DIABETES MELLITUS, CHRONIC COMPLICATION IN PATIENTS WITH ACROMEGALY: CASE REPORT AND REVIEW OF THE LITERATURE

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DIABETES MELLITUS, CHRONIC COMPLICATION IN PATIENTS WITH ACROMEGALY: CASE REPORT AND REVIEW OF THE LITERATURE (Abstract): Disturbances of glucose metabolism are frequently observed in patients with acromegaly. Excess amounts of GH and IGF1 interacts with metabolic regulation, and indeed, GH hypersecretion is associated with hepatic and peripheral insulin resistance; this and also other mechanisms are involved in the development of diabetes mellitus. It can quickly improve if the levels of GH decline after the therapy.

Case report: We present a patient of 54 years old, admitted in the clinic in 2009, with diagnosis of acromegaly. MRI scan reveals an expansive pituitary tumor 15/16/17 mm. Values of GH, IGF1 and blood glucose were much above normal. Body mass index 27, 5 kg/m². After 12 months of a medical treatment with somatostatin analogues, the evolution of blood parameters was favorable, but the patient has discontinued his treatment. At the hospitalization in 2012 there is a precarious control of the diabetes under oral antidiabetic agents. A new treatment has been applied: it was practiced surgical transsphenoidal ablation. At last admit, May 2014, the value IGF1 has been normal, GH has been below 1 ng/mL, and HbA1c was 5.27%. Dyslipidemic syndrome has been constantly present; the values of triglycerides and cholesterol should be a little more upper limit. Conclusions: Following successful treatment of acromegaly with surgery, glucose tolerance improves. Balancing type 2 diabetes, with return to normal HbA1c and the decrease in cholesterol and triglycerides values, represents the result of favorable normalization GH in our patients with acromegaly.

Keywords: DIABETES, ACROMEGALY, TRANSSPHENOIDAL SURGERY.

Acromegaly is a condition characterized by oversecretion of growth hormone (GH) and insulin-like growth factor 1 (IGF1). In 98% of cases hypersecretion due, to a pituitary somatotrophic adenoma; in the other cases (less than 2%) it is the result of over-secretion of Growth Hormone Releasing Hormone (GHRH) from a hypothalamic lesion or from a carcinoid tumor of the gut or pancreas(1). Occasionally acromegaly is found in association with glands, pancreatic islet cells, tumors like glucagonoma, insulinoma and gastrinoma, cutaneous tumors that include multiple angiofibromas, as part of Multiple Endocrine Neoplasia syndrome (MEN) Type 1 (2).
Disturbances of glucose metabolism are frequently observed in patients with acromegaly. The correlation between acromegaly and diabetes was noted as early as 1884 by Loeb (3). Some studies have shown that the incidence of hyperglycemia and glycosuria in acromegalic patients may vary between 10-40 % (4, 5, 6) or over 60% of patients with acromegaly include diabetes mellitus, impaired glucose tolerance and impaired fasting glucose (7, 8). French Acromegaly Registry reported a 22.3% incidence of diabetes mellitus (DM) in acromegalic patients (9). The diagnosis of acromegaly is usually delayed for years, exposing patients to slowly evolving chronic complications (8), that may include: high blood pressure (hypertension) cardiovascular disease, particularly enlargement of the heart (cardiomyopathy), osteoarthritis, diabetes mellitus, precancerous growths (polyps) on the lining of colon, sleep apnea, carpal tunnel syndrome, reduced secretion of other pituitary hormones (hypopituitarism), uterine fibroids, benign tumors in the uterus, spinal cord compression, vision loss. The development of carbohydrate metabolism disorders and/or progression to diabetes in patients with acromegaly may depend on several factors, such as age and gender (10), the levels of GH (11), as well as the duration of acromegaly and duration of exposure to elevated GH levels (9,11). A further possible factor involved in the early development of diabetes is a positive family history of DM (10, 12). A final factor that may also influence the development of glucose disturbances is the specific treatment for acromegaly. Somatostatin analogues may influence glucose metabolism both by lowering insulin secretion and by lowering GH and IGF1 levels (13, 14). The average interval between the onset of acromegaly and that of DM was 9.5 years; however, simultaneous onset of acromegaly and diabetes mellitus was noted in as many as 46.8% patients (9).

**CASE REPORT**

We present a patient of 54 years old, admitted in the clinic in 2009, with diagnosis of acromegaly. MRI scan reveals an expansive pituitary tumor 15/16/17 mm. Value of GH has been 74ng/mL, (N: 0-3), IGF1 has been 477 ng/mL (N: 93-410) and blood glucose was 168mg/dL. Body mass index (BMI) was 27.5 kg/m². A medical treatment with somatostatin analogues was initiated.

After 12 months of Sandostatin LAR- 20 mg/28 days, the evolution of blood parameters was favorable, but the patient has discontinued his treatment. At the hospitalization in 2012 there is a precarious control of the diabetes under oral antidiabetic agents: blood glucose was 325 mg/dL, HbA1c value was 9 % and the GH increased at 104ng/mL. A new treatment with the intention of the decrease in the GH has been applied: it was practiced surgical transsphenoidal ablation. The cyto-pathological interpretation: pituitary adenomas with somatotroph cells. Evolution after surgery was favorable. At last admit, May 2014, the value IGF1 has been normal, GH has been below 1 ng/mL, and HbA1c was 5.27 %. Joint dyslipidemic syndrome has been constantly present; the values of triglycerides and cholesterol should be a little more upper limit. BMI = 27 kg/m².

