Effect of somatotropin and IGF1 secretion on glucose metabolism: Diabetic ketoacidosis as first manifestation of acromegaly

Mª Joana Santos¹, Rui Almeida²,³, Olinda Marques¬¹³
1. Department of Endocrinology; 2. Department of Neurosurgery; 3. Pituitary Tumours Group, Hospital de Braga, Portugal

Introduction
Somatotropin (GH) and insulin have opposite effects in glucose and lipids metabolism and synergistic effects in the promotion of protein synthesis. In a healthy individual, in the postprandial period, insulin is the most important anabolic hormone as it promotes glucose and lipids storage. During fasting, the action of GH predominates, switching the preferential energetic substrate through stimulation of lipolysis and sparing the stored proteins. Through this mechanism, GH increases plasmatic free fatty acids and ketone bodies concentration, promoting hepatic and peripheral insulin resistance (Table 1).

Acromegaly
- Lipolysis and glycogenogenesis induced by GH may lead to decreased pancreatic insulin secretion, changes in the expression of the insulin gene and increased beta cell apoptosis.
- If insulin production is not able to counterbalance the increased insulin resistance, glucose intolerance or diabetes may appear. Rarely, when there is a relative/absolute insulin deficit and an excess of counterregulatory hormones, diabetic ketoacidosis may occur.
- The severity of glucose metabolism disturbance may be related to GH plasmatic concentrations (>25ng/ml).

Clinical cases (Table 2)

<table>
<thead>
<tr>
<th>Clinical cases (Table 2)</th>
<th>Case 1 Male, 26 years</th>
<th>Case 2 Male, 27 years</th>
<th>Case 3 Male, 35 years</th>
</tr>
</thead>
</table>
| Clinical presentation    | • Diabetic ketoacidosis as first manifestation of DM  
                         • No family history of DM  
                         • Clinically evident acromegaly → Pituitary macroadenoma |
| DM treatment             | Metformin 2g/day  
                         Insulin 0,26U/Kg/day |
|                         | Metformin 3g/day  
                         Insulin 1,28U/Kg/day |
|                         | No antidiabetic drugs in the first 2 months.  
                         Metformin 2g/day, Insulin 0,8U/Kg/day |
| Transsphenoidal surgery  | Partial remotion of the adenoma (January 2013) |
| Histologia               | GH diffuse  
                         GH dense |
| Evolution DM treatment   | Suspension after 8 m  
                         Metformin 3g/day, sitagliptin 100mg/day; insulin suspension after 3 months. |
| Acromegaly treatment     | Octreotide LAR 30mg  
                         Initial clinical presentation: pituitary apoplexy and panhypopituitarism.  
                         Octreotide LAR 20mg |
| Future                   | Radiosurgery |
|                         | Surgery |
|                         | Treatment: prednisolone, levothyroxine, testosterone. |

Conclusion:
Diabetic ketoacidosis is a very rare event in patients with acromegaly (1%). In our patients, its prevalence was 6,4% (N=47). In cases 1 and 2, initial GH secretion was very high and GH reduction led to a significant improvement in metabolic control. In case 3, glycemic control worsened probably due to the iatrogenic effect of prednisolone in a pancreas recently exposed to the glucolipotoxicity caused by GH. Somatotropin effects in carbohydrate metabolism and in the appearance of diabetic ketoacidosis in acromegaly are complex and not totally understood, but may be reversible with the reduction or normalization of GH levels.

Bibliography
2. Zuidam G. et al., Effects of growth hormone on glucose and insulin metabolism in healthy subjects: a randomized, double-blind, placebo-controlled trial, J Clin Endocrinol Metab. 1992 Dec;75(6):1673-7
3. Chen P. R., Salome P., Acromegaly, Endocrinol. 2006 Jan;251(S):17