Archives of Surgical Oncology

Abdel-Misih and Hornor, Arch Surg Oncol 2016, 2:4
DOI: 10.4172/2471-2671.1000115

Case Report Open Access

Surgical Treatment for Hypoglycemia: A Case Report

Sherif Abdel-Misih* **and Melissa Hornor***

The Ohio State University Wexner Medical Center and Arthur G. James Cancer Hospital, USA

***Corresponding authors:** Melissa Hornor, MD, 395 W. 12th Ave., 6th Floor, The Ohio State University Wexner Medical Center and Arthur G. James Cancer Hospital, Columbus, OH 43210, USA, Tel: (614)293-8704; Fax: (614)293-4063; E-mail: Melissa.Hornor@osumc.edu

Sherif Abdel-Misih, 395 W. 12th Ave., 6th Floor, The Ohio State University Wexner Medical Center and Arthur G. James Cancer Hospital, Columbus, OH 43210, USA, Tel: (614)293-7171; Fax: (614)366-0003

Received date: May 13, 2016; **Accepted date:** July 15, 2016; **Published date:** July 20, 2016

Abstract

A 55 year old female presented large left upper quadrant mass and episodes of recurrent hypoglycemia. Preoperative laboratory testing revealed normal insulin, IGF-I and IGF-II levels. Big-IGF-II levels were unable to be measured because the laboratory test was unavailable. A CT scan of her abdomen and pelvis revealed a large 19 × 15 × 12 cm left upper quadrant mass appearing to involve the pancreas, spleen, and left kidney. The mass was surgically extirpated and was consistent with a hemangiopericytoma. Subsequently, her hypoglycemic attacks along with abdominal symptoms resolved. We hypothesize that this patient's hypoglycemic attacks were a consequence of tumor secretion of a pro-hormone form of IGF-II called 'Big IGF-II'.

Introduction

Sarcomas are soft tissue tumors of mesenchymal origin, comprising about 1% of all adult malignancies. Sarcomas are a heterogeneous group of malignancies of many different histological types that are varyingly aggressive in nature. Soft tissue solitary fibrous tumor (SFT), otherwise known as hemangiopericytoma, is a rare tumor that represents less than 2% of sarcomas [1]. SFT usually presents in patients 40-50 years of age with an equal distribution in both sexes. About 80% of SFT's are benign in nature. Histopathologically, the tumor is composed of small cells individually separated by thin bands of collagen fibers. The most sensitive and specific marker is CD34. Histologic signs of malignancy are increased cellularity, pleomorphism, and mitotic count more than 4 per 10 high power fields [2]. The 5-year local recurrence and metastasis rate is 29% and 34% respectively [3]. Tumors located in the mediastinum, abdomen, and retroperitoneum are more likely to metastasize compared to malignancies in the extremities. When SFT's do metastasize, they tend to travel to lung, bone, or liver [4]. The most important determinant of local recurrence or metastasis is resectability of the tumor, with complete surgical resection being the only chance for a cure [4]. SFT's have been known to cause paraneoplastic syndrome, particularly hypoglycemia related to insulin mimicking peptides [4]. The tumors can be found anywhere in the body, but they are most commonly located in the pleura, with only about 7.5% of cases reported in the literature localized to the retroperitoneum [4].

The treatment for SFT is surgical extirpation and occasionally radiation therapy if the mass is unable to be fully excised. The symptoms are often non-specific, and the mass is usually diagnosed once it grows large enough to affect surrounding structures or abut peritoneal nerve fibers. In rare cases, however, the mass is associated with symptomatic hypoglycemia, especially when the mass is located in the retroperitoneal or pelvic location. The hypoglycemia is attributed to the secretion of insulin-like growth factors (IGFs) that are produced by the tumor. Because of this, the hypoglycemic episodes have been shown to resolve following surgical resection of the tumor.

Case Presentation

A 55 year old female with history of ulcerative colitis presented to the hospital with complaints of fatigue, nausea, episodic diaphoresis, tachycardia, and vague, intermittent left upper quadrant pain that started about three months prior. Due to her left upper quadrant pain, she had previously underwent laparoscopic cholecystectomy at an outside hospital on the basis of her abdominal pain and an abnormal HIDA scan (Ejection Fraction 26%). However, her nausea and pain failed to resolve. Soon thereafter she developed intermittent hypoglycemia (serumglucose level as low as 38 mg/dL) prompting further evaluation. A CT scan of her abdomen and pelvis was performed with discovery of a large 19 × 15 × 12 cm left upper quadrant mass appearing to involve the pancreas, spleen, and left kidney. She was referred to The Ohio State University Wexner Medical Center and Arthur G. James Cancer hospital for evaluation and management (Figure 1).