**DISCUSSION**

Disturbances of glucose metabolism in acromegaly can be explained by the direct hyperglycemic effects of GH excess. Excess amounts of GH and IGF1 interacts with
metabolic regulation, GH hyper-secretion is associated with hepatic and peripheral insulin resistance (15). Insulin resistance is also worsened by the lipolytic action of GH generating non-esterified fatty acids that act on the liver to increase hepatic glucose production and inhibit muscle utilization of glucose. Nabarro et al. (11) have reported the results of a large cohort of 208 patients among which 48 had diabetes. They found a significant correlation between age, duration of evolution of acromegaly, and GH level with the presence of diabetes but only by univariate analysis because of the insufficient size of the cohort. Biering et al. (16) have identified age but not GH level as risk factor for diabetes. Møller et al. (17) have studied insulin resistance in acromegalic patients before and after adenomectomy. They have demonstrated that insulin resistance in acromegalic patients is relieved after adenomectomy. The precise mechanism of insulin resistance in the presence of excessive chronic GH is still not clear. GH has a short-term insulin-like effect, but chronic exposure impairs insulin response. Cross talk between GH receptors and insulin receptors have been demonstrated. Hyperinsulinism, insulin resistance, and diabetes are well-recognized cardiovascular risk factors in general population and may contribute to the increased cardiac morbidity and mortality of acromegalic patients (18-21). Clinically, therefore, diabetes in acromegaly resembles Type 2 Diabetes. Diabetic complications, such as retinopathy, are rare but can be seen occasionally. Diabetic ketoacidosis is rare. Age at diagnosis of acromegaly, body mass index, hypertension and duration of evolution of acromegaly were significant independent risk factors associated with development of diabetes. For an acromegalic patient, the risk for the presence of diabetes was increased by 4.4% by age and 12.9% by additional BMI (kg/m²). Presence of hypertension increased the risk of diabetes by 2.5%. Prevalence of diabetes compared the studies, may be very different: The Spanish (22) and the Belgian registries (23) found a still higher incidence of 37.6 and 25.3% respectively. In the French Acromegaly Registry (9), the prevalence of diabetes was 22.3%. In a study published previously which observed the prevalence of DM in 213 patients with acromegaly, we found 24 cases of DM which represent 11.2 % (5). Diabetes was diagnosed at the same time as acromegaly in 46.8% of patients (9). For other patients, the discovery of diabetes predated the diagnosis of acromegaly with a mean duration of 5.8 years (9) or mean duration of active acromegaly before diagnosis 7.5 years as well as discrete female predominance (5, 12, 13). Although based on the clinical estimation and patient anamnesis, diabetes was present before the presumed beginning of acromegaly in 9.8% of patients (9) or in 20.8% (5). Complications are frequent and the consequences of a delayed diagnosis 5% of patients presented with arterial hypertension (5, 9) rheumatologically complications or pituitary deficiencies.

Diabetes was treated with diet, metformin alone, sulfonylureas associated with metformin, and insulin in 17.6-30% of patients (5, 9). Furthermore, after treatment of acromegaly, diabetes disappeared in 30% of the cases and treatment could be reduced in a number of other cases. Another question is the impact of different treatments of acromegaly in the evolution of diabetes. Ronchi et al. (24) have compared two somatostatin analogs (octreotide LAR versus lanreotide SR) describing a decrease in insulin resistance with both drugs, oc-
significant change was noted in acromegaly and Cushing syndrome.

HOMA-R and HOMA-b significantly decreased. Møller et al. (17) have showed a complete reversal of insulin resistance and glucose and lipid metabolism in acromegalic patients cured by adenomectomy. In a study by Kinoshita et al. (26), glucose metabolism in patients cured by surgery was improved when patients had preserved b-cell function.

CONCLUSIONS

In our patients with acromegaly, balancing type 2 diabetes, with return to normal HbA1c and the decrease in cholesterol and triglycerides values, represents the result to favorable normalization of GH.

REFERENCES


### NEWS

**SINGLE INCISION TRANS-UMBILICAL TOTAL HYSTERECTOMY: ROBOTIC OR LAPAROSCOPIC?**

The aim of this study was to compare the early surgical outcomes in patients who underwent total hysterectomy with laparoendoscopic single-site surgery (LESS-TH) versus robotic single-site total hysterectomy (RSS-TH). Methods: Twenty-four patients who underwent RSS-TH and thirty-four patients who underwent LESS-TH were retrospectively evaluated. Patient characteristics, operation time, intraoperative data (conversions, complications, estimated blood loss, etc.) and postoperative pain scores were compared. Results: The total operation time was significantly longer in the robotic surgery group, with a time of 98.5 vs. 86 min (p = 0.013), while vaginal closure time was significantly higher in the laparoscopic surgerygroup (p = 0.011). Intraoperative outcomes and postoperative pain scores were similar in the two groups. Conclusion: RSS-TH helps surgeons to overcome the technical disadvantages of LESS-TH, particularly vaginal cuff closure, ergonomics and instrument crowding and clashing. Early surgical outcomes are comparable in the two groups, and both techniques are safe and feasible. (Akdemir A, Yildirim N, Zeybek B, Karaman S, Sendag F. Single Incision Trans-Umbilical Total Hysterectomy: Robotic or Laparoscopic? Gynecol Obstet Invest 2015 Jan 27. Epub ahead of print)

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