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## Case Report

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# KETOACIDOSIS AS THE PRIMARY MANIFESTATION OF ACROMEGALY

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**Although diabetes mellitus is common in acromegaly, diabetic ketoacidosis (DKA) is rarely reported in this disease. Herein, we reported on a 41-year-old man with acromegaly whose first presentation was DKA. After treatment of acromegaly, his diabetes subsided. We concluded that, even in nondiabetic individuals, a high level of growth hormone can rarely cause DKA.**

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**Keywords:** Acromegaly • diabetic ketoacidosis • growth hormone

### Introduction

**A**lthough impaired glucose tolerance affects 36% and overt diabetes mellitus can be seen in 30% of cases with acromegaly,<sup>1</sup> diabetic ketoacidosis (DKA) is rarely reported in this disease. So far, only nine cases of acromegaly and DKA have been reported in the literature and in only four of them, DKA was the first presentation of acromegaly.<sup>2-5</sup>

### Case Report

A 41-year-old man was brought to the emergency room due to a decreased level of consciousness since 12 hours before admission. Since three weeks prior to admission, he had developed polyuria and polydipsia for which, he was visited by a local physician. Laboratory data, then, showed hyperglycemia and hypertriglyceridemia. Glibenclamide, 15 mg/day and clofibrate, 1000 mg/day were administered. Nonetheless, no significant improvement was achieved. Since three days before admission, his symptoms aggravated and he developed weakness and repeated episodes of vomiting and gradually became stuporous.

There was no history of fever. His family history was positive for the presence of hypertriglyceridemia in his father and brother, but there was no history of diabetes in his family. On admission, he was stuporous, severely dehydrated, and had Kussmaul respiration. Urinalysis revealed 3+ ketonuria and glucosuria. He had a plasma glucose of 893 mg/dL, a BUN of 25, K of 4.6 mEq/L, and Na of 135 mEq/L. Arterial blood gas analysis showed severe acidemia (pH: 6.94), an arterial PO<sub>2</sub> of 86 mmHg, bicarbonate level of 3.6 mEq/L, and severe hypocapnia (PCO<sub>2</sub>: 17.5 mmHg). Serum ketone was strongly positive with nitroprusside test in a ¼ dilution. With impression of DKA, treatment with intravenous fluid, potassium chloride, and insulin infusion, 10 U/hr was started. For a poor initial response, insulin dosage was increased to 20 U/hr. His serum ketone became negative after 14 hours. Later on, his blood sugar was controlled with 70 units of human NPH insulin. During the hospital course, he was noted to have acromegalic features (Figure 1). On direct questioning, he mentioned an enlarged shoe size during recent years, but he denied headache or visual disturbance. The diagnosis of acromegaly was established by finding a raised basal growth hormone (GH) level of 56 ng/mL, which increased to 62 ng/mL, 90 minutes after a 75 g oral glucose load. Hormonal assays revealed a luteinizing hormone level of 4.5 mIU/mL (NL: 0.5 – 11.2), follicle stimulating hormone of 6 mIU/mL (NL: 0.6 – 8.6), testosterone of 6 ng/mL (NL: 3 – 10),

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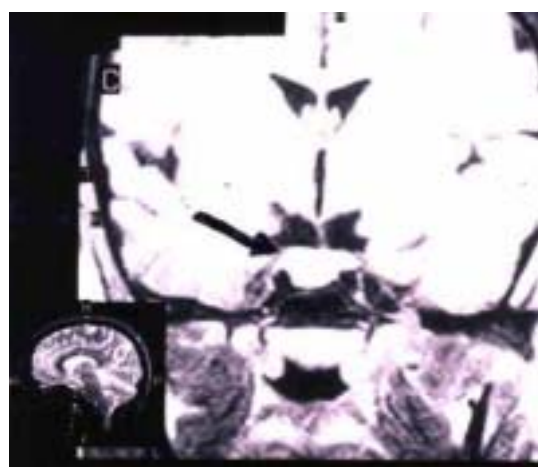
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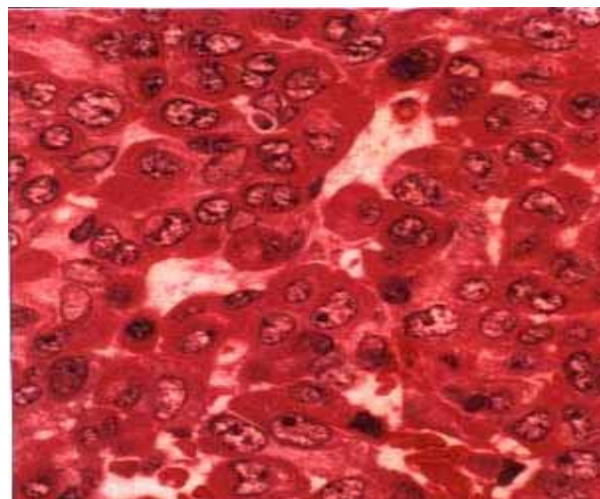
**Figure 1.** The patient's picture shows acromegalic features.

