

Resistant macroprolactinoma and infertility: a difficult challenge

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Introduction:

Dopamine agonist resistance is rare in prolactinoma (10%). Doses of cabergoline of up to 2.0 mg/week are usually effective in controlling prolactin (PRL) secretion and reducing tumor size. Surgical treatment is rarely indicated.

Case report:

An 18-year-old female presented in 2002 with a 2-year history of amenorrhea and galactorrhea.

Hormonal investigation:

- *Hyperprolactinemia (4800 mUI/l)
- *integrity of the other pituitary axis.
- *The acromegaly was excluded.

MRI:

- *2 cm pituitary adenoma with suprasellar extension.

Visual field :

- *central bilateral scotoma.

Ttt :

The patient was initiated on bromocriptine, which was titrated to a daily dose of 15 mg.

Evolution:

- *Subsequent MRI showed a decrease in the pituitary mass to 11mm
- * PRL never normalized during 6 years of bromocriptine and ranged from 1677 to 3074 mUI/l.
- *In 2010, she switched to cabergoline, which was titrated to a weekly dose of 2.5 mg.
- *Subsequent MRI showed no amelioration, prolactin never normalized and the patient was always in amenorrhea, despite compliance to cabergoline and increasing to a weekly dose of 6mg.

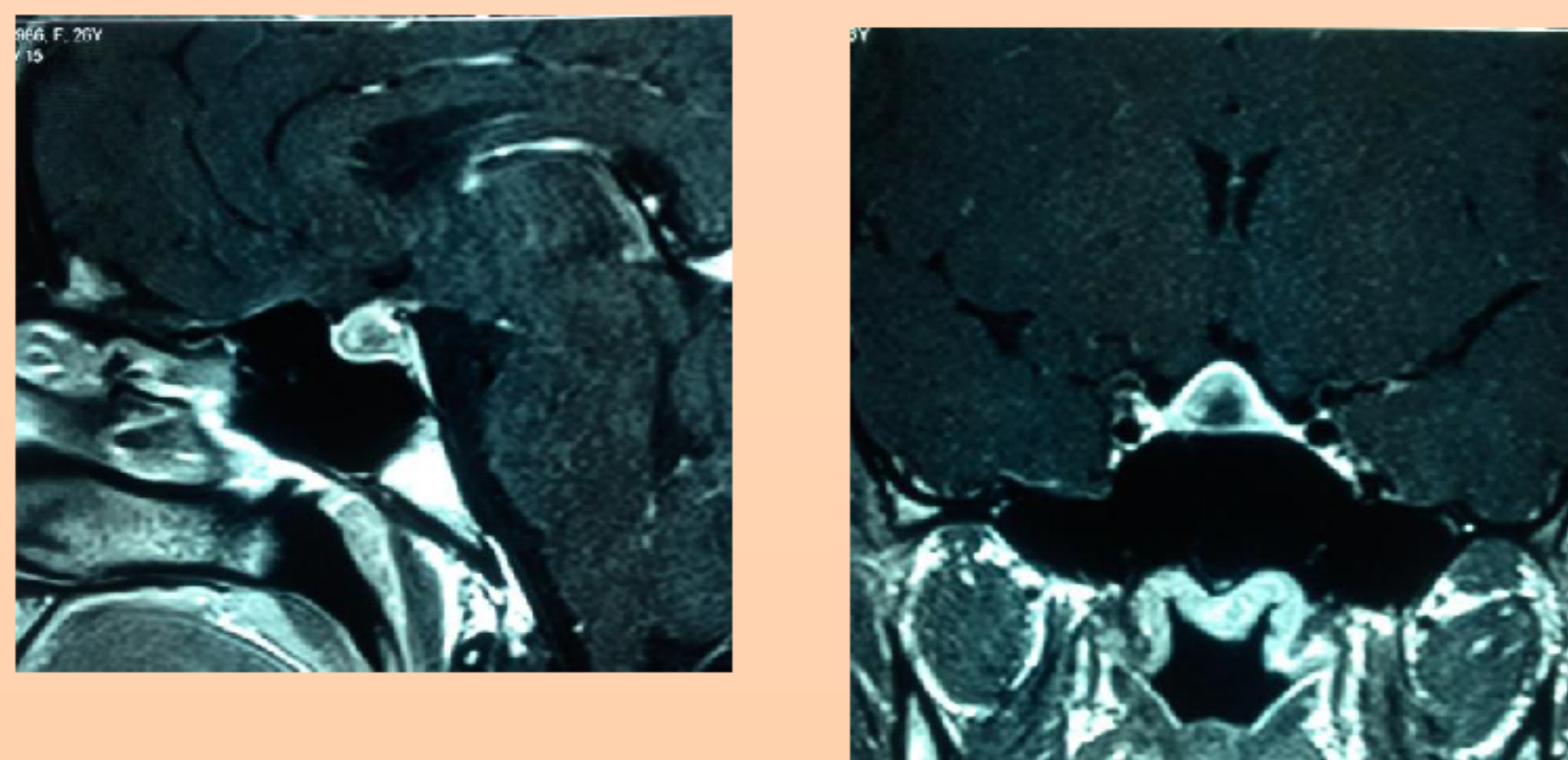


Fig: Preoperative pituitary MRI showing a pituitary mass of 11mm

*Finally, she was referred to neurosurgery and she underwent a transsphenoidal endoscopic resection of the pituitary adenoma.

*The immunohistochemical analysis demonstrated positive staining for PRL (+++) and LH(+). Ki-67 nuclear labeling was estimated at 1%.

*The patient had no postoperative complications, with integrity of corticotrope and thyretrope axis.

*Three months after the surgery, she had no resumption of menses and the hormonal exploration showed a hyperprolactinemia (2668 mUI/l). The serum HCG level was elevated. A spontaneous pregnancy of 13 weeks of amenorrhea was diagnosed.

Discussion:

*There are several possible approaches for treatment of patients who are resistant to dopamine agonists (DAs). Patients taking bromocriptine should simply be converted to cabergoline, because most will then respond (1).

*For the patient resistant to cabergoline, the most common approach is to increase the dose of cabergoline, as long as a reduction in PRL levels can be demonstrated with each stepwise increase. Patients generally tolerate such dose increases quite well. (2)

*Because medical treatment is so highly efficient, transsphenoidal surgery has become less and less used, thus explaining the fact that recent surgical series are rare and often contain a limited number of patients.

*Surgery usually allow a subsequent normalization of PRL concentrations, with a lower dose of DA in nearly half of the resistant patients. Resistance to DAs or even the need to utilize a higher-than-standard dose of cabergoline to control PRL and tumor volume may therefore be considered as valid indications for surgical resection of prolactinomas.

*There was, however, no difference in the percentage of reduction of PRL levels under DA treatment before or after surgery. This indirectly suggests that the sensitivity of the tumoral cells to dopaminergic inhibition most likely did not change with surgery. (3)

*As shown by Caccavelli *et al.* (4)intrinsic sensitivity of the tumor to DA is essentially related to D2 dopamine receptor expression on pituitary tumor cells, a parameter which should not be affected by partial resection of the adenoma.

Conclusion:

Although rarely indicated, the surgical treatment is interesting in resistant prolactinoma, especially in young woman with infertility.

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