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The impact of lipomatous tumors on type 2 diabetes: are adipose-derived tumors metabolically active?

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ABSTRACT

Background: The metabolic and immunologic properties of adipose tissue are linked to the pathogenesis of type 2 diabetes mellitus. Lipomatous tumors, such as liposarcomas, are rare but can reach significant size. We hypothesized that some lipomatous tumors are metabolically active and can alter systemic glucose homeostasis.
Methods: We performed a retrospective study of patients who underwent resection of a lipomatous tumor at a tertiary cancer referral center (2004-2015). We divided patients into nondiabetics, well-controlled diabetics (hemoglobin A1c [HbA1c] < 7), and poorly controlled diabetics (HbA1c ≥ 7). We compared patient demographics, tumor characteristics, and measures of glycemic control among these groups before and after tumor resection.
Results: We reviewed 217 operations for lipomatous tumors. No differences were observed in tumor characteristics in patients with and without diabetes. However, tumor characteristics differed significantly between the well-controlled and poorly controlled diabetics groups. Patients with poorly controlled diabetes had larger tumors that were more likely to be malignant, retroperitoneal, and well-differentiated. Tumor resection had no detectable impact on diabetes, as assessed by HbA1c, and requirement for diabetic medications.
Conclusions: Poorly controlled diabetes was linked to the presence of large, malignant, and retroperitoneal lipomatous tumors. However, in limited follow-up, no detectable impact of tumor resection was apparent on glycemic control. These data suggest that most lipomatous tumors do not exert a clinically relevant impact on glucose homeostasis.

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Introduction

The metabolic and endocrine properties of adiposity contribute directly to insulin resistance and the development of type 2 diabetes.[1] Lipomatous tumors are derived from adipose tissue and arise both peripherally and centrally within the retroperitoneum, presumably from subcutaneous and visceral adipose cell precursors, respectively.[2] These tumors, particularly malignant liposarcomas, can reach a significant size. Some lipomatous tumors retain many features of mature adipocytes (e.g., well-differentiated liposarcomas), while others become dedifferentiated and are composed of a mixture of mesenchymal cell types.[3]

Adipose tissue does more than just storing lipids; it is an endocrine organ, secreting adipokines.[4] In the obese, adipose tissue attracts and becomes engorged with macrophages and other leukocytes becoming, by mass, the largest immune organ of the body.[5] Adipose tissue can also be classified based on metabolic properties. In contrast to the more common white adipocytes, brown adipocytes are thermogenic and, under activating conditions, can reduce body weight.[6] Beige adipocytes describe another subtype that, under specific conditions, can be induced to differentiate into brown fat.[6] Moreover, the distribution of adipose tissue in the body is linked to its metabolic implications—e.g. visceral adiposity, as opposed to peripheral, is associated with insulin resistance and other metabolic diseases.[1,7]

We hypothesized that some lipomatous tumors exhibit metabolic activity and alter systemic insulin resistance. Diabetes improvement following liposarcoma excision has been reported in a single case series from 2010, but no other literature has otherwise explored the link between lipomatous tumors and diabetes.[8] Based on our hypothesis, we predicted that some patients with large, metabolically active lipomatous tumors would exhibit perturbed systemic glycemic control. Given the diverse properties of precursor adipose cells, we predicted that only a subset of lipomatous tumors—those derived from metabolically "bad" adipose cells—would affect systemic metabolism. In patients with metabolically active lipomatous tumors, resection would therefore lead to immediate improvements in glycemic control.

We performed a retrospective analysis of patients treated surgically for lipomatous tumors at a single, tertiary referral center. We identified 217 cases of adipose-derived tumors, and we assessed measures of glycemic control related to tumor characteristics, as well as the impact of resection.

Materials and methods

With institutional review board approval and waiver for obtaining informed consent, we performed a retrospective study of patients who underwent resection of a lipomatous tumor at a tertiary cancer referral center between 2004 and 2015. Patient demographics, measures of glycemic control, and tumor pathology and characteristics were reviewed in detail. We studied patients both with liposarcoma and with lipoma. Of patients with liposarcoma, all four subtypes—well-differentiated, dedifferentiated, pleomorphic, and myxoid—were represented in our cohort. We excluded a single case of hibernoma.

Patients who had a preoperative diagnosis of type 2 diabetes mellitus recorded in their past medical history were identified, and hemoglobin A1c (HbA1c) measurements were reported in all patients in whom levels were collected. Based on the most recent preoperative HbA1c, and in accordance with the American Diabetes Association guidelines for treatment goal,[9] we divided patients into well-controlled diabetics (HbA1c < 7) and poorly controlled diabetics (HbA1c ≥ 7). We compared patient demographics, body mass index (BMI), tumor characteristics and pathology, and measures of glycemic control between these groups both before and after tumor resection. In patients with a preoperative diagnosis of diabetes, we also compared the need for diabetic medications before and after lipomatous tumor resection.

Tumor details included size and lipomatous tumor subtype. Tumor size was recorded as three-dimensional measurements that are meant to represent length, width, and height of the tumor mass, the largest of which was considered the diameter of the tumor. We excluded lipomas with diameters of less than 5 cm. Preoperative measurements of random serum glucose and BMI were compared to measurements of random serum glucose and BMI at 6 mo and 12 mo after surgery. We chose to report measurements 6 mo after surgery to allow for random serum glucose and BMI to stabilize after the procedure. With regard to preoperative serum glucose, we reported serum glucose measurements taken as close to, but greater than 24 h before, the time of surgery. If there were more than one glucose measurements recorded on that day, we reported the mean serum glucose. Similarly, for postoperative serum glucose, we reported measurements that were recorded as close as possible to 6 mo and 12 mo after the date of tumor resection.

Several patients underwent more than one operation for tumor resection. Because patients' glycemic control and BMI, as well as tumor characteristics, varied for each procedure, each operation was treated as a separate entity.

The results are presented in median (and interquartile range). Wilcoxon rank-sum test was utilized. *P* values less than 0.05 were considered statistically significant. Statistical analysis was carried out using SPSS, version 16 (SPSS Inc, Chicago, IL).

Results

Between February 2004 and May 2015, we identified 217 cases of lipomatous tumors at a tertiary referral site. Resections of liposarcoma accounted for 147 of the operations we studied, and 70 operations involved excision of lipomas that were preoperatively suspicious for malignancy. Liposarcomas resected had a median diameter of 18.4 cm (with a range of 1.6-53 cm), 6.3 cm greater than the median diameter of lipomas ($P < 0.05$), which was 12.1 cm (5.0 cm to 29 cm). Of the 217 operations, 31 were performed on patients carrying a diagnosis of type 2 diabetes mellitus. Twelve nondiabetic patients had partial pancreatectomy as a part of their tumor resection; no diabetic patients underwent partial pancreatectomy.