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A Rare Metabolic Paradox: Diabetic Ketoacidosis Presenting as the Initial Symptom in Undiagnosed Acromegaly

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ABSTRACT

Acromegaly is a rare endocrine disorder resulting from the chronic hypersecretion of growth hormone, usually as a result of a pituitary adenoma. While insulin resistance and secondary diabetes mellitus are common metabolic complications of acromegaly, diabetic ketoacidosis is an extremely rare manifestation of the disease. In this report, we present a case of a 28-year-old female patient who presented with vomiting, abdominal pain, and shortness of breath to the emergency department and was found to have severe hyperglycemia and metabolic acidosis consistent with DKA. The patient had the characteristic signs of acromegaly, including an enlarged jaw, macroglossia, coarse facial features, and enlarged hands and feet. The patient's imaging studies revealed a 2.2x2.9x2.2 cm sellar-suprasellar mass with extension into the cavernous sinus, consistent with a pituitary macroadenoma. The patient was managed with the standard DKA protocol and then referred for endocrine evaluation and management of her acromegaly. This case report highlights the extremely rare occurrence of DKA as a possible cause of undiagnosed and untreated acromegaly and the importance of a thorough clinical evaluation and early diagnosis of endocrine disorders in patients with acute metabolic

decompensation syndromes. Diabetic ketoacidosis is an extremely rare cause of acromegaly. High insulin resistance caused by growth hormone can rarely cause dysfunction of the pancreatic beta cells and ketoacidosis. The presence of characteristic signs of acromegaly in patients with diabetic ketoacidosis can aid in early diagnosis and endocrine treatment.

Keywords: Acromegaly; Diabetic ketoacidosis; Pituitary macroadenoma; Insulin resistance; Secondary diabetes mellitus

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INTRODUCTION

Acromegaly is a chronic endocrine disorder characterized by excessive production of growth hormone (GH) following epiphyseal closure, usually as a result of a pituitary adenoma secreting growth hormone (1). The excess growth hormone is converted into insulin-like growth factor-1 (IGF-1), which in turn leads to the characteristic somatic changes of the disease, including enlargement of hands and feet, prognathism, macroglossia, frontal bossing, and deepening of the voice (1). Due to the insidious onset of the disease, it is usually diagnosed after a delay of several years following the onset of the first symptoms.

In addition to the somatic changes of the disease, acromegaly is associated with a variety of systemic complications, including hypertension, cardiomyopathy, obstructive sleep apnea, and metabolic disturbances (2). Amongst these, glucose metabolism disturbances are particularly common in patients with acromegaly. Growth hormone has anti-insulin effects, which are mediated through its ability to stimulate gluconeogenesis, glycogenolysis, and lipolysis, as well as reducing glucose uptake in the body (4). These effects of growth hormone can cause insulin resistance and secondary diabetes mellitus in a significant proportion of patients with acromegaly (4, 8). Approximately one-third of patients with acromegaly are known to develop diabetes mellitus during the natural course of their illness (4). However, diabetic ketoacidosis is seldom described in these patients. The prevalence of DKA in patients with acromegaly is estimated to be around 1% (3). This is primarily due to the fact that in acromegaly, insulin resistance is more common than insulin deficiency. However, there are some reported cases of DKA presenting as the initial manifestation of acromegaly (5, 7). We are presenting this rare case of diabetic ketoacidosis in a patient with previously undiagnosed acromegaly, which highlights the need to diagnose subtle phenotypic manifestations of this endocrine disorder in emergencies.

Case History and Examination

A 28-year-old female from Kalar Sayedan, Rawalpindi, presented to the Emergency Department of Holy Family Hospital on 21st October 2025 complaining of a two-day history of vomiting and abdominal pain, and a one-day history of shortness of breath. The vomiting was sudden in onset, persistent, non-projectile, and contained gastric contents. It was accompanied by headache, dizziness, and somnolence. Her abdominal pain was described as

sudden, continuous, crampy, and mild-to-moderate in intensity, with no radiation, aggravating, or relieving factors. The patient also reported progressive exertional dyspnea over the preceding 24 hours, with no associated orthopnea, paroxysmal nocturnal dyspnea, fever, cough, or chest pain.

