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Pituitary apoplexy as the first manifestation of non-functioning pituitary neuroendocrine tumour

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A 45-year-old male presented to the emergency department with a one-week history of bilateral visual deterioration (but with a clear left-side predominance), including blurred vision, diplopia, and visual field defect. The visual symptoms progressed over the week, with a sudden worsening accompanied by nausea and severe dull headache on the day of hospital admission. His vital signs were normal, and his past medical history was significant for arterial hypertension treated with amlodipine and ramipril. On the ophthalmological examination, the visual acuity in the left eye was limited to hand motion and in the right eye was decreased to 0.5. The visual field examination revealed a profound visual field constriction in the left without deficits in the right eye. Apart from the visual impairment, the neurological examination was normal. Initial laboratory tests showed mild hyponatraemia (sodium [Na^+]: 131 mmol/L) and hyperglycaemia (random plasma glucose: 203 mg/dL). A brain computed tomography revealed a haemorrhagic sellar mass with suprasellar extension (Fig. 1A). Subsequent magnetic resonance imaging (MRI) confirmed a large pituitary lesion measuring 20 × 27 × 29 mm with signs of intratumoural bleeding. The mass was compressing and displacing the optic chiasm, compressing the posterobasal part of the frontal lobes, and reaching the third ventricle floor (Fig. 1B–C). The hormonal evaluation showed central hypothyroidism, the corticotroph axis was preserved with serum cortisol concentration adequate for the patient's state. The medical examination and initial hormonal assessment did not indicate the hormonal activity of the tumour. The hormonal findings are summarized in Table 1. The patient underwent endoscopic endonasal transsphenoidal surgery with perioperative hydrocortisone cover. A total resection of the pituitary lesion was achieved. Pathological examination revealed a gonadotroph pituitary neuroendocrine tumour (PitNET) with positive FSH, LH, and alpha-subunit staining.

Due to the postoperative hypopituitarism, the patient was started on hydrocortisone and levothyroxine. Due to hyperglycaemia and an elevated glycated haemoglobin (HbA_{1c}) (7.4%), he was diagnosed with diabetes mellitus and prescribed metformin. During the 3-month follow-up, he complained of muscle

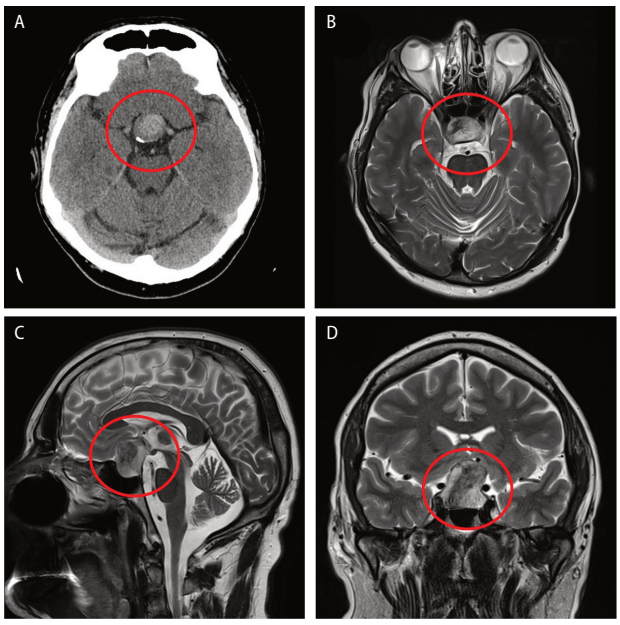

Figure 1. *Computed tomography (CT) (***A***) and magnetic resonance imaging (MRI): axial (***B***), sagittal (***C***), coronal (***D***) scans presenting a large sellar mass with suprasellar extension and intratumoural haemorrhage*

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Table 1. *Hormonal parameters at the time of pituitary apoplexy diagnosis and in the 12-month follow-up*

Parameter	Time					
	At the time of diagnosis	1 month after the surgery	3 months after the surgery	6 months after the surgery	12 months after the surgery	Reference range
ACTH [pg/mL]	25.3	3.27	–	2.76	12.17	6.0–48.0
Cortisol [μg/dL]	21.4	< 0.3	–	< 0.3	< 0.3	3.7–19.4
TSH [μIU/mL]	0.761	0,181	–	0.027	< 0.08	0.35–4.95
FT4 [ng/dL]	0.69	0.6	0.73	1.1	1.22	0.7–1.48
FT3 [pg/mL]	1.69	1.71	2.12	2.56	2.81	1.58–3.91
LH [μIU/mL]	1.8	0.3	–	–	–	0.6–12.1
FSH [mIU/dL]	8.26	1.07	–	–	–	0.95–11.95
Testosterone [nmol/L]	0.69	0.07	22.39	25.60	24.23	12.0–32.0
IGF-1 [ng/mL]	129.6	54.38	58.00	34.88	147.75	44–248
Prolactin [mIU/mL]	89.1	–	–	241.6	–	72.7–407.4

ACTH — adrenocorticotropic hormone; TSH — thyroid-stimulating hormone; FT3 — free triiodothyronine; FT4 — free thyroxine; LH — luteinizing hormone; FSH — follicle-stimulating hormone; IGF-1 — insulin-like growth factor

weakness, decreased libido, and erectile dysfunction. Testosterone replacement therapy with testosterone enanthate was introduced. At the 6-month follow-up, decreased insulin-like growth factor (IGF-1) concentration was noted (35 ng/mL, RR: 44.0–248), indicating growth hormone (GH) deficiency. Thanks to the National Program of Severe Growth Hormone Deficiency Treatment in Adults in Poland [1], recombinant human GH (rhGH) therapy was implemented. He required hydrocortisone and levothyroxine dose adjustments during the rhGH introduction and dose titration.

The patient is still followed up at our department. The ophthalmological deficits improved but did not resolve completely. The hormonal parameters during the 12 months of observation are summarized in Table 1.

The presented case illustrates pituitary apoplexy (PA) in the patient as the first manifestation of non-functioning PitNET (NF-PitNET). PA is a rare and potentially life-threatening neuroendocrine emergency that is a complication of acute intratumor ischaemia and/or haemorrhage of PitNET [2, 3]. NF-PitNETs, especially macroadenomas, seem to have a higher risk of apoplexy [4]. However, NF-PitNETs are usually larger and more frequent than functional adenomas, which could be the explanation of PA prevalence in these tumours [3]. Males are affected more frequently than females [2]. Various factors have been suggested to increase the risk of PA in patients with PitNETs. However, the latest large, last-decade-based analysis identified arterial hypertension, diabetes mellitus, and anticoagulation/antiplatelet therapy as the most frequent comorbidities (or risk factors) [3]. The presented patient suffered from arterial hypertension before PA and was diagnosed with diabetes shortly thereafter. Thus, he had 2 main risk factors for PitNET PA occurrence.

The ideal management protocol for PA remains debated. Acute adrenal insufficiency is the main cause of mortality in PA; therefore, prompt glucocorticoid administration is mandatory. Conservative treatment with careful monitoring is recommended in patients with or without mild and non-progressive neuro-ophthalmological deficits. On the other hand, in the case of more severe clinical presentation, neurosurgical intervention is required [2, 5]. The described patient presented with significant visual impairment accompanied by compression and displacement of the optic chiasm. Therefore, he underwent urgent decompressive surgery with gross tumour resection. PA management should be individualized in each case and result from a multidisciplinary decision.

Conflict of interest

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