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Prolactinomas in men: management challenges
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Introduction: Prolactinomas are the most common pituitary adenomas (Pas), with an estimated higher prevalence in women. Over 90% of prolactinomas are small, intrasellar tumors that rarely increase in size, but occasionally, these PAs can be aggressive or locally invasive and cause compression of vital structures. Usually, prolactinomas in male patients are large, invasive, but the reasons for the more aggressive course remain poorly understood. Also, male prolactinomas have a lower expression of estrogen receptor alpha (ERα), which is associated with higher proliferation rates, resistance to dopamine agonists and a poor prognosis (1).

Objective: To investigate the impact of sex-related differences in prolactinomas. Material and Methods: We analyzed 76 patients with confirmed diagnosis of prolactinomas. The patient’s information was collected retrospectively between 2018 and 2021. The patients had a mean age of 40.9 years old (range 18-77) and the majority were males (56.75%). We identified 15 patients (11 males, 4 females) with prolactin (PRL) secreting macroadenomas who underwent pituitary surgery (transsphenoidal, ten patients; transcranial five patients, and three of them had two transsphenoidal interventions and one of them had two transcranial interventions), four had also radiotherapy (three patients had high voltage radiation therapy and one had gamma knife radiosurgery). In the group of patients who underwent pituitary surgery, mean pre-operative maximal diameter was 35.65 ± 14.83 mm (6 giant prolactinomas, all of them in males) with mean PRL levels at presentation of 3640 ng/ml (range 560–16000), with significant higher levels observed in
male patients. Eleven patients had visual field defects and the same number had panhypopituitarism with hormonal replacement therapy. Only two patients (females) are now normoprolactinemic without treatment with dopamine agonists. Nine tumors were considered invasive, according to Knosp classification (grade 3-4). Two female patients had remission of the disease following surgery. Nine patients had residual tumors after surgery, with controlled PRL secretion under treatment with dopamine agonists. The nuclear positive cells for Ki-67 were quantified by bright field microscopy (magnification x200) using QuantCenter software, its values ranging from 1% to 20%, with a value of 15-20% in the case of a male patient with giant prolactinoma with cavernous sinus invasion.

**Conclusion:** Significantly higher prolactin concentrations are observed in men as compared to women, in PRL secreting pituitary adenomas. The reasons for a more aggressive course of prolactinomas in men remain poorly understood, the higher rates of proliferation markers, such as the Ki-67 labeling index or the mitotic count, the low expression of ERα may explain the more aggressive behavior in men.


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