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Pasireotide treatment in giant prolactinoma resistant to dopamine agonists

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Giant prolactinomas (GP), defined as tumours > 40 mm, are a scarce subtype of lactotroph plurihormonal pituitary neuroendocrine tumours (PitNET) (accounting for 2–3%), occurring predominantly in young men. Treatment of GP is often challenging and requires a multimodal approach [1]. Resistance to dopamine agonists (DA) is defined as a lack of normalisation of prolactin serum levels or lack of at least 30% reduction in maximum diameter of the tumour treated with standard dopamine agonist doses (7.5–10 mg/day of bromocriptine or 2.0 mg/week of cabergoline) for at least 6 months [2].

We present a case of a 17-year-old male with a DA-resistant GP treated with a second generation of somatostatin analogue-pasireotide LAR. In August 2022, the patient was admitted to the Endocrinology Department. He had been receiving cabergoline since 2020 and underwent 2 neurosurgical procedures in Ukraine (July 2020 and January 2021) due to severe headaches and vision disturbances. On admission, he complained of diplopia, temporal visual field deficits, persistent headaches (4/10 on the numerical rating scale [NRS]), presented with obesity, and symptoms of hypogonadism. Significantly elevated prolactin concentration [43.211 μIU/mL, reference range (RR): 86–324 μIU/mL], with decreased testosterone, low follicle-stimulating hormone (FSH), and luteinising hormone (LH) accompanied by thyroid-stimulating hormone (TSH) and free thyroxine (fT4) indicative of central hypothyroidism were detected. Magnetic resonance imaging (MRI) from July 2022 revealed a residual pituitary tumour (38 × 34 × 33 mm) infiltrating the right cavernous sinus and right optic nerve (Fig. 1AB). No heart valves abnormalities were found on echocardiography. The dose of cabergoline was increased to 3.5 mg/week. Levothyroxine (50 mcg/day) and testosterone injection (1×/2 weeks) were commenced. Due to high prolactin values (51,247 μIU/mL), cabergoline was uptritated to 4.5 mg/week. In May 2023, through the dopamine agonist resistance, a therapy with pasireotide LAR was implemented at the dose of 20 mg/month (increased to 40 mg/month after 6 months). After pasireotide commencement, the tumour dimensions stabilised (Fig. 1CD), and signs of tumour cystic degeneration occurred (Fig. 1EF). The patient reported remarkable headache alleviation (0/10 on the NRS scale), the appearance of facial hair, and body weight reduction. The ophthalmologic examination showed an improvement in the visual field. The prolactin level decreased to 35,000 μIU/mL (32% of the baseline concentration from September 2022).

Most GPs are benign; however, due to tumour dimensions, they might show aggressive behaviour, infiltrating the optic chiasm, sphenoid sinuses, or cavernous sinuses [1]. GPs usually respond well to DA therapy; cabergoline is the most effective DA [2]. Surgical treatment is indicated in pituitary apoplexy, cerebrospinal fluid leakage, and tumour growth despite optimal treatment. GPs are more often non-resectable and prone to postoperative recurrence; therefore, the surgeries are associated with significant mortality [1, 3]. Moreover, extracellular extension and cavernous sinus invasion (evaluated by Knosp

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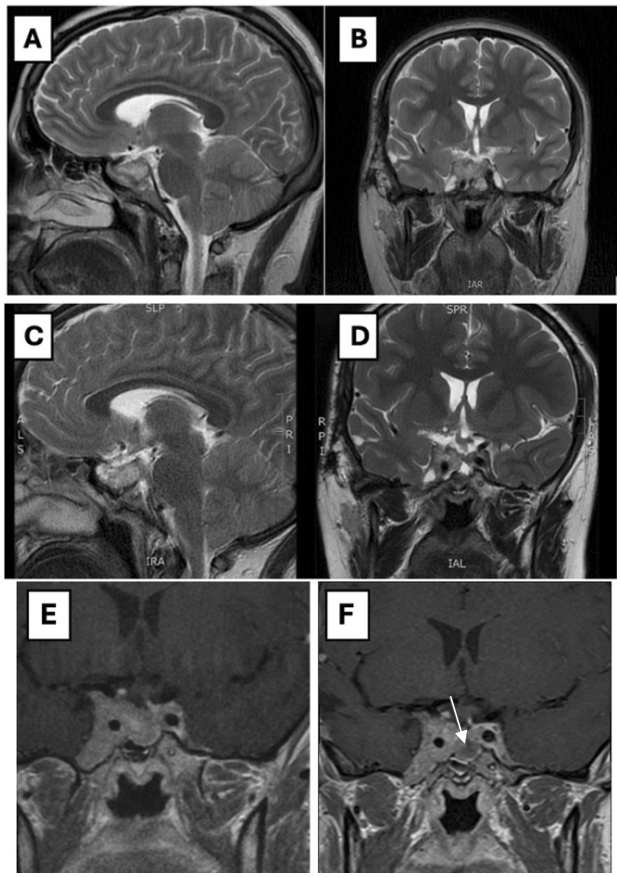

Figure 1A, B. *Sagittal T2 (***A***) and coronal T2 (***B***) magnetic resonance imaging (MRI) (July 2022) showing pituitary tumour (38 × 34 × 33 mm) infiltrating the right cavernous sinus and right optic nerve;* **C, D.** *Sagittal T2 (***C***) and coronal T2 (***D***) MRI (July 2023) showing stable dimensions of the tumour after pasireotide implementation;* **E, F.** *Coronal T1 MRI (July 2022) and coronal T1 MRI (July 2024) comparing the part of the tumour without (***E***) and with (***F***) a cystic degeneration of the tumour (arrow)*

classification) are associated with lower remission rates [3]. The prognostic factor associated with early remission after transsphenoidal surgery was lower prolactin concentration on the first postoperative day [3]. The current consensus is that temozolomide is usually recommended as a treatment option for aggressive prolactinoma with persistent growth [2]. However, there is increasing evidence that pasireotide can be successfully introduced due to its potential antitumor and analgesic effect [4, 5]. This case emphasises that GPs require an individualised therapeutic approach. Pharmacological therapy with pasireotide in DA-resistant GPs should be regarded as the first-line treatment. Alleviation of headaches, decreased prolactin, tumour stabilisation, and cystic degeneration are considered satisfactory outcomes [4, 5]. Further studies should be conducted to evaluate the effectiveness of pasireotide in GPs.

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