

Catarina Cidade Rodrigues¹, Ariana Maia², Isabel Ribeiro³, Cláudia Amaral²

1 – Endocrinology department, Centro Hospitalar do Tâmega e Sousa, Portugal, 2 – Endocrinology department, Centro Hospitalar Universitário do Porto, Portugal, 3 – Neurosurgery department, Centro Hospitalar Universitário do Porto, Portugal

Introduction:

- Prolactinomas are prolactin-secreting pituitary tumours with a prevalence of 50 per 100,000⁽¹⁾. They account for up to 40% of total pituitary adenomas⁽²⁾ and 44-67% of functioning pituitary adenomas⁽³⁾.
- Microprolactinomas occur more frequently in women, whereas macroprolactinomas occur more frequently in men⁽⁴⁾. When in men they are usually larger, more resistant to medical treatment and often show aggressive features⁽⁵⁾.
- We present the case of a male patient with a resistant and aggressive macroprolactinoma, treated with temozolomide.

Case report:

- ♂, caucasian, date of birth: 06/04/1981. First consult: December 2010.

Presenting symptoms:

- Headaches and reduced libido with 6 months duration. No visual impairment.
- No past medical history, chronic medication or relevant family history.

Physical examination:

- Weight 89 kg, height 1,80 m, BMI 27.4 kg/m². Bilateral nonpainful gynecomastia.

Initial blood workup: Table 1. **Pituitary MRI:** Figure 1.

Analytical parameter (units)	Result	Reference range
Prolactin (ng/mL)	3152	4.04-15.2
Morning cortisol (µg/dL)	16.3	6.2-19.4
IGF-1 (ng/mL)	311	117-329
Total testosterone (ng/mL)	0.382	2.8-8.0
FSH (µUI/mL)	4.1	1.5-12.4
LH (µUI/mL)	2.7	1.7-8.6
TSH (µUI/mL)	3.09	0.38-5.33
Free T4 (ng/dL)	0.6	0.54-1.24
Sodium (mmol/L)	137	135-145
Potassium (mmol/L)	4.66	3.5-5.0
Total calcium, corrected for albumin (mmol/L)	2.18	2.2-2.7

Table 1: Initial blood workup.

