Hemorrhagic Rathkes Cleft Cyst Apoplexy Post COVID-19 Vaccination

Sir,

A 25-year-old man developed an acute-onset headache, vomiting and altered sensorium 2 days after taking the Pfizer BioNTech Covid-19 vaccine taken in Kuwait. The patient did not have any rash but had fever and vaccination site arm pain for 2 days post vaccination. His CRP and ESR levels were elevated. The patient was noted to have severe hyponatremia with serum sodium of 104 mmol/l. The patient was euvolemic with low serum osmolality of 210 mOsm/kg. MRI Brain revealed presence of sellar cyst with nodule and haemorrhage. The patient did not have any visual field deficits. Pituitary-specific endocrionological evaluation revealed low testosterone and thyroid-stimulating hormone levels. Cortisol, Prolactin and IGF1 levels were noted to be in normal range. There was no medical history of polyuria, lethargy and cold intolerance. His sensorium improved post-correction of hyponatremia. Hydrocortisone and thyroxine were also started suspecting apoplexy.

Initial MR images demonstrated a 26 mm-sized sellar mass with suprasellar component of heterogeneous signal intensity with peripheral rim enhancement. The lesion had mixed signal intensities on both T1- and T2-weighted scans, with an intracystic fluid level [Figure 1]. These findings suggested the presence of haemorrhage in a pituitary adenoma, Rathke Cleft Cyst (RCC), or craniopharyngioma. In absence of significant endocrinological dysfunction and visual field deficit, option of conservative management with radiological follow-up was discussed with the patient. However, due to the large size of the sellar suprasellar mass and lack of histological diagnosis, the option of surgical intervention was offered after discussion with the multidisciplinary team. Trans-sphenoidal microsurgery encountered a bulging of the sella floor which was quite thinned out. Upon opening of the dura mater, there was an immediate expression of a bloody serous, mucinous and yellowish substance. Cyst contents were completely evacuated and the cyst wall was partially excised. Histology revealed the lesion to be a sellar cyst with epithelial linings (cytokeratin and Epithelial Membrane Antigen (EMA) positive) which was suggestive of Rathke Cleft Cst (RCC). No squamous metaplasia was noted. There was evidence of

