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Association of gonadotroph pituitary macroadenoma and contiguous brain chordoma in a young woman with ovarian hyperstimulation syndrome

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Background

Gonadotroph pituitary adenomas account for 15-40% of all pituitary tumors. More than 80% of clinically nonfunctioning pituitary adenomas are estimated to be gonadotroph-derived, accounting for approximately half of all macroadenomas.

These adenomas often arise in middle-aged men, who may have low testosterone levels with high LH and FSH levels, suggesting a diagnosis of primary hypogonadism.

Women with gonadotroph adenomas and supra-normal FSH levels are generally not recognized as exhibiting a syndrome, because many are over 45 years of age with ovaries devoid of pre-antral follicles, and are insensitive to the action of FSH.[1]

Ovarian Hyperstimulation Syndrome (OHSS) has been reported in patients aged 10-39 years, with pituitary tumors varying in size from 8 mm diameter to huge invasive adenomas.

We present here an interesting case of premenopausal women with FSH-secreting and clinically functioning adenoma, manifesting with enlarged multicystic ovaries and with abdominal pain; associated to a incidentally diagnostic chordoma of the preponic cistern, that have tight anatomic contact with the pituitary adenoma.

Case Report

A 33-year old woman with a 10 years history of sterility with dysmenorrheal and pelvic pain in relation with recurrent ovarian cysts for 1 year.

Because of gradually increasing pelvic pain associated with headache, the patient presented to our outpatient clinic for evaluation. She had no neurologic or visual complaints. Clinical examination was normal apart from obesity (BMI : 30 kg/m²; WC : 111 cm)

Ultrasound examination revealed bilaterally enlarged ovaries containing multiple 2- to 3-cm cysts. (Figure 1)

Endocrine evaluation (Table I) was very suggestive of a gonadotroph adenoma.

Cerebral magnetic resonance imaging examination revealed two masses, the first within the pituitary gland and the second was a cystic tumor inside the preponic cistern (Figure 2).

She had moderate limitation of bitemporal visual fields, with enlargement of the blind spot .

The patient underwent a transphenoidal resection of both tumors.

Histologic examination was consistent with a benign pituitary gonadotroph adenoma with cytoplasm immunoreacting with antibodies against FSH and LH and in lower degree TSH. The second tumor was a chordoma.

Adjuvant Radiotherapy was indicated for the residual tissue.

The follow-up was marked by the disappearance of pelvic pain and normal ovaries without cysts in the postoperative ultrasound examination. However, the patient remains in amenorrhea because of postoperative gonadotroph deficiency. Post-operative hormonal results are shown in **table I**.

Table I – Pre- and post-operative (4 months after surgery) levels of hormones assessed

Hormonal results (units)	Normal Range	Pre-operative levels	Post-operative levels
FSH (mU/mL)	1,5 - 9	9,5	3.8
LH (mU/mL)	1 - 12	0,3	2.7
E2 (pg/mL)	30 - 200	990 -1100	45
Testosterone (ng/mL)	0.1 – 0.7	0,5	0.5
Prolactin (μU/mL)	72 - 480	680	320
TSH (mU/L)	0,25 – 4,5	0,77	1.05
FT4 (pmol/L)	7 - 19	10,4	1.44
GH (ng/ml)	0 - 10	0.2	
ACTH (pg/mL)	< 50	11	12
1μg-Synacthen test : Cortisol peak (ng/ml)	>200		470
α-subunit (ng/mL)	0.02 – 0.9	1.2	0.03
Inhibin B (ng/L)	15 - 200	222	
AMH (μg/l)	2.00 – 6.80	1.37	
GnRH test: Baseline → peak			
LH (mU/mL)		< 0.2 → 1.5	
FSH (mU/mL)		7.3 → 11	
α-subunit (ng/mL)		0.4 → 0.48	



Figure 1 – Bilaterally enlarged ovaries : 110 x 100 x 65 (Right Ovary , RO), 80 x 95 x 70 (Left Ovary , LO). Multiple cysts measuring up to 35 mm hyperechogenous stroma. Thickened endometrium.

