0.6 mIU/mL (n.v. 1.3- 8)	D-dimer: 0.59 mg/l (n.v. < 0.5)
Testosterone 0.29 ng/ml (n.v. 2.35-3.5)	

DISCUSSION

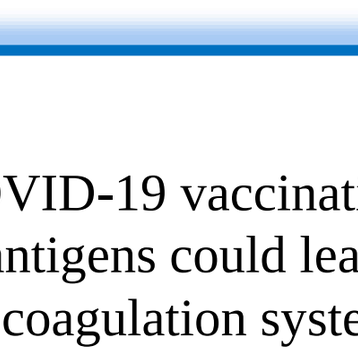
✓ There are few reports of pituitary apoplexy after COVID-19 vaccination and infection.

✓ The cross-reaction between SARS-CoV-2 proteins and tissue antigens could lead to pituitary autoimmunity

✓ COVID-19-associated coagulopathy includes activation of the coagulation system, inhibition of fibrinolysis and release of prothrombotic mediators, causing microemboli that might lead to infarction of the pituitary adenoma

✓ Pituitary stimulation and cytokine storm occurring in the infectious state may lead to acute increased pituitary blood demand precipitating apoplexy

✓ The development of anti-PF4/heparin antibodies after vaccine administration may occur, determining complement activation and induction of both coagulopathy, thrombocytopenia and bleeding



✓ Ours is the first case of SARS-CoV-2 evidence in pituitary tissue, suggesting that, possibly, endothelial infection of pituitary vessels might be present before vaccination, supporting the hypothesis that the patient could have experienced an asymptomatic SARS-CoV-2 infection that persisted at CNS level, which could be implicated in the apoplexy onset. Our case underlines that SARS-CoV-2 can associate with apoplexy by penetrating into CNS, even in cases of negative nasal swab.

✓ Patients with underlying diagnosed or undiagnosed pituitary tumours may be exposed to COVID-19 and may be at increased risk of pituitary apoplexy, therefore clinicians should be conscious of this risk, investigating pituitary hormones.