Title: Unusual Presentation of the Rathke Cleft Cyst: A 25-Year-Old Female

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Abstract:

Introduction: Rathke cleft cysts (RCC's) are cystic sellar and supra sellar benign lesions which are thought to originate from the remnants of Rathke's pouch.

There are no specific clinical or radiological signs to differentiate them from other pituitary lesions.

Presentation of Case: We report a 25-year-old female presented with hyperandrogenism and menstrual disorder, with the preliminary diagnosis of pituitary adenoma, based on clinic or radiologic features. The patient underwent endoscopic trans-sphenoid surgery, with the final histopathologic diagnosis of Rathke cleft cyst.

Discussion: Rathke cleft cysts (RCC) are generally asymptomatic, and the most common clinical findings are headache, pituitary dysfunction and visual disturbances It is important to diagnose the patient's problem at an early stage, based on the history, hormone profile, laboratory and radiologic findings.

Conclusion: The presented case highlights the challenging pre-operative diagnosis of Rathke's cyst.

Keywords: Rathke cleft cyst**,** Sellar and supra sellar lesions, Endoscopic trans-sphenoid surgery.

Introduction:

Rathke cleft cysts (RCC's) are benign lesions which originate from congenital remnants of the Rathke pouch and typically arise within the sella between the anterior and posterior lobes of the pituitary (1).

Martin H. Rathke, who proposed that the anterior lobe of the pituitary gland originated from an evagination of the stomodeal epithelium in 1839, is the source of the name RCC (2). Afterward, Goldzieher described the first case of RCC as an incidental postmortem finding in 1913 (3).

Although RCC is usually asymptomatic, it may have debilitating symptoms such as headache, endocrine dysfunction, and occasionally visual disturbances due to mass effect on surrounding neurovascular structures (4,5,6).

In the last decades, neuroimaging techniques improvement has bettered the detection of RCC. So, it is important to differentiate RCC from other cystic lesions with same region clinically like craniopharyngioma, cystic pituitary adenoma, and etc. Therefore, accurate preoperative diagnosis can be difficult (7). We reported one case of Rathke cleft cyst with primary diagnosis of pituitary adenoma with clinical manifestations of hyperandrogenism and menstrual disorder who underwent trans-sphenoidal surgery.

Case presentation:

A 25-year-old female with menstrual disorder (oligomenorrhea) and weight gain from 3 years ago, presented to the endocrinology clinic, Loghman Hakim hospital, Tehran, Iran. Other chief complains were hair loss, fatigue, excessive body hair (hirsutism). She had temporal and occipital region headache from many years ago and She took a variety of medications for headache.

She had irregular menstrual periods and her first menstruation was at the age of 13;other

Past medical and surgical history, family history and drug history were all unremarkable. Upon Physical Examination, her vital signs were all within normal ranges , BMI (body mass index):29.68 and the Ferriman-Gallwey score for hirsutism was 10.

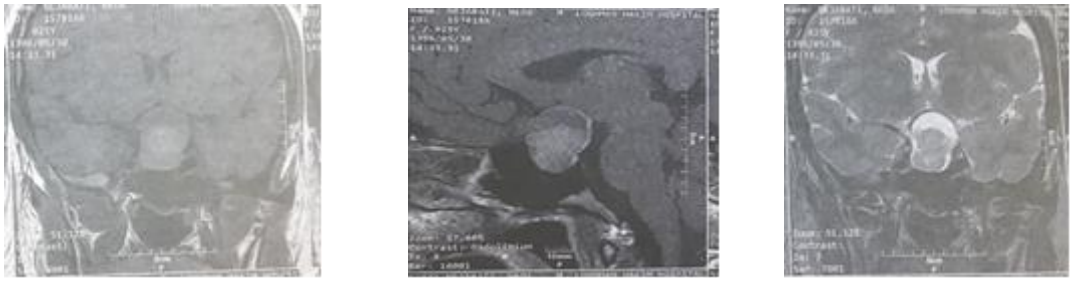
There was no finding in favor insulin resistance or Cushing syndrome.

According to the hyperandrogenism feature and menstrual disorder, the patient was diagnosed with polycystic ovarian disease (PCOD) and other related disorders; lab tests were requested in the second day of menstruation which were shown in (table1, part a) ; *pelvic sonography* was normal.

