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INTRODUCTION

Pituitary apoplexy is an uncommon endocrine emergency due to infarction and/or hemorrhage of pituitary gland while hypophysitis is also an extremely rare inflammation of pituitary gland. We report a case of apoplexy with hypophysitis possibly related to *ChAdOx1 nCoV-19 (AZD1222)*, AZ vaccination.

CASE

A healthy 24-year-old female with chronic unilateral headache presented with an acute severe left sided throbbing, retro-orbital headache, and associated with nausea. There were no visual and neurological disturbances. She received her second dose of AZ 7 days prior. CT brain was done to rule out post-vaccination central venous thrombosis and revealed a well defined lobulated sellar mass with compression to left cavernous sinus (**Figure 1**). This was followed by a contrasted MRI showing pituitary apoplexy with mass effect to the optic chiasm (**Figure 2**). She was initially treated for pituitary apoplexy and acromegaly with hydrocortisone and ocreotide. Her Pituitary Apoplexy Score = 0 (PAS<4 for conservative treatment). However, acromegaly was later ruled out after a normal Overnight Dexamethasone Suppression Test. The alternative diagnosis of hypophysitis was made. Throughout this time, she had multiple visits to ED for throbbing headache. Repeated MRI four weeks later showed reduction in the size of the mass by 50% (**Figure 3**). The combination of persistent headache and recent MRI findings makes hypophysitis more likely. Hydrocortisone was changed to high dose of dexamethasone which successfully controlled the headache. Further plan is to repeat the MRI in 3-months to confirm the diagnosis of hypophysitis after completed course of dexamethasone.

Investigations results:

Hormone	Result	Normal value
FT4	19.4	12 – 22 pmol/L
TSH	1.090	0.27 – 4.2 mIU/L
LH	12.9	Follicular: 3.5-12.6 IU/L
FSH	7.3	Follicular: 2.4-12.6 IU/L
Estradiol	427.9	Follicular: 98.1-571 pmol/L
Morning cortisol	505	101-537.7 nmol/L
prolactin	119.5	<550 mIU/L
Serum IGF-1	417	98.7 - 289 ng/mL
Overnight Dexamethasone Suppression Test	48.4	<50 nmol/L
Synacthen test	normal	

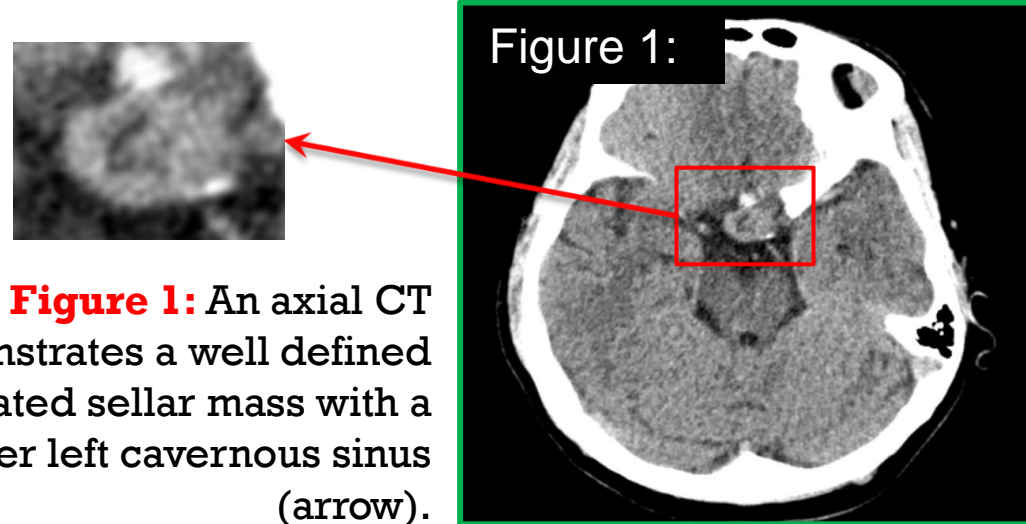


Figure 1: An axial CT demonstrates a well defined lobulated sellar mass with a fullness over left cavernous sinus (arrow).

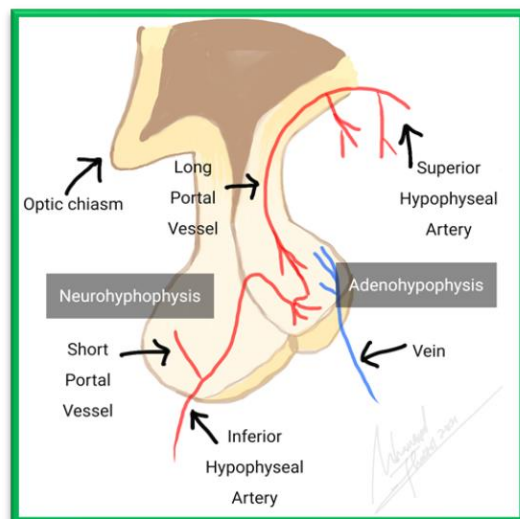


Figure 4: An illustration shows rich and complex networks of vessels supply the pituitary gland.

DISCUSSION

Apoplexy has a 5.4 greater chance of bleeding in pituitary adenoma than other brain tumors due to its complex vascular structure (**Figure 4**). Due to adenoma, the blood vessels are more friable and easily bleed. Robust immune response after vaccination could lead to pituitary adenoma and causing apoplexy. Apoplexy is typically diagnosed with MRI. Hypophysitis also requires radiological diagnosis which is 92% sensitive and 99% specific.