Upon further evaluation, the patient noted a progressive enlargement of her hands, feet, jaw, and tongue over the past seven years. She also reported left-sided headaches that were gradual in onset and progressive, though she denied any history of seizures, visual disturbances, photophobia, or focal weakness. One week before admission, she experienced polyuria, polydipsia, and polyphagia, alongside a deepening of her voice, increased skin pigmentation on her face, axilla, and posterior neck, and excessive hair growth on her face and extremities. Progressive joint pain, primarily involving the knees, was partially managed with over-the-counter analgesics. She had no known prior history of hypertension or diabetes mellitus.

Her past surgical history included an uncomplicated right oophorectomy for an ectopic pregnancy in 2019 and a lower-segment cesarean section in 2021, both performed at Holy Family Hospital. There were no complications from these surgeries.

The patient's vital signs were as follows: blood pressure 140/90 mmHg, pulse rate 89 beats per minute, respiratory rate 26 breaths per minute, and temperature 97°F. Oxygen saturation was 98% on room air, and her capillary blood glucose was markedly elevated at 438 mg/dL. Distinct acromegalic features were noted, including macroglossia, thick and greasy skin with excessive hair growth, and a pronounced enlargement of the nose, ears, and jaw. The patient remained conscious but was in evident respiratory distress.

Diagnosis, Investigations, and Differentials

Based on the presenting signs, the differential diagnoses focused on diabetic ketoacidosis, hyperosmolar hyperglycemic state, acute pancreatitis, and metabolic acidosis secondary to severe infection. Laboratory workup confirmed a diagnosis of severe diabetic ketoacidosis, revealing profound hyperglycemia, metabolic acidosis, and ketonemia. Baseline arterial blood gas analysis showed a pH of 7.06, PCO₂ of 15.6 mmHg, and HCO₃ of 4.4 mEq/L. Serum ketones were positive, and the remaining complete blood count parameters fell within normal limits. Subsequent endocrine workup revealed markedly elevated serum Growth Hormone levels at 99 ng/ml (normal: 2–5 ng/ml) and a serum IGF-1 level of 813.7 ng/ml (normal: 135–449 ng/ml). Other pituitary hormone axes were unremarkable. Within two days of standard management, metabolic parameters normalised, yielding a pH of 7.43, PCO₂ of 25.3 mmHg, and HCO₃ of 17.1 mEq/L. Urinalysis confirmed significant ketonuria.

Magnetic resonance imaging (MRI) of the brain using a dedicated pituitary protocol revealed a large sellar-suprasellar mass measuring 2.2 x 2.9 x 2.2 cm. The lesion demonstrated extension into the left cavernous sinus and the infratemporal fossa, meeting criteria for Knosp Grade 4. The mass directly involved the optic chiasm, and the left internal carotid artery was noted to be enlarged, highly suggestive of an invasive pituitary macroadenoma.

Treatment, Outcomes, and Follow-up

The patient was immediately stabilised using the standard diabetic ketoacidosis protocol, comprising aggressive intravenous fluid resuscitation, continuous insulin infusion, and careful electrolyte replacement. Hyperglycemia and metabolic acidosis were successfully corrected over 48 hours. Following stabilization, her care was co-managed with endocrine and neurosurgical teams for definitive intervention of the pituitary macroadenoma. The patient and her family were thoroughly counseled on management pathways, including transsphenoidal surgery and medical management utilizing dopamine agonists or somatostatin analogues. She was discharged with instructions for close outpatient follow-up to monitor glycemic control, hormonal status, and tumour progression.

DISCUSSION

Acromegaly is a chronic endocrine disorder involving prolonged exposure to excessive amounts of growth hormone and increased levels of insulin-like growth factor-1. It is usually the result of a pituitary adenoma (1). Due to the slow and insidious nature of the disease's progression, the diagnosis is frequently not made until several years after the initial symptoms. Metabolic abnormalities are the most common complication in patients diagnosed with acromegaly. Growth hormone has considerable anti-insulin effects on the body. It increases the production of glucose in the liver and decreases the uptake of glucose in the periphery (4, 8). Consequently, insulin resistance occurs in many patients suffering from acromegaly and can eventually result in impaired glucose tolerance and diabetes mellitus (4, 6). Diabetes mellitus occurs in 30-40% of the patients suffering from acromegaly (4).