Table1: Laboratory data from The Patient (a) on Presentation and (b) Subsequent results

	Initial Results (a)	Subsequent Results (b)	Normal range
White Cell Count (WBC)	7.6 k/uL	-	4-10
Hemoglobin (Hg)	13g/dL	-	12-16
Platelet count (Plt)	394 k/uL	-	150-450
Blood urea nitrogen (BUN)	20 mg/dL	-	8-23
Creatinine	1.1 mg/dL	-	0.7-1.3
Fasting blood sugar (FBS)	74 mg/dl	-	70-100
Insulin	5.5 µIU/ml	-	Up to 29
Thyroid Stimulation hormone (TSH)	*0.04 mIU/l,*	-	0.4-4
Thyroxine level (T4)	5.6µg/dl	-	4-12
Prolactin	1516 mu/L	-	< 400
Prolactin (dilution 1/10)		1520 mu/l	< 400
Prolactin (dilution 1/100)		1524 mu/l	< 400
17 hydroxy progesterone (17OHP)	**0.2 ng/ml**	-	<2
Luteinizing hormone (LH)	**1.6 IU/L**	-	2-12
Follicle-stimulating hormone, (FSH)	**5 IU/L**	-	2-12
Testosterone	**0.9 ng/mL**		**2.8-12**
Insulin growth factor-1 (IGF-1)	-	110ng/ml	115-300
Cortisol level	-	12 µg/dl	5-20
Adrenocorticothropic hormone (ACTH)	-	**14.76 pg/ml**	10-64

Based on the laboratory findings of hyperprolactinemia and secondary hypothyroidism; and absence of laboratory/sonographic evidence of hyperandrogenism, central nature of the disease was suspected. Therefore, Brain MRI was requested, which showed a 30 × 21 mm solid –cystic mass with suprasellar extension, High signal in T1and low or iso-signal in T2 (Figure 1).



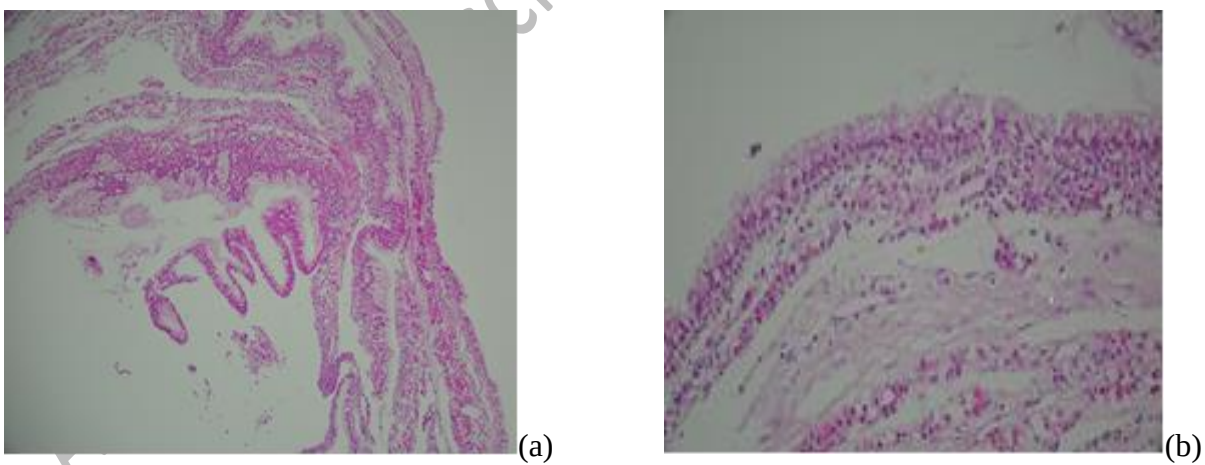
(a) (b) (c)

Figure 1: a) Preoperative imaging of a sellar Rathke cleft cyst with suprasellar extension coronal view (type II RCC) (b,c)T1-T2 weighted gadolinium–enhanced sagittal and coronal MRI.

Based on these findings, the main differential diagnoses were Craniopharyngioma and Cystic Pituitary adenoma. For evaluation of other evidences of hypopituitarism, such as diabetes insipidus (DI); Serum Cortisol, ACTH and IGF1 were measured, the results shown in (table1, part b); the urine output and osmolality were within normal limits.

Perimetry and visual field studies were unremarkable. The Patient underwent the endoscopic trans sphenoidal surgery (ETSS), with the pre-operative diagnosis of non-functional pituitary adenoma.

The received pathologic specimen consisted of several soft tan membranous tissue fragments aggregating to about 1.5×1×0.5 cm and 0.2 cm in maximal thickness, with the final histopathologic diagnosis of " Rathke cleft cyst".