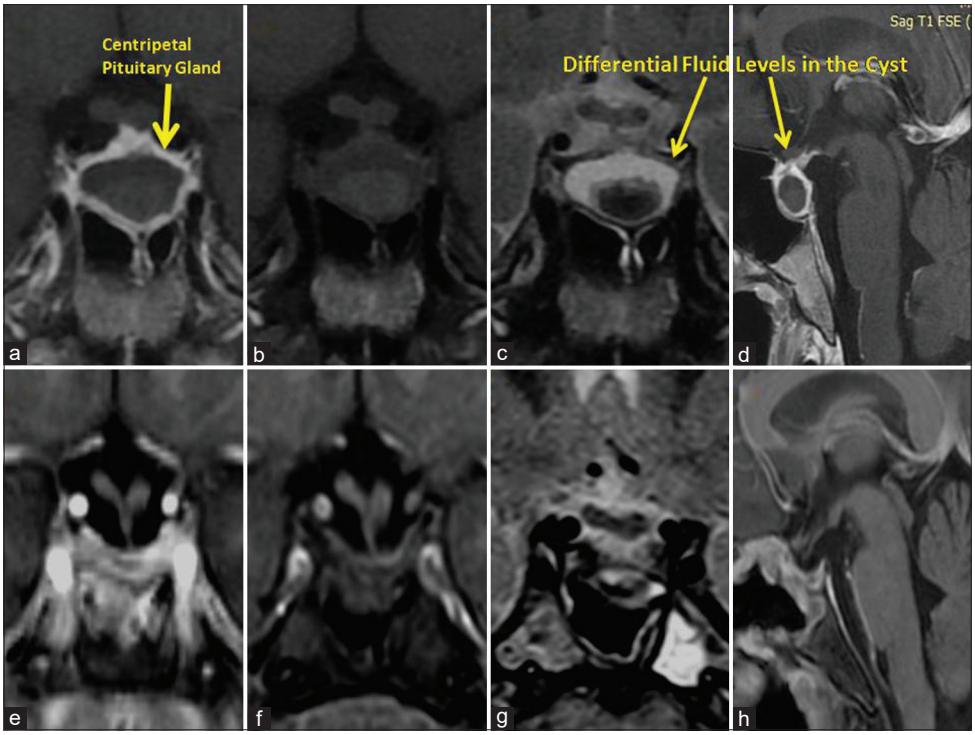

Figure 1: Classical features of Rathke cleft cyst on imaging. Top row showing preoperative imaging: (a) T1W contrast image shows ring enhancing pituitary gland displaced centripetally by Rathkes cleft cyst. (b) T1W image shows central hyperintense nodule with surrounding cystic collection; (c) T2W image shows central hypointense nodule with surrounding cystic collection (cyst, hematoma and nodule seen separately) and (d) T1W contrast sagittal image. The bottom row (e-h) shows corresponding postoperative images

acute haemorrhage mixed in with the contents of the cyst. Interestingly, predominant lymphocytosis and plasma cell infiltrates, suggestive of inflammation, were noted [Figure 2]. The postoperatively course was uneventful. The patient did not develop any diabetes insipidus after surgery. And preoperative mild endocrinopathies were resolved at 1-month follow-up. At 1-year follow-up, MR imaging revealed complete resolution of the lesion without any recurrence. [Figure 1] The patient is not on any hormone replacement and thereafter had vaccinations with two doses of Oxford – AstraZeneca COVID19 vaccine (Covishield).

Symptoms of RCC apoplexy are similar to those of pituitary apoplexy but less severe.[1] Symptomatic patients having RCC usually manifest headaches, endocrinopathies and visual disturbances secondary to supra-sellar extension. Even for pituitary apoplexy a recent meta-analysis revealed that there was no significant difference in the recovery of visual acuity and pituitary function between patients undergoing surgery as compared to those managed conservatively.[2] Euvolemic hyponatremia has been well reported as the presenting symptom in RCC.[3] The reason why RCC should have a higher incidence of hyponatremia at presentation in comparison to other suprasellar neoplasms needs further evaluation.

Controversies still exist regarding indications for surgery and the extent of cyst wall resection in the surgical management of RCC. Trans-sphenoidal surgical decompression of symptomatic RCC is noted to be efficient in relieving 92–98% of compressive symptoms like vision and mild endocrinological abnormalities.[4] The extent of cyst wall excision during surgery has not been associated with increased recurrence. Partial excision of the cyst wall for biopsy with drainage of cyst contents seems to be effective in managing these cases. The incidence of new hormone deficiencies and diabetes insipidus are significantly higher in the few patients who undergo complete or aggressive cyst wall resection. Higher rates of recurrence have been associated with suprasellar location, reactive squamous metaplasia in the cyst wall, superinfection of the cyst and the use of a fat graft into the cyst cavity.[4]

Although a few authors have analysed the imaging characteristics of RCCs, it can still be difficult to distinguish the intracystic nodule of an RCC from acute haemorrhage seen in pituitary apoplexy.[5] Nonenhancing nodule in the cyst with the presence of differential fluid level and a centripetally stretched pituitary could help in predicting the presence of underlying haemorrhagic RCC apoplexy. This nodule most commonly appears as an area within the cyst that exhibits T1-weighted hyperintensity, T2-weighted hypointensity and no gadolinium enhancement. The pituitary gland is usually displaced centripetally by the cyst [Figure 1].

