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EDITORIAL

Giant prolactinomas: Multi-modal approach to achieve tumor control

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Prolactinomas, the most common pituitary adenomas depicted, occur in ~5/10,000 subjects. Among the affected patient population, females usually harbor microadenomas, whereas the larger macroadenomas are diagnosed in males and post-menopausal women. The very large and invasive prolactin (PRL)—secreting tumors measuring ≥40 mm in diameter with baseline PRL levels >1000 ng/ml but typically much higher, the giant prolactinomas, represent 3–5% of all PRL-adenomas, and appear with a male to female ratio of about 9:1 [1, 2]. Usually, there is an association between tumor size and baseline serum PRL level, but this association is not always kept. Prolactinomas mostly respond to dopamine agonists, with a 90% remission rate when treated with cabergoline as primary treatment [3]. However, with increasing adenoma size, PRL normalization rate decreases and seen in 70–80% of macroprolactinomas [4].

In this issue of Endocrine Andujar-Plata P et al. [5] summarized their clinical experience with 16 adults presented with giant prolactinomas. Interestingly, almost half of the patients (7/16) were women, with a median delay of 150 months in diagnosis in females vs 12 months in men. Three of the women were post-menopausal, and one was a 16-year-old adolescent. Eleven patients started with dopamine agonist treatment as first-line approach, the other five had pituitary surgery as primary treatment (due to compressive symptoms in three patients, intratumoral hematoma and patient preference–one patient each). All patients received dopamine agonists, but only 4 patients started medical therapy without further treatment on follow-up. Altogether, 11 patients had pituitary surgery (69%), however, no patient was cured by surgery. Seven patients received two treatment modalities, and five underwent three modalities including dopamine agonists, 1-2 operations and/or radiotherapy. After nine years of treatment, PRL reached normal values in 7 patients (44%) or near-normal (<2× upper limit of normal) levels in 6 out of 16 patients. Three patients still had high PRL values. Thus, half of this cohort showed dopamine resistance, at least partially, and most of the patients required other treatment modalities to achieve tumor control. Noteworthy, all patients presented with hypogonadism, but only in two the gonadal axis recovered. This cohort of giant PRL-tumors illustrates the difficulties to achieve biochemical control and alleviate mass effects in patients diagnosed with aggressive prolactinomas, commonly requiring several treatment modalities.

Two series published recently, one with 47 (5 females, 42 males) patients with giant prolactinomas [6] and the other with 18 patients (2 females, 16 males) with giant tumors larger than 60 mm [7] reported fairly good response to cabergoline treatment with PRL normalization in 68 and 61% of patients, and recovery of gonadotrophic axis in 32 and 37%, respectively. Six (13%) and nine (50%) of the patients included in these two cohorts had pituitary surgery compared to 69% in the current series [5]. Maiter D & Delgrange E summarized the efficacy of primary treatment with dopamine agonists in 13 other cohorts of patients with giant prolactinomas including 140 subjects (86% males) [1]. PRL normalized in 60% of the patients treated with cabergoline, bromocriptine, or pergolide, and the tumors have shrunk (>30% decrease in tumor diameter, or >65% reduction in tumor volume) in 74% of the subjects. However, it is difficult to compare efficacy rates among

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different cohorts, due to the variability in patients and adenomas characteristics, dopamine agonists used and medication doses. Moreover, these are retrospective small cohorts composed of patients treated by several physicians using different treatment attitudes. Importantly, a decision to refer a macroprolactinoma patient with chiasmal compression and visual damage for decompressive pituitary surgery or to prefer primary medical treatment may change, according to the treating physician's experience and the availability of a dedicated skilled pituitary neurosurgeon.

Anyway, as for the smaller macroprolactinomas, we have learned that the majority (60%) of giant prolactinomas will respond to high dose dopamine agonist therapy with PRL normalization, tumor mass reduction and improvement in visual deficits. The minority who are resistant or respond partially to medical treatment or develop acute complications, will require debulking surgery to improve response to dopamine agonists, or adjuvant irradiation in certain circumstances. Nevertheless, the chance to achieve hormonal control with pituitary surgery is very low [5, 7] and the risk for surgical complications including diabetes insipidus, anterior pituitary deficiency or cerebro-spinal fluid leak should be considered. Thus, primary medical therapy should be tried as first option in most patients, and surgery be reserved only for patients with severe visual damage, or in cases of dopamine agonist resistance.

Compliance with ethical standards

Conflict of interest The author declares no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by the author.

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