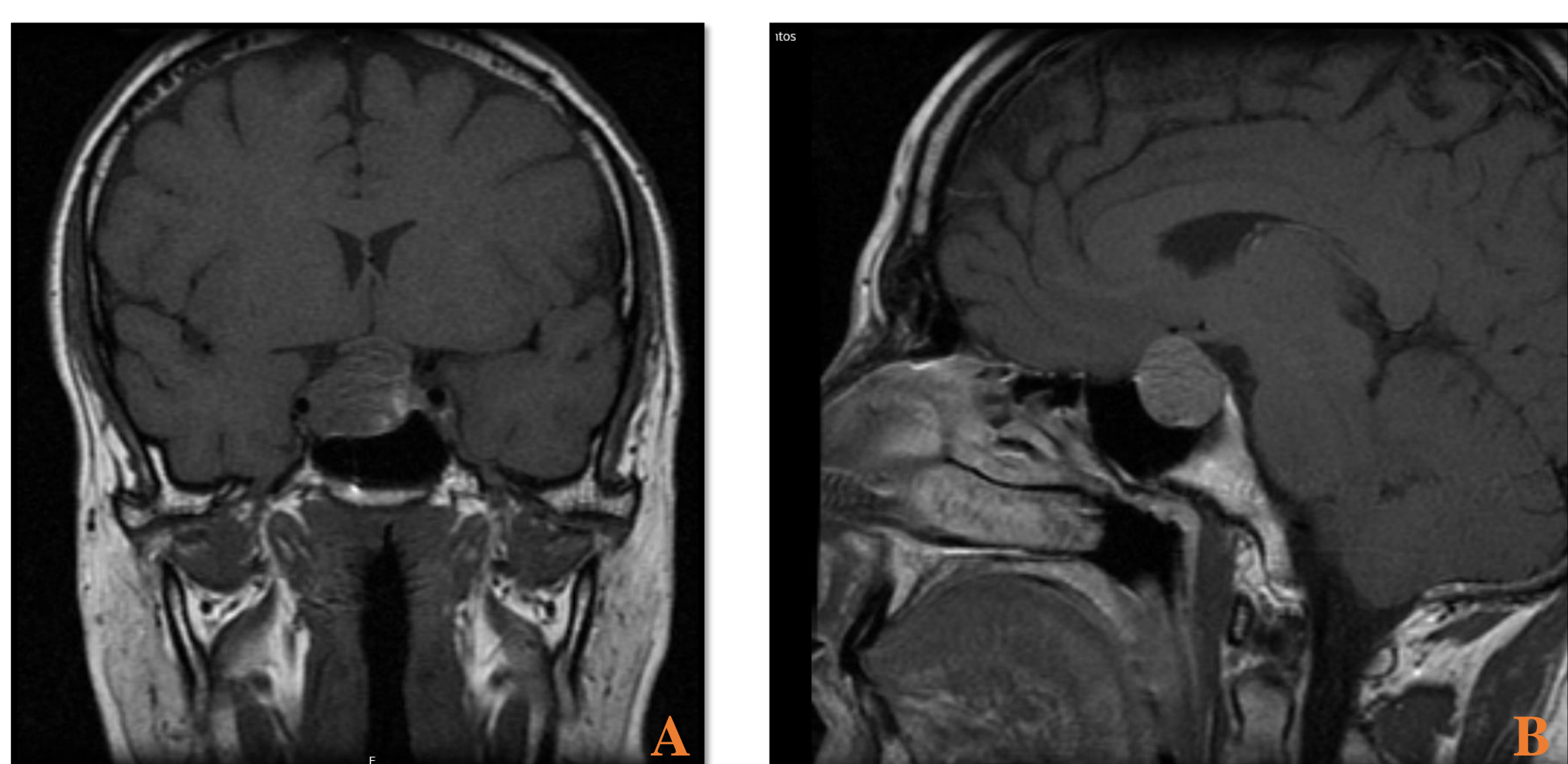
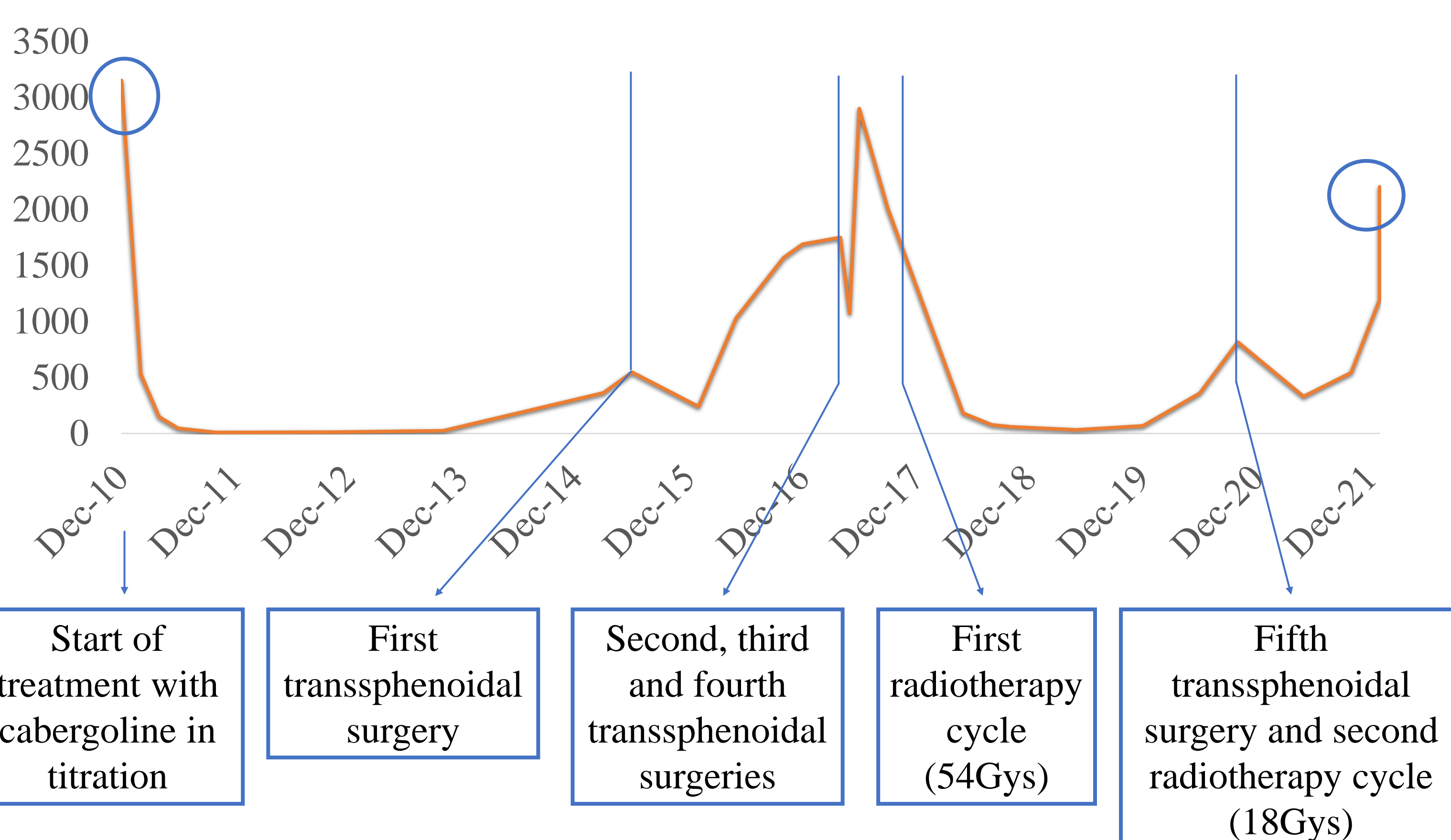