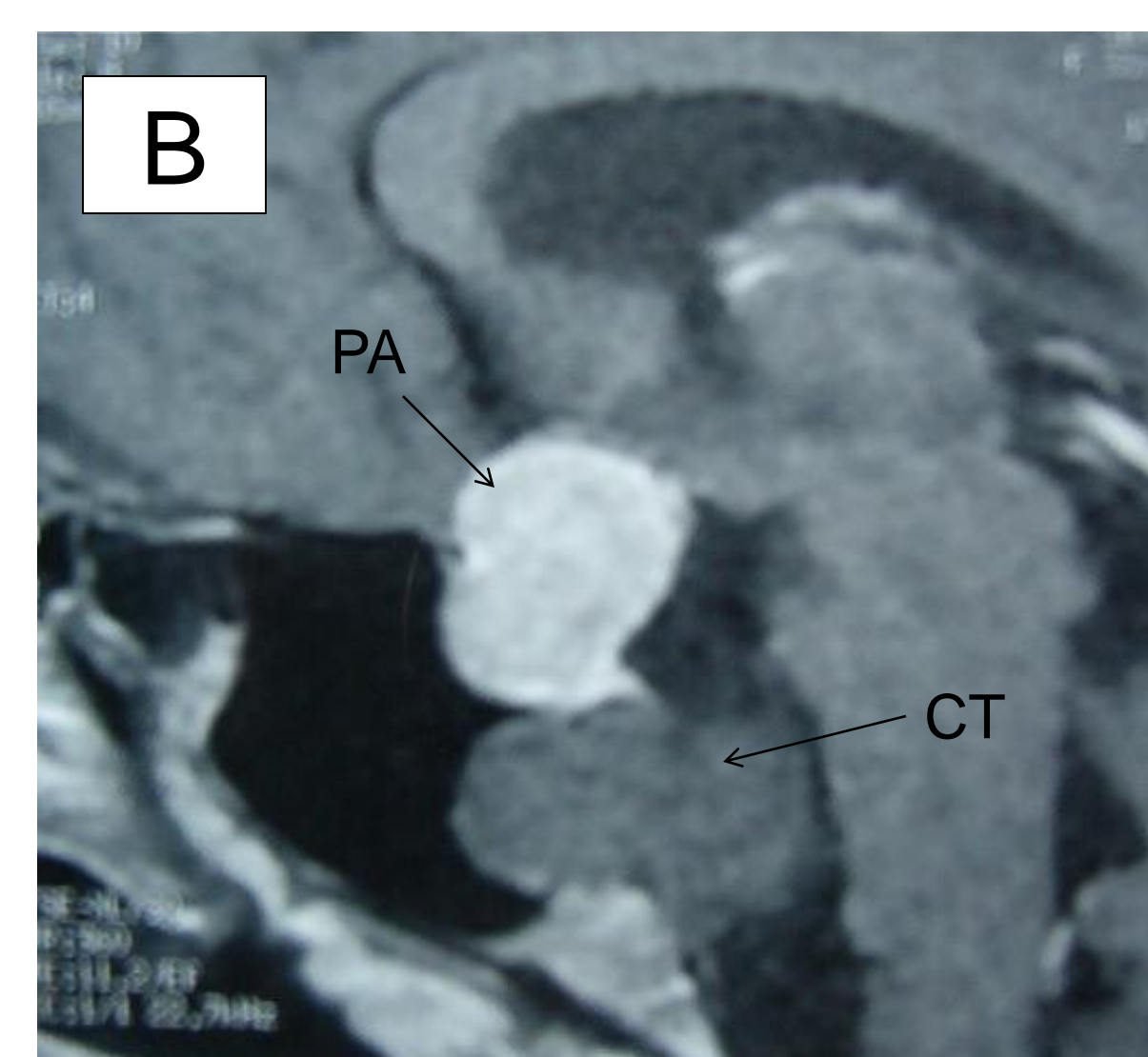
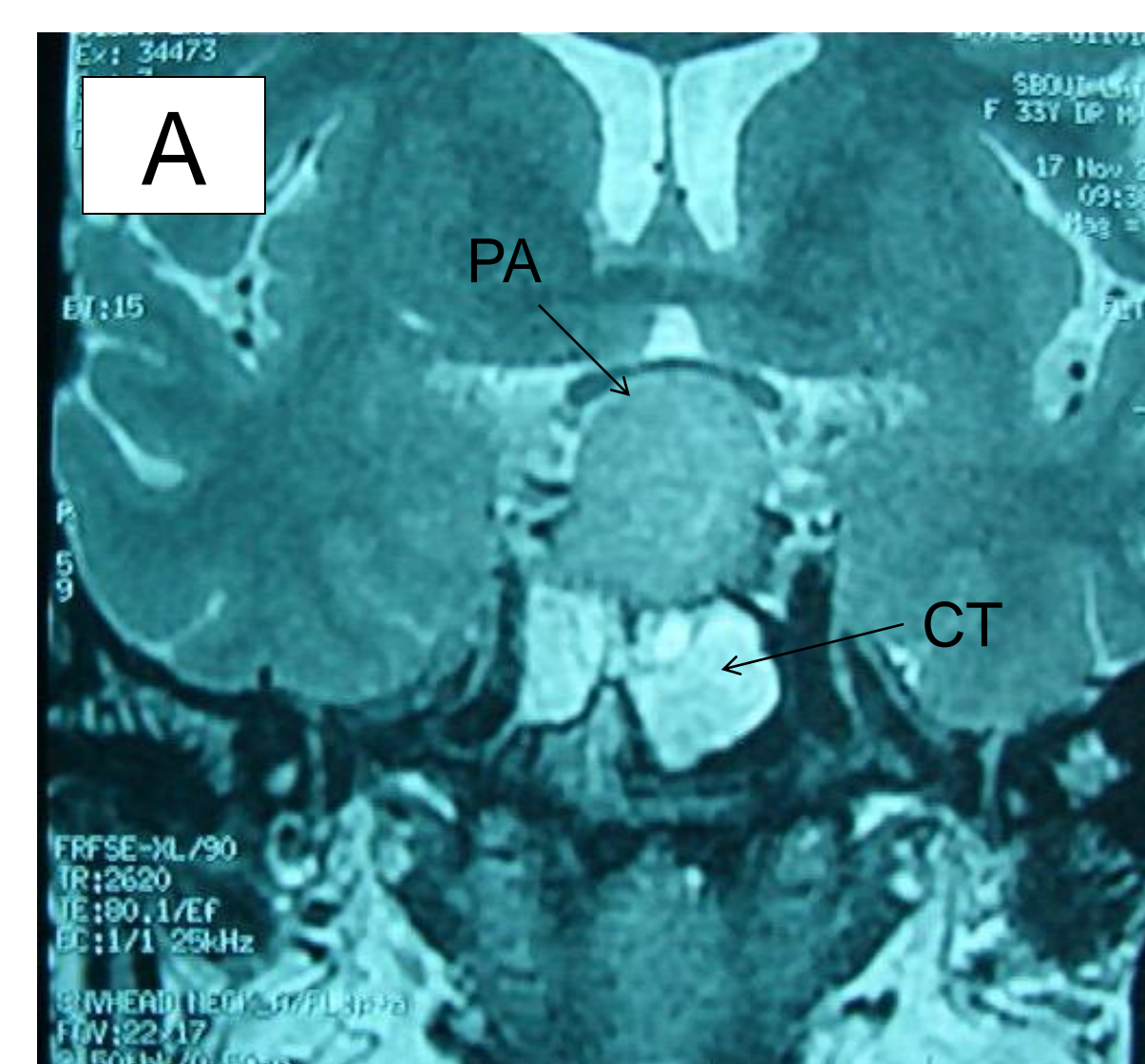