Several vaccines have been approved worldwide for the prevention of morbidity and mortality against severe acute respiratory syndrome coronavirus 2. However, the development of these vaccines has raised concerns regarding their adverse effects. Herein, we report the first case of RCC

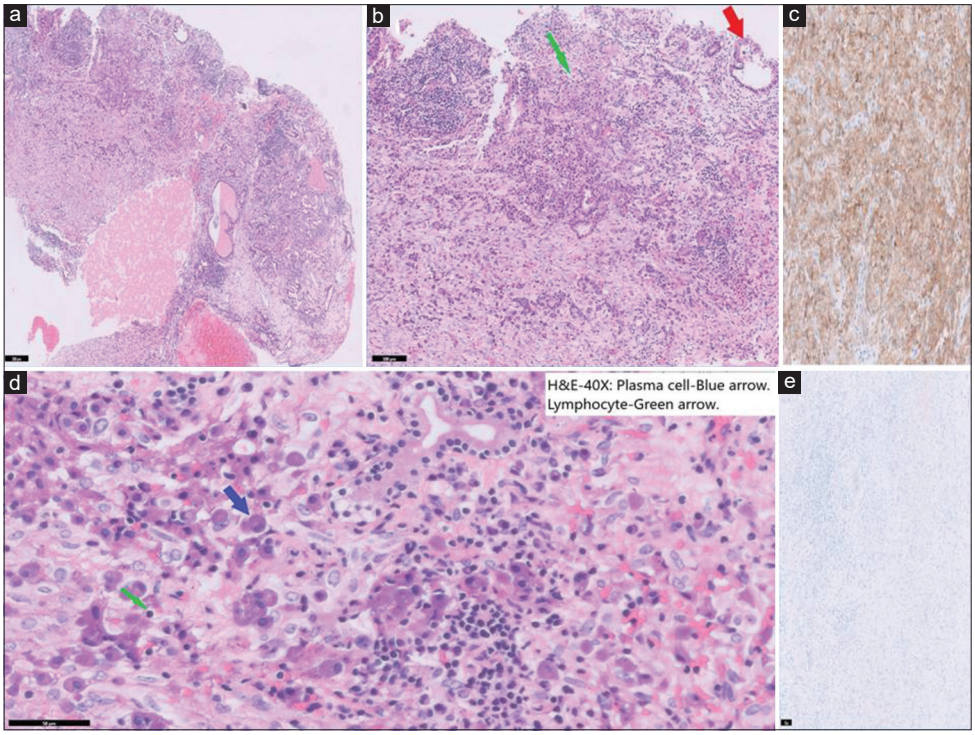

Figure 2: Histology. Haematoxylin and Eosin Stain with (a) 5× magnification shows cyst wall epithelium and dense inflammation; (b) 20× magnification with cyst epithelium (red arrow) and inflammation (green arrow); (c) 40× magnification shows plasma cell (blue arrow) and lymphocyte (green arrow); (d) immunohistochemistry with 20× magnification shows Synaptophysin positivity in residual pituitary and (e) absence of LH, FSH, GH, ACTH and prolactin-secreting cells

haemorrhage probably due to vasculitis after the first dose of mRNA vaccine (BNT162b2, Pfizer/BioN-Tech). In this case, the presence of significant lymphocytosis and plasma cell infiltrates in the cyst wall specimen were suggestive of inflammation leading us to presume vaccination-induced secondary vasculitis or portal vein thrombosis as a probable cause of the RCC apoplexy in this case. The pathogenesis of vasculitis following vaccination remains unclear, although an autoimmune mechanism mediated by vaccine proteins has been proposed.[6,7] Although this case cannot demonstrate a direct relationship between COVID-19 vaccination and haemorrhage in the RCC, the clinical and histological features of this patient are circumstantially consistent with the adverse effects of COVID-19 vaccine.

Informed consent

Informed consent was obtained from the individual participant's family to use MRI images included in the study. Identifying information regarding participants is not included in the study.

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Conflicts of interest

There are no conflicts of interest.

Tarang K. Vora, Rahul Lath, Meenakshi Swain[1], Amitava Ray

Departments of Neurosurgery and [1]Pathology, Apollo Hospital, Jubilee Hills, Hyderabad, Telangana, India

Address for correspondence: Dr. Amitava Ray, Department of Neurosurgery, Apollo Health City, Jubilee Hills, Hyderabad - 500 096, Telangana, India.
E-mail: amitray0407@gmail.com

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