thyroid stimulating hormone of 1.2  $\mu\text{U/mL}$  (NL: 0.4 – 5.0), thyroxin level of 9.2  $\mu\text{g/dL}$  (NL: 5 – 12), a  $\text{T}_3$  resin uptake of 32% (NL: 25% – 35%), prolactin of 13 ng/mL (NL: 1.6 – 18), basal cortisol level of 12  $\mu\text{g/dL}$  (NL: 5 – 25), and a cortisol level after ACTH stimulation of 25  $\mu\text{g/dL}$  (NL: >18). Magnetic resonance imaging (MRI) of sella showed a macroadenoma of pituitary with extension to the left cavernous sinus (Figure 2).

Transsphenoid surgery was carried out one month after presentation. Pathological study of the pituitary mass revealed an acidophilic adenoma (Figure 3). The patient also received a course of radiotherapy. Basal GH, two months after the operation became 4.8 ng/mL that was suppressed to 2 ng/mL after a glucose load. Because of a repeated hypoglycemia in the second month post-operatively, the insulin dose was tapered down and then discontinued. In the fourth month post-



**Figure 2.** Magnetic resonance image of pituitary gland demonstrates macroadenoma.



**Figure 3.** A section of pituitary tumor revealing acidophilic adenoma (H & E  $\times 400$ ).

operatively, his fasting plasma glucose was 104 mg/dL. Two hours after giving 75 g glucose, it increased to 134 mg/dL. The patient has been followed up for three years and his fasting blood sugar has remained within the normal range, without taking any medication. His acromegaly is also in remission.

## Discussion

The effect of GH on glucose metabolism is complex. It has an acute insulin-like effect and a chronic insulin-antagonistic and diabetogenic action.<sup>6</sup>

So far, a number of mechanisms have been proposed for the diabetogenic effects of GH; GH causes impairment of the insulin action within 2 to 12 hours, with no effect on glucose-mediated insulin secretion.<sup>7</sup> The insulin resistance occurs primarily in muscles and is due to a postreceptor defect.<sup>7</sup> At the postreceptor level, GH decreases autophosphorylation of the insulin receptor and glucose transporters.<sup>8</sup> An increase in the hepatic glucose output has also been implicated as a cause of hyperglycemia in acromegaly.<sup>9</sup> The role of GH in DKA is not well-known. Some degree of insulin resistance is present in most patients with DKA.<sup>10</sup> However, an elevated plasma GH is not necessary for maintaining the insulin resistance during DKA.<sup>11</sup> These findings suggest that GH has at most, a small role in the pathogenesis of DKA, which explains the rarity of DKA in patients with acromegaly. In acromegaly, the glucagon level, not suppressible by glucose load, is increased.<sup>12</sup> Glucagon induces hepatic ketogenesis and is

important in the pathogenesis of DKA.<sup>13</sup> Moreover, certain GH by-products such as hGH 172 – 191 have more diabetogenic effects.<sup>14</sup> DKA occurs when the levels of counterregulatory hormones are significantly in excess of insulin. As a consequence, in a few patients with acromegaly, the levels of GH—including its more diabetogenic by-products—and glucagon are high enough so that even in the presence of insulin, can shift hormonal balance towards ketogenesis and ultimately to DKA. The mean basal GH level in previously reported cases of DKA and acromegaly (56 ng/mL), as that was observed in our patient, was higher than that in usual patients of acromegaly.<sup>15</sup>

Our patient and other reported cases needed higher doses of insulin for treatment of their DKA, which was due to the insulinresistance caused by excess amounts of GH. In three other reported cases,<sup>2, 4, 5</sup> as in our patient, diabetes was completely subsided after the acromegaly had been treated. This demonstrates that, even in nondiabetic individuals, excess GH can rarely cause DKA.

Although it is very rare, but DKA could be the primary manifestation of acromegaly.

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