Figure 2 – Brain MRI images (A : Coronal view ; B : Sagittal view) showing homogeneously enhancing mass of 21 x 22 x 18 mm within the pituitary (PA), extending to the optic chiasm and to sphenoid and a second cystic tumor (CT) inside the preponic cistern.

Discussion

This case of gonadotroph pituitary macroadenoma (GPM) presents several particularities :

1. It occurs in young woman, so that it was responsible of an OHSS. When OHSS is caused by an FSH-secreting adenoma, FSH levels are usually elevated, LH is suppressed, and estradiol levels are elevated up to 80 times the normal levels. Women suffering from OHSS usually develop enlarged multicystic ovaries associated with abdominal pain. Interestingly, GPM are more common in postmenopausal women, who are relatively insensitive to ovarian hyperstimulation.[1]
2. Enlarged ovaries with multiple cysts and moderately elevated prolactin could mislead to the diagnosis of PCOS in premenopausal woman with dysmenorrhea and obesity. However, the absence of hirsutism and normal androgens and AMH levels are against that diagnosis. Moreover, the detection of elevated prolactin levels then triggers the ordering of a pituitary MRI, which will reveal the presence of a pituitary adenoma.
3. Surgical resection is the definitive and primary therapy for OHSS due to gonadotropin-secreting adenomas. Infact, it commonly results in normalization of gonadotropin and estradiol levels. In our case, gonadotropin deficiency secondary to large pituitary surgery and radiotherapy explains amenorrhea [3].
4. To our knowledge, this is the first case describing an association of GPM and contiguous chordoma. It may be a hazardous association. However, it may rise questions about interactions, neuromediator interactions, tumor genesis and local factors that are able to enhance gonadotropins secretion (by analogy with brain tumors responsible for precocious puberty in children).

Conclusion

This case highlights the importance of endocrine assessment in the case of recurrent ovarian cysts.

Moreover this case arise the question of a potential link between gonadotroph tumors genesis and a contiguous tumor.

Finally, we note the difficulty of management of such tumors especially after surgical treatment and radiotherapy in regards to fertility.

References

- [1] Chaidarun SS and Kibanski A (2002) Gonadotropinomas. Semin Reprod Med 20: 339-348.
- [2] Roberts JE et al. (2005) Spontaneous ovarian hyperstimulation caused by a follicle-stimulating hormone-secreting pituitary adenoma. Fertil Steril 83: 208-210.
- [3] Cooper O, Geller JL, Melmed S. Nat Clin Pract Endocrinol Metab. 2008;4(4):234-238.