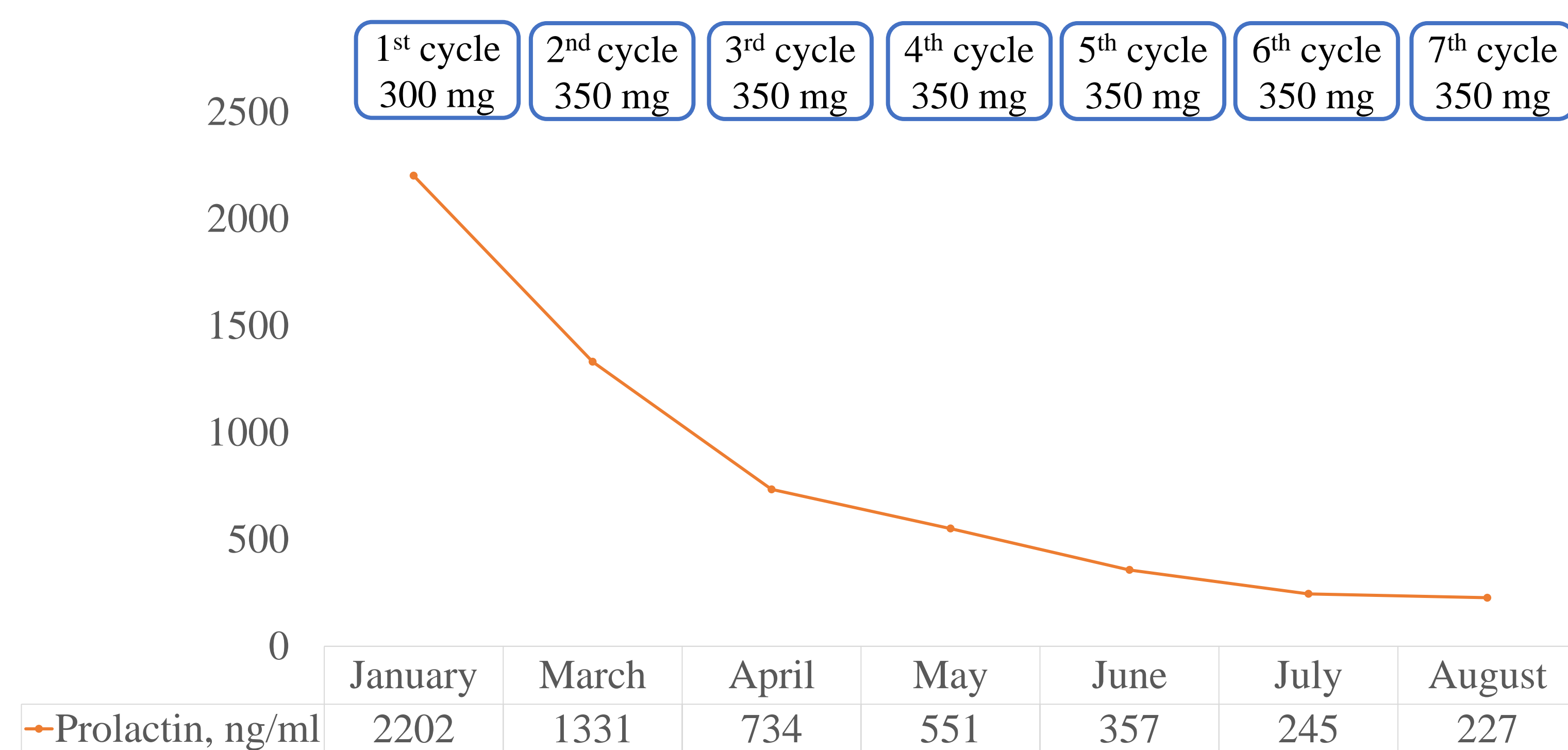
Figure 1: Initial pituitary MRI, documenting an intrasellar round mass, 19x26x22mm, consistent with macroadenoma, not invading the cavernous sinus, but touching the optic chiasm. Panel A: T1 coronal view; Panel B: T1 sagittal view.

Diagnosis: Prolactinoma and hypogonadotropic hypogonadism.