Despite the strong association between the two endocrine disorders, diabetic ketoacidosis is an extremely rare complication. Several institutional studies found the incidence of diabetic ketoacidosis as the initial manifestation in a small fraction of patients suffering from acromegaly (3). The rarity of DKA in acromegaly can be explained by the underlying pathophysiological mechanisms. Although the pathophysiological mechanisms underlying acromegaly involve insulin resistance as the main effect of GH, the pathophysiological mechanisms underlying DKA involve absolute insulin deficiency as the main cause. However, it is possible that the effects of prolonged insulin resistance could eventually lead to exhaustion and impaired function of the pancreatic beta-cells, which could eventually cause ketosis and metabolic acidosis. In the above case, the patient has a seven-year history of progressive acromegaly, which could indicate that the effects of the underlying pathophysiological mechanisms have persisted over the years, eventually leading to the development of diabetic ketoacidosis.

The treatment of acromegaly involves both surgical and medical management. The first-line treatment for the management of pituitary adenoma is transsphenoidal surgery. The medical management involves the administration of somatostatin receptor ligands, dopamine receptor agonists such as cabergoline, and GH receptor antagonists (9). The administration of cabergoline has been found to be effective in the treatment of acromegaly, especially in the subgroup of patients with adenomas that secrete co-existing prolactin (9). This case also emphasizes the need to perform a thorough physical examination to identify the typical features

of acromegaly in the setting of acute metabolic disorders. Early identification of subtle phenotypic features may lead to early diagnosis, thereby preventing the long-term consequences of untreated or delayed disease. However, this report also has some limitations in that, being a case report, the findings cannot be generalized to the general population. Secondly, markers of pancreatic beta-cell function, such as C-peptide levels, were not measured, making it difficult to differentiate between relative and absolute insulin deficiency. Thirdly, follow-up data regarding glycemic control were not available.

This case report contributes to the sparse literature regarding diabetic ketoacidosis as a presenting feature of undiagnosed acromegaly, and the need to maintain a high degree of suspicion in patients presenting with clinical features suggestive of this condition. This case illustrates a rare metabolic paradox, wherein severe diabetic ketoacidosis presented as a late complication of long-standing undiagnosed acromegaly in a young woman without prior diabetes, a phenomenon observed in fewer than 1% of acromegaly patients, predominantly males. In contrast to prior reports of early metabolic decompensation, our patient exhibited seven years of progressive acromegalic features, markedly elevated GH (99 ng/mL), and a Knosp grade 4 macroadenoma with invasion of the cavernous sinus, internal carotid artery, and optic chiasm, accompanied by hirsutism, hyperpigmentation, and arthralgias—features suggesting substantial tumor burden contributed to beta-cell exhaustion amid GH-induced insulin resistance. These findings emphasise the need for careful clinical evaluation of acromegalic signs in patients with acute metabolic disturbances to facilitate early diagnosis and intervention.

CONCLUSION

This case represents an unusual metabolic paradox where severe diabetic ketoacidosis developed as a complication of long-standing undiagnosed acromegaly. Although glucose metabolism abnormalities are common in patients with acromegaly, DKA is a rare complication, occurring in fewer than 1% of patients and usually with severe metabolic stress or beta-cell dysfunction. In this case, the presence of a large Knosp Grade 4 Pituitary Macroadenoma with markedly elevated GH levels and long-standing undiagnosed disease likely caused severe insulin resistance and subsequent beta-cell exhaustion. The case represents the importance of recognizing the phenotypic features of undiagnosed patients with acromegaly presenting with acute metabolic crises. By recognizing the phenotypic features of this patient with undiagnosed acromegaly presenting with an acute metabolic crisis, appropriate treatment of the underlying endocrine abnormality may be implemented to avoid further metabolic crises.

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Data Availability Statement

The data were taken from a patient who presented to our hospital; all data and references are publicly available on databases such as PubMed and Google Scholar.

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