(a) (b)

Figure 2: Cyst wall lined by columnar epithelium with goblet cells, accompanied with remnants of adenopituitary tissue in adjacency. (a) Magnification x 100 (b) Magnification x 400

After surgery, the patient's headache improved and she was on hormone replacement therapy with hydrocortisone, levothyroxine and DDAVP (desmopressin nasal spray) for post-surgery pan hypopituitarism. For lack of menstruation after ETSS, replacement therapy with estrogen

and progesterone agents began up to 3 months but it was discontinued because of pulmonary embolism. The reports of MRI 3 months and 1 year after surgery were normal (Figure 3).

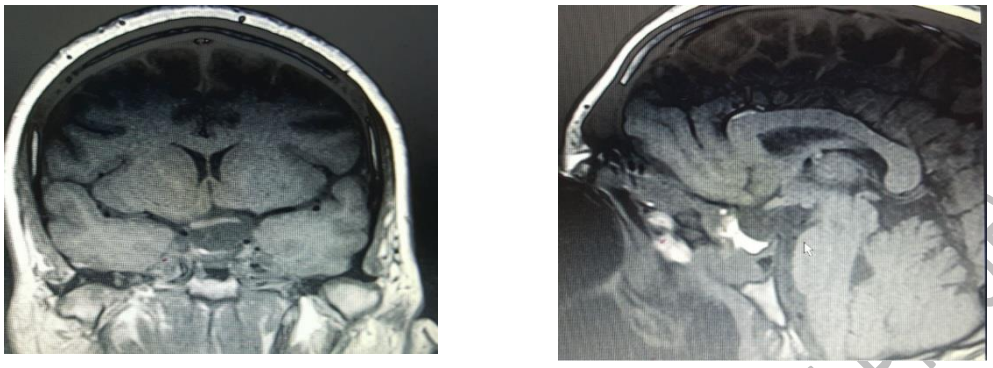


Figure3. Postoperative imaging a normal sella T1-weighted gadolinium–enhanced coronal and sagittal MRI.

Discussion:

Pituitary adenoma is the most frequent benign lesion in the sellar area, followed by RCC (8). International studies have found significantly more symptomatic RCC occur in women and the overall female to male ratio is near 2 to 1. The late 30s represented the median age of detection (8-9). The most frequently reported symptom in the meta-analyses performed by Mendelson et al. in 2014 was headache, followed by pituitary dysfunction and visual abnormalities (9). Galactorrhea, amenorrhea, DI, and panhypopituitarism are symptoms of pituitary dysfunction (10). In this case, headache was the initial symptom that accompanied with weight gain and menstruation abnormality and hirsutism. We thought about PCOD which was the most prevalent differential diagnosis.

The reason of hyperandrogenism feature can be due to high bodyweight and high BMI. According to no findings for hyperandrogenism in lab tests (normal testosterone) and high PRL and low T4 and TSH as well as history of headache, we consider secondary cause (hypothalamus and pituitary origin) , and brain MRI was done. MRI has evolved into the gold standard for evaluating sellar-suprasellar lesions and serving as a framework for surgical planning. RCCs have a wide range of MRI appearances, making neuroimaging diagnosis of an RCC problematic (10-11). RCCs usually look hyperintense on T2 weighted imaging on MRI. On T1-weighted imaging, the cyst's signal intensity changes depending on the protein concentration in the intra cystic contents, and can be hyper intense in 50% of patients, iso or hypo intense in others, and hyper intense (70%) or iso or hypo intense in others on T2

weighted imaging (12). The central site of RCC without stalk deviation and the positioning of the cyst between the anterior and posterior glands when examined in sagittal cuts, are major differences between RCC and an adenoma (13). Early detection and proper preoperative diagnosis are essential because it changes the management protocol. According to anatomical classification (14) this case was Type II RCCs because of being in sella and suprasellar extension. The cornerstone of treatment for symptomatic RCC is surgical treatment. Transsphenoidal surgery has become the usual treatment for intrasellar lesions, and it's becoming more popular for individuals with suprasellar extension (15).

The histopathological examination is the mainstay of the diagnosis, revealing cystic lesion lined by ciliated columnar epithelium with goblet cells. (16, 17)

In conclusion we reported a symptomatic RCC case which presented with hyperandrogenism features and menstrual disorders that led us to central origin, and RCC.

It is important to be able to diagnose the patient's problem at an early stage based on their history, hormonal profile, laboratory results and radiological view. Today, with the advancement of radiology techniques, we are optimistic to distinguish the RCC from adenomas and other differential diagnoses and make the best treatment decisions.

Conflict of interest:

There was no conflict of interest in this study.

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