This patient presents as diagnostic conundrum for endocrinologist. Her radiological findings are more in keeping with apoplexy, but her blood parameters and symptoms regression with glucocorticoid point towards hypophysitis. The definitive diagnosis of hypophysitis requires histo-pathological examination, which is not a palatable option. Having said that, there has been a case report on hypophysitis presenting as apoplexy.

The UK Covid-19 astra-zeneca vaccine analysis print identified two possible cases of apoplexy. Our patient had severe headache after her second dose of AZ. Although the apoplexy and hypophysitis could still be coincidental, this case illustrates a possible connection with AZ vaccine.

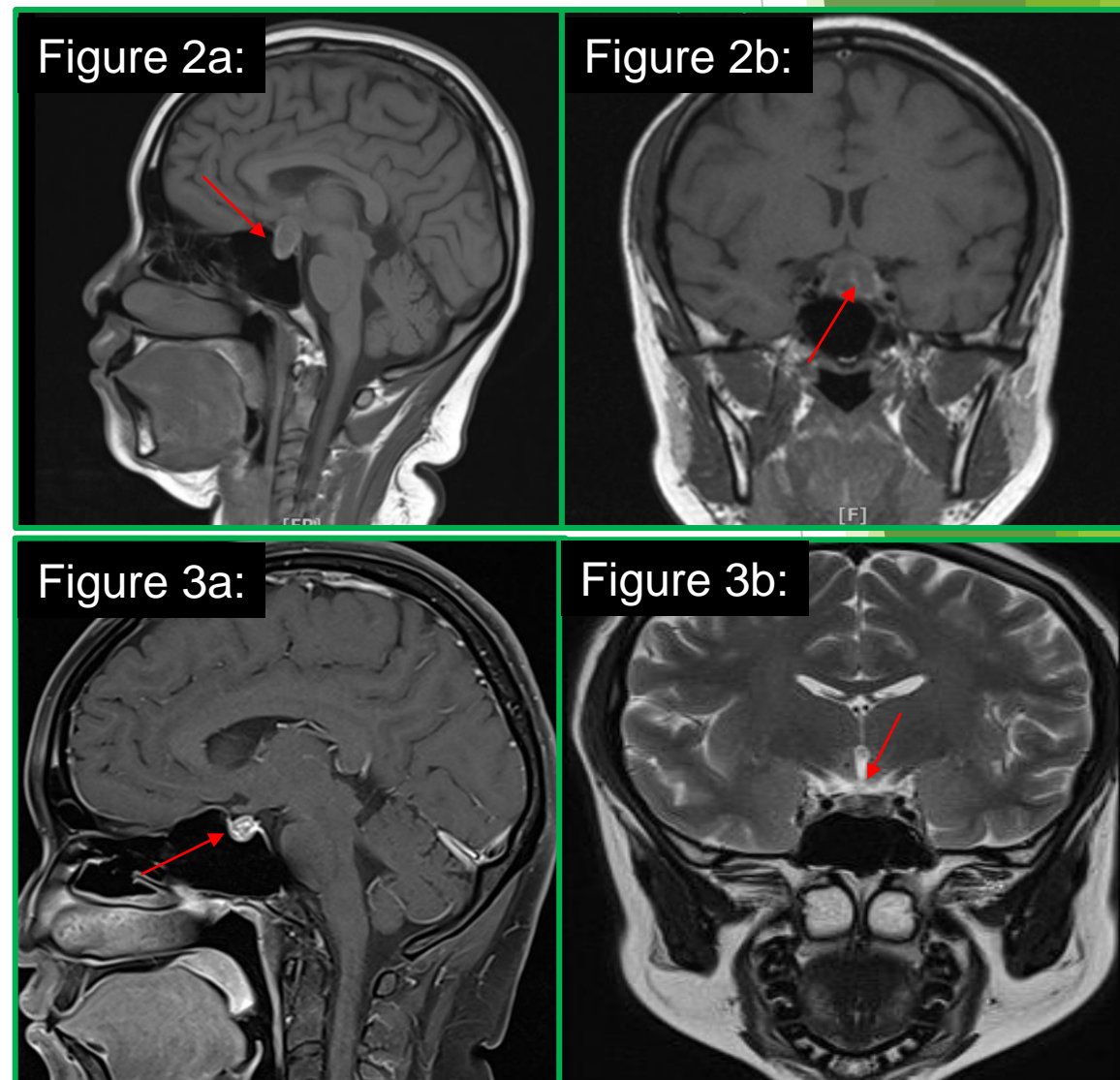


Figure 2a: Sagittal MRI demonstrates an enlarged pituitary gland with compression to pituitary stalk (arrow).

Figure 2b: Coronal MRI shows enlarged pituitary with apoplexy, and mass effect to optic chiasm measuring 1.1x1.8x1.9cm (APxWxCC), hypointense centrally with high signal in the periphery (arrow).

Figure 3a: Sagittal repeated MRI demonstrates a smaller enlarged pituitary gland with persistent compression to stalk (arrow).

Figure 3b: Coronal repeated MRI shows resolved mass effect to the optic chiasm (arrow).

CONCLUSION

At present there is no concrete evidence to link apoplexy and hypophysitis with *ChAdOx1 nCoV-19* vaccine. The vaccine is still being administered worldwide. The association can only be determined when more reports of side effects emerge.

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