Functional Gonadotroph Adenoma

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Introduction

- The most common form of non-functional adenomas are gonadotroph adenomas. They usually do not secrete significant quantities of functional hormones.
- Functional gonadotroph adenomas are rare, secrete biologically active hormones and can result in ovarian hyperstimulation syndrome in premenopausal women.

Case presentation

- A 39-year-old female presented for evaluation of headaches and sellar mass on CT.
- She had an IUD placed in 2012 after childbirth and reported continued lactation for 2 years after cessation of breastfeeding.
- Galactorrhea continued to occur 5-6 times per year since. She underwent a gastrectomy in 2018 and noted 3 months of significant spotting postoperatively despite IUD use.
- She reported decreased libido and vaginal dryness.
- MRI brain revealed a sellar and suprasellar mass with pituitary stalk deviation and optic chiasm displacement (Figure 1).
- Formal visual field testing was normal.
- Prolactin and Estradiol (E2) were elevated (Table 1).
- US pelvis showed a large right complex ovarian cyst favored to be functional.
- To rule out inefficient prolactinoma, she was started on cabergoline. Prolactin levels normalized but repeat MRI showed no change in adenoma size.
- Transsphenoidal adenomectomy was performed due to the invasive nature of the lesion.
- The surgical pathology report noted that the tissue morphology and positive staining for GATA-3, FSH and LH supported the diagnosis of gonadotroph pituitary adenoma.
- Estradiol levels normalized after surgery (Table 2).

Findings

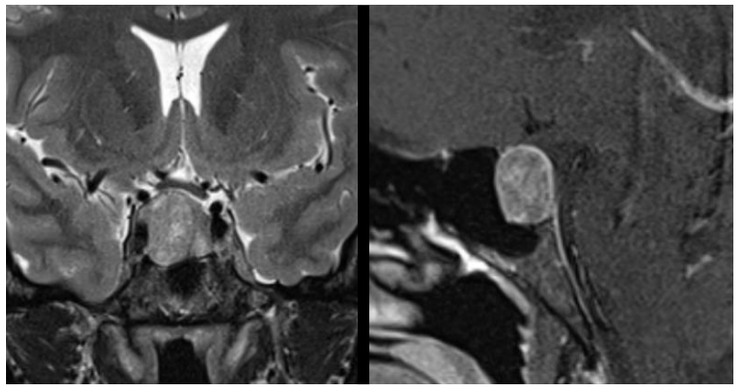

Figure 1. MRI finding of pituitary adenoma - measuring 14 x 19 x 17 mm.

Table 1
Initial lab results

Lab	Value
Prolactin	**210 ng/ml**
ACTH	8.0 pg/ml
Cortisol	16.2 ug/ml
TSH	1.9 uIU/ml
T4	8.6 ug/dl
IGF-1	102 ng/ml
FSH	9.7 mIU/ml
LH	2.5 mIU/ml
Alpha Subunit	0.75 ng/ml
E2	**1496 pg/ml**

Table 2
Lab result trend

Date	PRL	FSH	LH	E2
3/20/19	**210**	9.7	2.5	**1496**
4/12/19	**149**	13.4	-	**601**
7/23/19 [a]	11	6.4	10.6	**581.4**
1/14/20 [b]	28.9	5.0	5.5	**210.7**

[a] After commencing cabergoline
[b] Postoperative lab values

Discussion

- Non-functioning adenomas are most often composed of gonadotroph cells.[1]
- They are usually clinically silent, presenting with mass effect or discovered incidentally on imaging.
- Approximately 35% produce enough FSH or LH to raise serum gonadotropin levels but do not result in clinical syndromes.[2]
- Functional gonadotroph adenomas are uncommon and present with hyperstimulation syndromes:
  - Testicular enlargement
  - Precocious puberty
  - Ovarian hyperstimulation in premenopausal women
- In women, the typical pattern is elevated FSH and E2. Persistent elevation in FSH leads to recruitment of multiple dominant follicles and high E2 concentrations. Women present with:
  - Amenorrhea or oligomenorrhea
  - Vaginal bleeding/spotting
  - Abdominal distension
- There is limited role for medical therapy though there are reports of dopamine agonists resulting in improved symptoms of OHSS without affecting adenoma size.[3]
- Surgical removal of adenoma is the preferred treatment based on limited data. If successful, it will lead to normalization of gonadotropin secretion and ovarian function.
- Mildly elevated prolactin can be seen with macroadenomas due to tumor disruption of normal dopaminergic inhibition of lactotroph cells.

Conclusion

- Functional gonadotroph adenomas are rare and can present with hyperstimulation syndromes. Non-surgical treatment can be trialed, but surgical resection is the best treatment to address the tumor.

References

1. Chaidarun SS, Klibanski A. Gonadotropinomas. Semin Reprod Med. 2002 Nov;20(4):339-48. doi: 10.1055/s-2002-36708. PMID: 12536357.
2. Ho DM, Hsu CY, Ting LT, Chiang H. The clinicopathological characteristics of gonadotroph cell adenoma: a study of 118 cases. Human pathology. 1997 Aug 1;28(8):905-11.
3. Georgia Ntali, Cristina Capatina, Ashley Grossman, Niki Karavitaki, Functioning Gonadotroph Adenomas, *The Journal of Clinical Endocrinology & Metabolism*, Volume 99, Issue 12, December 2014, Pages 4423–443.
4. Bergsneider M, Mirsadraei L, Yong WH, Salamon N, Linetsky M, Wang MB, McArthur DL, Heaney AP. The pituitary stalk effect: is it a passing phenomenon? J Neurooncol. 2014 May;117(3):477-84. doi: 10.1007/s11060-014-1386-5. Epub 2014 Feb 19. PMID: 24549751.