Graphic 1: Changes in prolactin levels (ng/mL) during follow-up and timing of surgical and radiotherapy treatments.

- **Histopathology (2021):** round, hyperchromatic and pleomorphic nuclei, granular and chromophobe cytoplasm, abundant mitosis, immunoreaction for PRL and PIT1. Ki-67 >3%. p53+.
- *AIP* gene mutation: negative.
- After the fourth surgery, he developed hypopituitarism and started testosterone, levothyroxine and prednisolone supplementation.
- **Whole body and brain CT:** no signs of metastasis.
- In February 2022, he started treatment with temozolomide.
- Adverse effects reported: epigastric pain, nausea, constipation and transient asthenia.



Graphic 2: Changes in prolactin levels (ng/mL) during treatment cycles with temozolomide.

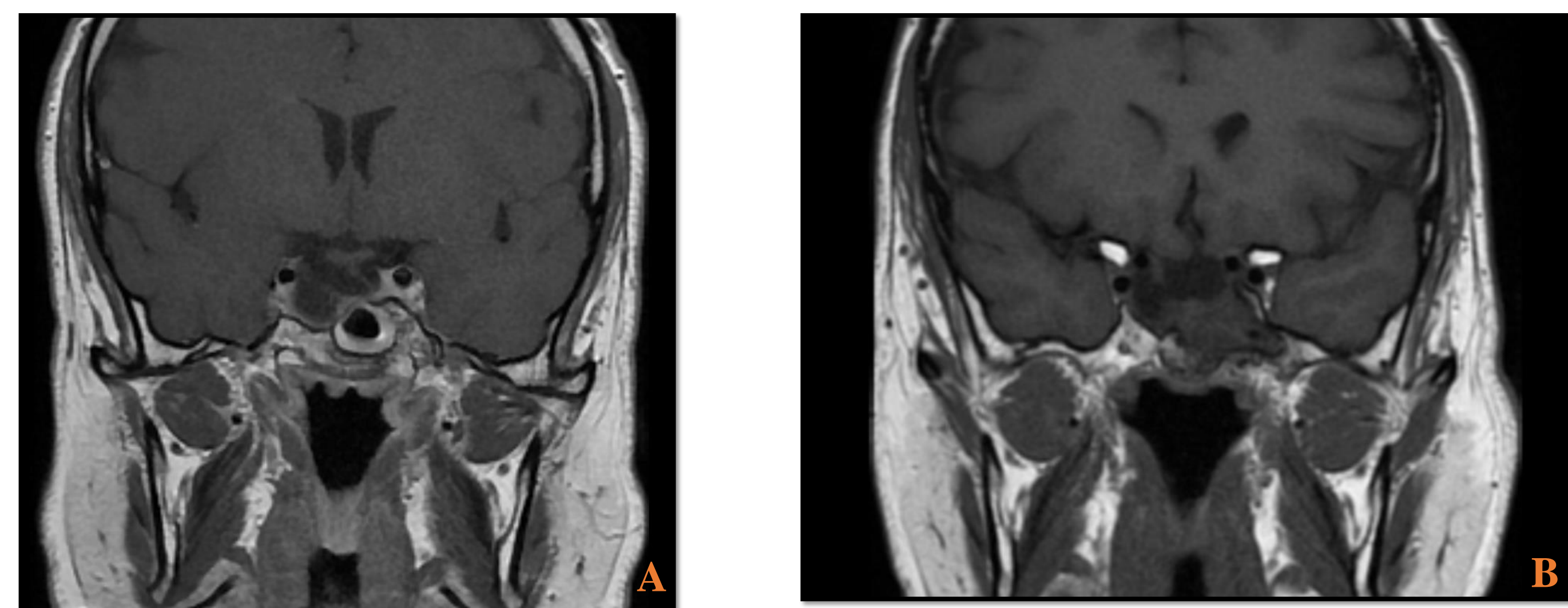


Figure 2: Pituitary MRI before and after 3 cycles of temozolomide treatment, evidencing no tumour size progression. Panel A: T1 coronal view, December 2021 (before treatment); Panel B: T1 coronal view, May 2022 (after treatment).

Discussion:

- Resistant prolactinomas are a therapeutic challenge, especially when additional features of aggressiveness are present.
- Although temozolomide is recommended as fourth-line treatment in these cases⁽⁶⁾, success rates are around 40-70%, depending on the criteria considered⁽⁷⁾.
- In our patient, there seems to be a good initial response to this treatment and no tumour size progression.
- However, other therapies need to be considered in case of future relapse or progression, such as somatostatin analogues, tyrosine kinase inhibitors, mTOR inhibitors and peptide receptor radionuclide therapy⁽⁶⁾.

References:

