Growth Hormone-Mediated Diabetic Ketoacidosis: A Rare Presentation of Acromegaly

Waraporn Polamuang[1], Thanyaporn Angsuwatcharakorn[2,3], Sakun Santisukwongchote[4], Sarat Sunthornyothin[3,5], Thiti Snabboon[3,5,*]

ABSTRACT

Acromegaly is a chronic disorder caused by pathological hypersecretion of growth hormone (GH), most commonly due to pituitary somatotroph adenomas. Excess GH leads to elevated insulin-like growth factor 1 (IGF-1) levels, which together mediate progressive physical changes and a wide range of systemic complications. A key metabolic abnormality in acromegaly is impaired glucose metabolism, which may result in diabetes through mechanisms of insulin resistance. This report describes a case of diabetic ketoacidosis (DKA), a severe complication of relative insulin deficiency, presenting as a rare initial manifestation of acromegaly. Following surgical intervention and remission of acromegaly, the glycemic control of the patient significantly improved, underscoring the importance of addressing the underlying endocrinopathy. This report highlights the critical need for comprehensive clinical evaluations in patients with common metabolic disorders, such as diabetes mellitus, to identify rare underlying causes and ensure timely diagnosis. Furthermore, it examines potential mechanisms of ketosis in acromegaly and reviews current approaches to glycemic management in this population, where evidence-based guidelines remain limited.

KEYWORDS

diabetic ketoacidosis; acromegaly; pituitary adenoma; hyperprolactinemia

AUTHOR AFFILIATIONS

[1] Department of Medicine, Prapokklao Hospital, Chanthaburi province, Thailand
[2] Department of Medicine, Somdet Phra Phutthaloetla Hospital, Samut Songkhram province, Thailand
[3] Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[4] Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[5] Excellence Centre in Diabetes, Hormone and Metabolism, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand
* Corresponding author: Excellence Centre in Diabetes, Hormone and Metabolism, Division of Endocrinology and Metabolism, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Rama IV Road, Patumwan, Bangkok 10330, Thailand; Thiti.S@chula.ac.th

Received: 10 September 2025
Accepted: 6 March 2026
Published online: 26 May 2026

Acta Medica (Hradec Králové) 2026; 69(1): 32–36
https://doi.org/10.14712/18059694.2026.14

INTRODUCTION

Acromegaly is an endocrine disorder characterized by chronic hypersecretion of growth hormone (GH), most commonly resulting from a pituitary somatotroph adenoma. Excess GH and its downstream effector, insulin-like growth factor-1 (IGF-1), result in characteristic phenotypic changes and a broad spectrum of systemic complications, including cardiovascular, respiratory, metabolic, musculoskeletal, and neurological involvement (1, 2). In addition, tumor mass effects may cause headaches or visual disturbances.

A major metabolic consequence of acromegaly is impaired glucose homeostasis, with diabetes mellitus reported in up to 53% of affected patients (3, 4). Furthermore, the prevalence of acromegaly among individuals with diabetes is 25- to 75-fold higher than in the general population (3, 5). The presence of diabetes in acromegaly is associated with diminished quality of life and adverse long-term prognosis. While insulin resistance is the principal mechanism underlying metabolic complications in acromegaly (6), this report describes a case of diabetic ketoacidosis (DKA), indicative of an absolute or relative insulin deficiency state, as the initial clinical manifestation of acromegaly. This study also discusses the underlying pathophysiology and therapeutic strategies for managing diabetes in this context.

CASE REPORT

A 46-year-old woman presented with a 5-day history of epigastric pain and dyspnea. Her medical history was notable for unintentional weight loss of 6 kg over the preceding 4 months. On admission, she was febrile (37.8 °C), tachycardic (120 beats/min), and exhibited Kussmaul respirations, with a blood pressure of 136/90 mmHg and a body mass index (BMI) of 28.48 kg/m² (weight 72 kg). Initial laboratory studies showed severe hyperglycemia, a plasma glucose level of 503 mg/dL and an HbA1c of 12.3%. Serum b-hydroxybutyrate was elevated at 3.9 mmol/L (reference 0.2–0.27 mmol/L; enzymatic spectrophotometric assay). Mild azotemia was present, with blood urea nitrogen of 50 mg/dL (reference 7–20 mg/dL) and serum creatinine of 1.9 mg/dL (reference 0.6–1.1 mg/dL). Serum electrolytes showed sodium 133 mmol/L, potassium 3.8 mmol/L, chloride 105 mmol/L, and bicarbonate 11 mmol/L, with an anion gap of 17 mmol/L. Venous blood gas analysis indicated metabolic acidosis with pH 7.254, pCO_2 15.1 mmHg, and HCO_3 6.7 mmol/L. Serum lactate was normal at 0.9 mmol/L

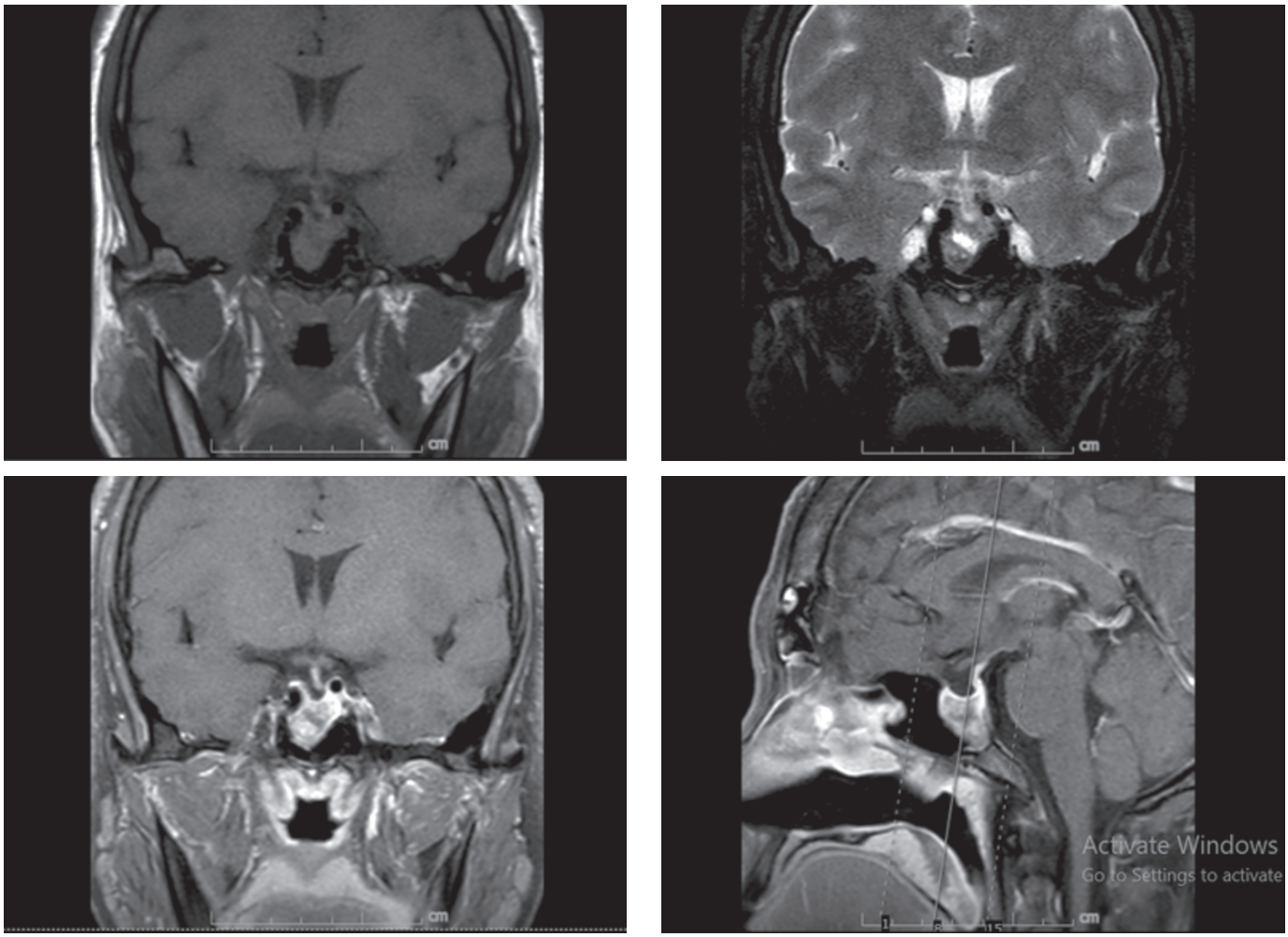

Fig. 1 Pituitary MRI showing a heterogeneously enhancing intrasellar mass (1.7×1.9×1.9 cm) with inferior extension into the sphenoid sinus. Coronal views: (A) T1-weighted, (B) post-contrast T1-weighted, (C) T2-weighted; (D) sagittal view.

(reference 0.5–2.0 mmol/L) and the effective serum osmolarity was 293 mOsm/kg (reference 275–295 mOsm/kg). Complete blood count revealed leukocytosis (white blood cell count, 12.0×10⁹/L) with marked neutrophilia (92%). The patient was diagnosed with DKA precipitated by primary *Klebsiella pneumoniae* bacteremia without an identifiable source of infection. Management was initiated according to institutional DKA protocols, including aggressive intravenous fluid resuscitation with isotonic saline, continuous intravenous insulin infusion at 7 units/hour, potassium supplementation, and close biochemical monitoring. Ketoacidosis resolved within 12 hours, after which insulin therapy was transitioned to a subcutaneous basal-bolus regimen, with subsequent normalization of renal function and serum electrolytes. Intravenous ceftriaxone was started based on antimicrobial susceptibility testing and subsequently de-escalated to oral amoxicillin-clavulanate on hospital day 7 to complete a 14-day course. The patient was discharged in stable condition on subcutaneous premixed insulin, with a total daily dose of 90 units.

Further history revealed progressive facial changes, a 10-kg weight gain, increased snoring, and amenorrhea over the past 6 years. Re-examination revealed distinctive acromegalic features, including frontal bossing, macroglossia, prognathism, and spade-like hands. Ophthalmologic evaluation demonstrated normal visual fields and fundoscopic findings. Hormonal evaluation confirmed the diagnosis of acromegaly, with markedly elevated IGF-1 levels at 662 ng/mL (reference 74–196 ng/mL) and non-suppressible GH during an oral glucose tolerance test (OGTT) (nadir GH 22.8 ng/mL; normal <1 ng/mL). Prolactin was moderately elevated at 100.3 ng/mL (reference 5.2–26.5 ng/mL). Thyroid function tests showed euthyroid state: thyroid-stimulating hormone (TSH) 1.028 mIU/mL (reference 0.70–1.48 mIU/mL), free thyroxine (FT_4) 0.99 ng/mL (reference 0.35–4.94 ng/mL). Morning cortisol was within normal ranges at 7.0 mg/dL (reference 3.7–19.4. mg/dL). Gonadotropin levels were follicle-stimulating hormone (FSH) 11.0 mIU/mL (reference 3.03–8.08 mIU/mL), luteinizing hormone (LH) 3.1 mIU/mL (reference 1.8–11.78 mIU/mL), and estradiol < 5.00 pg/mL (follicular-phase reference 21–251 pg/mL), consistent with hypogonadism. Pituitary magnetic resonance imaging (MRI) identified a macroadenoma without optic chiasm compression (Figure 1). The patient underwent transsphenoidal surgery with complete tumor resection, and histopathological examination confirmed a mammosomatotroph adenoma (Figure 2). At the 6-month follow-up, biochemical remission was achieved, with normalized IGF-1 levels (160.2 ng/mL), appropriate GH suppression, and normal prolactin levels. Follow-up MRI demonstrated

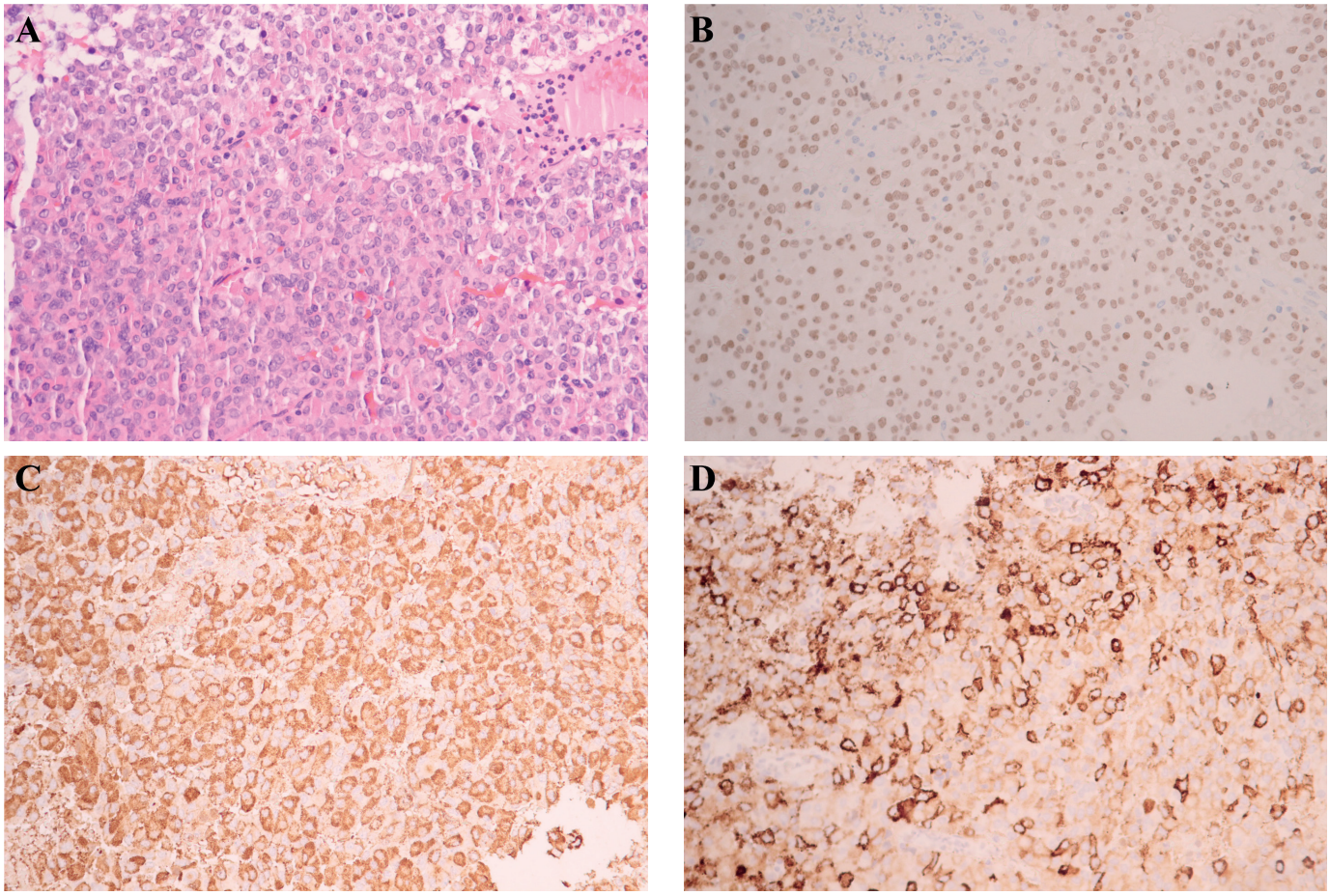

Fig. 2 Histology of the pituitary tumor. (A) H&E stain (40×) showing tumor cells with round nuclei, distinct nucleoli, stippled chromatin, and eosinophilic cytoplasm. Immunohistochemistry showing positive staining for (B) nuclear PIT-1, (C) cytoplasmic GH, and (D) cytoplasmic prolactin.

no residual tumor. Glycemic control improved significantly, with HbA1c decreasing to 6.5%, allowing discontinuation of insulin therapy. Subsequent evaluation revealed preserved b-cell function (C-peptide 3.0 ng/mL; reference 0.78–5.19 ng/mL) and negative anti-glutamic acid decarboxylase (anti-GAD) antibodies. Optimal glycemic control was maintained with combined dipeptidyl peptidase-4 (DPP-4) inhibitor and metformin therapy.

DISCUSSION

Acromegaly presents a significant diagnostic challenge due to its insidious clinical progression and frequent misdiagnosis as more common conditions. Consequently, diagnosis is often delayed by five to ten years (7), which increases the risk of preventable complications such as cardiovascular diseases, metabolic derangements, and malignancies (1, 8). This case report illustrates that GH excess can precipitate severe dysglycemic states, notably DKA, and also highlights the diagnostic and therapeutic challenges of managing diabetes secondary to acromegaly.

The metabolic actions of GH and IGF-1 mediate the disordered carbohydrate metabolism observed in acromegaly. GH exerts predominantly diabetogenic effects by inducing hepatic and peripheral insulin resistance, which results in reduced glucose uptake and increased hepatic gluconeogenesis. In contrast, IGF-1 enhances insulin sensitivity and stimulates pancreatic b-cell insulin secretion; however, these compensatory mechanisms are insufficient to overcome GH-induced insulin resistance, resulting in net hyperglycemia (2, 3, 6). Notably, the characteristics of insulin resistance in acromegaly differ from those observed in type 2 diabetes, as it is primarily mediated by GH excess rather than obesity or visceral adiposity. The severity of these metabolic complications correlates with circulating GH levels and is further influenced by factors such as age, disease duration, BMI, hypertension, female sex, and family history of diabetes (4, 5, 8).

DKA is a life-threatening acute metabolic complication of diabetes mellitus, characterized by hyperglycemia, ketosis, and high-anion gap metabolic acidosis. It results from absolute or relative insulin deficiency, typically in the setting of an elevated glucagon-to-insulin ratio. In acromegaly, chronic GH excess promotes lipolysis, resulting in elevated circulating free fatty acids that enhance hepatic ketogenesis and contribute to b-cell dysfunction through glucolipotoxicity. Consequently, in addition to its effects on insulin resistance, prolonged GH exposure may induce a state of relative insulin deficiency (9, 10). In this patient, longstanding hyperglycemia, reflected by a markedly elevated HbA1c, was likely driven by undiagnosed acromegaly and precipitated into DKA by infection and dehydration. The absence of autoimmune markers and the recovery of endogenous insulin secretion following remission of acromegaly support the reversibility of this metabolically decompensated state. These findings highlight that acromegaly-associated diabetes may progress from isolated insulin resistance to compromised b-cell functional reserve, predisposing susceptible individuals to DKA during metabolic stress, consistent with a ketosis-prone phenotype (11). However, C-peptide, insulin, and glucagon levels were not measured during the acute episode, precluding confirmation of this proposed mechanism.

Diagnosing acromegaly in patients with diabetes presents additional challenges because poorly controlled hyperglycemia may suppress IGF-1 levels and compromise the reliability of the OGTT. Therefore, achieving glycemic control before the hormonal evaluation is essential for accurate interpretation (12, 13). Currently, disease-specific guidelines for managing diabetes secondary to acromegaly remain limited; thus, treatment generally follows standard protocols for type 2 diabetes mellitus (14). Metformin remains the first-line therapy due to its insulin-sensitizing effects and suppression of hepatic glucose production. Incretin-based therapies, including DPP-4 inhibitors and glucagon-like peptide-1 receptor (GLP-1R) agonists, as well as sodium-glucose cotransporter-2 (SGLT2) inhibitors, may be preferred over thiazolidinediones or insulin secretagogues (sulfonylureas and repaglinide) because of their cardiovascular benefits, which are particularly relevant for acromegaly patients at increased cardiovascular risk.

Surgical resection of the adenoma, the definitive treatment for acromegaly, significantly improves glucose tolerance, with diabetes resolving in approximately two-thirds of patients who achieve remission (6, 10). For those with persistent disease or requiring preoperative management, medical options including somatostatin receptor ligands (SRLs), dopamine agonists, and GH receptor antagonists are effective in controlling acromegaly and improving glycemic control. However, pasireotide, a second-generation multi-ligand SRL, may worsen glucose metabolism by suppressing insulin and incretin secretion; therefore, it should be avoided in patients with impaired glucose tolerance or poorly controlled diabetes (15). Radiotherapy, considered a third-line treatment for acromegaly, has inconclusive effects on glucose metabolism.