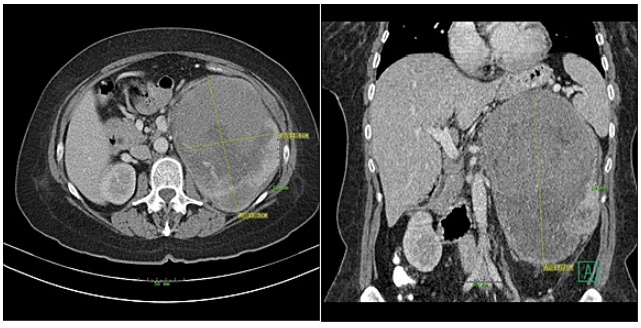

Figure 1: Computed tomography scans demonstrating a large left upper quadrant mass.

Biochemical testing was carried out to rule out functional neuroendocrine tumors of adrenal or pancreatic origin which all returned within normal limits. The patient also underwent a 72-hour

fast to determine the extent of her hypoglycemic episodes. She became hypoglycemic to the 30's 24 hours into her fast, at which point her serum glucose level recovered with the administration of glucagon and oral glucose supplementation. Her insulin and C-peptide levels were both normal.

A CT guided biopsy of the mass was performed and the histopathologic report was consistent with hemangiopericytoma. With this histology and hypoglycemia, there has been an association related to insulin like growth factors (IGF) I/II which were tested. The IGF-I level was low at 67 (normal 87-238 ng/ml) while IGF-II levels were within normal limits (433 with normal range of 288-736). The patient required periodic glucose infusion to maintain her serum glucose in the normal range. Due to the inability to safely prevent hypoglycemic episodes at home, the patient was prepped and consented for surgical resection of the mass (Figure 2).

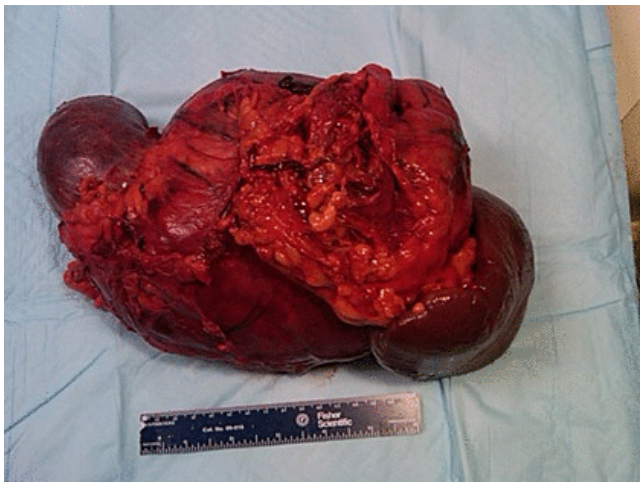

Figure 2: Gross photograph of specimen including mass, spleen, distal pancreas and left kidney.

The patient underwent an exploratory laparotomy, radical resection of the left upper quadrant mass inclusive of distal pancreatectomy, splenectomy and left nephrectomy. Gross pathologic examination revealed an intermediate grade (Grade II/III) hemangiopericytoma-SFT measuring 19.2 × 14.8 × 11.7 cm in size without lymphatic, vascular, or perineural invasion with 5 mitoses per 10 high-power fields, consistent with malignant SFT. The spleen, left kidney and adrenal gland were grossly involved, but were free of involvement histologically. The margins were negative except for focal involvement of the posterior margin. Although the mass did not infiltrate the descending colon, the left colon was divided to facilitate circumferential tumor exposure and dissection. Subsequently, a colocolostomy was undertaken.

Postoperatively, the patient's left upper quadrant pain and nausea resolved. Additionally, the patient's hypoglycemia resolved immediately without any further episodes requiring medical management. However, surgery was complicated by intraabdominal sepsis secondary to an anastomotic leak at the colocolostomy warranting reoperation with anastomotic resection and neo-colocolostomy with diverting ileostomy. She recovered well and subsequently underwent ileostomy reversal. She has continued radiographic surveillance with CT scan of her abdomen and pelvis every four months to assess for recurrence or metastasis. It has been 2.5 years since her operation and she has not had radiographic evidence of disease recurrence nor any episodes of hypoglycemia. She has regained a normal quality of life and returned to work full time (Figure 3).