In our patient, the pathological examination revealed a mammosomatotroph adenoma, a Pit-1 lineage tumor subtype that secretes both GH and prolactin (16). Clinically, this subtype closely resembles a densely granulated somatotroph tumor but is distinguished by more pronounced hyperprolactinemia and a higher prevalence among younger patients with acromegaly or gigantism. While data regarding medical treatment responses are limited, mammosomatotroph adenomas generally respond to somatostatin analogs and may also benefit from dopamine agonist therapy.

CONCLUSION

This case demonstrates DKA as a rare but preventable manifestation of acromegaly. It underscores the importance of comprehensive evaluation in patients with common disorders such as diabetes, which requires thorough history taking, careful physical examination, and appropriate investigations to identify underlying etiologies.

REFERENCES

1. Colao A, Grasso LFS, Giustina A, et al. Acromegaly. Nat Rev Dis Primers. 2019; 5: 20.
2. Gadelha MR, Kasuki L, Lim DST, Fleseriu M. Systemic complications of acromegaly and the impact of the current treatment landscape: an update. Endocr Rev. 2019; 40: 268–332.
3. Ferraù F, Albani A, Ciresi A, Giordano C, Cannavò S. Diabetes secondary to acromegaly: physiopathology, clinical features and effects of treatment. Front Endocrinol (Lausanne). 2018; 9: 358.
4. Rosario PW. Frequency of acromegaly in adults with diabetes or glucose intolerance and estimated prevalence in the general population. Pituitary. 2011; 14: 217–21.
5. Suda K, Fukuoka H, Iguchi G, et al. The prevalence of acromegaly in hospitalized patients with type 2 diabetes. Endocr J. 2015; 62: 53–9.
6. Esposito D, Boguszewski CL, Colao A, et al. Diabetes mellitus in patients with acromegaly: pathophysiology, clinical challenges and management. Nat Rev Endocrinol. 2024; 20: 541–52.
7. Ganokroj P, Sunthornyothin S, Siwanuwatn R, et al. Clinical characteristics and treatment outcomes in acromegaly, a retrospective single-center case series from Thailand. Pan Afr Med J. 2021; 40: 31.
8. Puder JJ, Nilavar S, Post KD, Freda PU. Relationship between disease-related morbidity and biochemical markers of activity in patients with acromegaly. J Clin Endocrinol Metab. 2005; 90: 1972–8.
9. Yoshida N, Goto H, Suzuki H, et al. Ketoacidosis as the initial clinical condition in nine patients with acromegaly: a review of 860 cases at a single institute. Eur J Endocrinol. 2013; 169: 127–32.
10. Moustaki M, Paschou SA, Xekouki P, et al. Secondary diabetes mellitus in acromegaly. Endocrine. 2023; 81: 1–15.
11. Yotsapon T, Sarat S. Clinical characteristics and long-term follow-up of ketosis-prone diabetes in Thai patients. Exp Clin Endocrinol Diabetes. 2014; 122: 303–7.
12. Rosario PW, Calsolari MR. Safety and specificity of the growth hormone suppression test in patients with diabetes. Endocrine. 2014; 48: 329–33.
13. Dobri G, Niwattisaiwong S, Bena JF, et al. Is GH nadir during OGTT a reliable test for diagnosis of acromegaly in patients with abnormal glucose metabolism? Endocrine. 2019; 64: 139–46.
14. Baroni MG, Giorgino F, Pezzino V, Scaroni C, Avogaro AJ. Italian Society for the Study of Diabetes (SID) / Italian Endocrinological Society (SIE) guidelines on the treatment of hyperglycemia in Cushing's syndrome and acromegaly. J Endocrinol Invest. 2016; 39: 235–55.
15. Melmed S, di Filippo L, Fleseriu M, et al. Consensus on acromegaly therapeutic outcomes: an update. Nat Rev Endocrinol. 2025 Nov; 21(11): 718–37.
16. Asa SL, Mete O, Perry A, Osamura RY. Overview of the 2022 WHO Classification of Pituitary Tumors. Endocr Pathol. 2022; 33: 6–26.