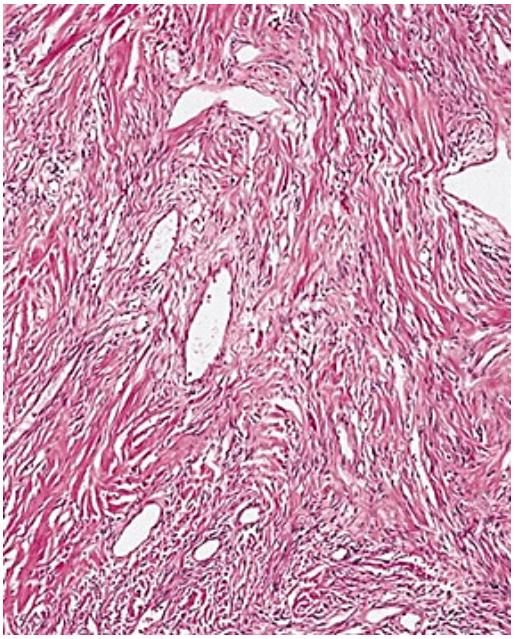

Figure 3: Histopathological specimen of solitary fibrous tumor [5].

Discussion

This is a rare case of retroperitoneal solitary fibrous tumor/hemangiopericytoma associated with hypoglycemia. The patient presented with complaints of persistent abdominal pain and nausea in addition to hypoglycemic episodes. Preoperative biochemical testing was relatively unremarkable. However, due to recurrent hypoglycemia, surgery was recommended. After surgical extirpation, her abdominal pain improved along with her hypoglycemia.

It is apparent that the hypoglycemic episodes were tumor related given the immediate normalization of blood glucose levels postoperatively. The preoperative biochemical testing did not reveal any abnormality associated with IGF's. However, previous studies have demonstrated the involvement of different IGFs and their effects on growth and physiologic functions including tumor-induced hypoglycemia [6-8]. A prohormone form of IGF-II ('Big IGF-II') identified to be secreted by some tumors functions to increase glucose uptake by the tumor as well as by insulin responsive tissues like muscle and fat. Big IGF-II also directly inhibits pancreatic beta cells' insulin secretion and hepatic glucose production. Indirect effects of big IGF-II include inhibition of pituitary growth hormone secretion which decreases IGF-I synthesis thereby affecting hepatic glucose production. With this complex IGF physiology previously studied, we hypothesize that big IGF-II was the major physiologic factor responsible for tumor induced hypoglycemia whose isoform was not assessed biochemically preoperatively. Further study is required to identify the frequency of this phenomenon and the implications of big IGF-II production in the prognosis of solitary fibrous tumors.

Genomic imprinting refers to the mono-allelic expression of certain genes according to their parent-of origin. In mammals, imprinted DNA methylation is directly controlled by DNA methyltransferases [9]. In addition, recent study has found histone methyltransferases G9a and GLP also plays a role in the maintenance of genomic imprinting [10]. IGF-II is one of the imprinted genes and its expression is regulated by the DNA methylation that presents at the IGF2/H19 imprinting control center (ICR) [11]. As loss of imprinting of IGF-II and H19 occurred in many cancers [12,13], it is essential to understand the link between aberrant expression of the enzymes associated with the maintenance of genomic imprinting and initiation of human carcinomas.

Regarding the patient's outcome, ongoing long-term follow-up is recommended due to the not insignificant recurrence risk for SFT's, particularly for large tumors (>10 cm), positive surgical margins, and with histological features of malignancy. Her surveillance follow up has consisted of clinic visits including a CT abdomen/pelvis with labs every four months. She has been followed in the outpatient setting for 3 years thus far without any signs of disease recurrence, despite this patient having a large tumor with histologic features of malignancy and positive focal margins. Importantly, she continues to be euglycemic without any hypoglycemic episodes since tumor extirpation.

Conclusion

This report describes an intermediate grade retroperitoneal SFT with hypoglycemia likely caused by excessive secretion of big IGF-II that was successfully treated with surgical extirpation. The hypoglycemia immediately improved following the surgery and the patient's disease has not recurred symptomatically or radiographically after five years.

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