Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Endocrinology

Comatogenic Hypoglycemia Secondary to Paraneoplastic IGF2 Secretion by a Malignant Solitary Pancreatic Fibrous Tumor

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DOI: https://doi.org/10.36347/sjmcr.2024.v12i11.004 | **Received:** 13.09.2024 | **Accepted:** 17.10.2024 | **Published:** 06.11.2024

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Abstract **Case Report**

Solitary fibrous tumors are rare mesenchymal tumors, most often developing in the pleura, but sometimes appearing in soft tissue or parenchymal organs, where their diagnosis is often problematic. Exceptionally they have been described in the pancreas. We report the case of a malignant solitary fibrous tumor of the pancreas occurring in a 58-year-old woman who consulted for comatogenic hypoglycemia associated with abdominal pain. Surgical resection of the tumor was performed, but the patient died of postoperative complications.

Keywords: Pancreatic Solitary Fibrous Tumor, IGF2, Comatogenic Hypoglycemia.

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INTRODUCTION

Solitary fibrous tumors of the pancreas are rare, of unknown etiology, most often discovered incidentally or during abdominal pain, rarely following hypoglycemia. They are characterized by excessive IGF2 secretion [1]. The only curative treatment is complete surgical removal of the tumors responsible. Pharmacological therapies such as glucocorticoids, glucagon and somatostatin analogues are also an option for alleviating hypoglycemia in multiple or unresectable tumors [2].

CASE DESCRIPTION

A 58-year-old female patient hospitalized for investigation of repeated comatogenic hypoglycemia reaching 0.2 g/l. On examination, she reported permanent cramp-like epigastralgia of moderate intensity, without irradiation, unrelated to eating, associated with nausea and no other digestive signs, notably no jaundice, no externalized upper or lower digestive bleeding. Clinical examination revealed a conscious patient, hemodynamically and respiratorily stable, apyretic, with a blood glucose level of 0.45 g/l, normotensive, normocardiac, diffuse abdominal tenderness, and a 20 cm hard, deep-lying impaction over the right hypochondrium and epigastrium extending beyond the umbilicus. Biological samples (Table 1), taken during hypoglycemia to 0.30 g/l, showed a collapse in C-peptide and insulin levels, with a very high IGF2 level.

Table 1: Results of hormone assays performed during hypoglycemia at 0.30 g/L

Dosage	Results	Norm
Peptide C	0.01 ng/mL	(1,10-3,3)
Insulinaemia	0.20 µUI/mL	(3-25)
IGF1	33.76 ng/mL	(46-238)
IGF2	1333 ng/mL	(396 - 1049)
IGF2/IGF1	39.48	< 10

Abdominal and pelvic CT revealed a voluminous, exophytic duodeno-pancreatic abdominal mass measuring 20cm×19cm, intensely and heterogeneously enhanced, with significant angiogenesis.

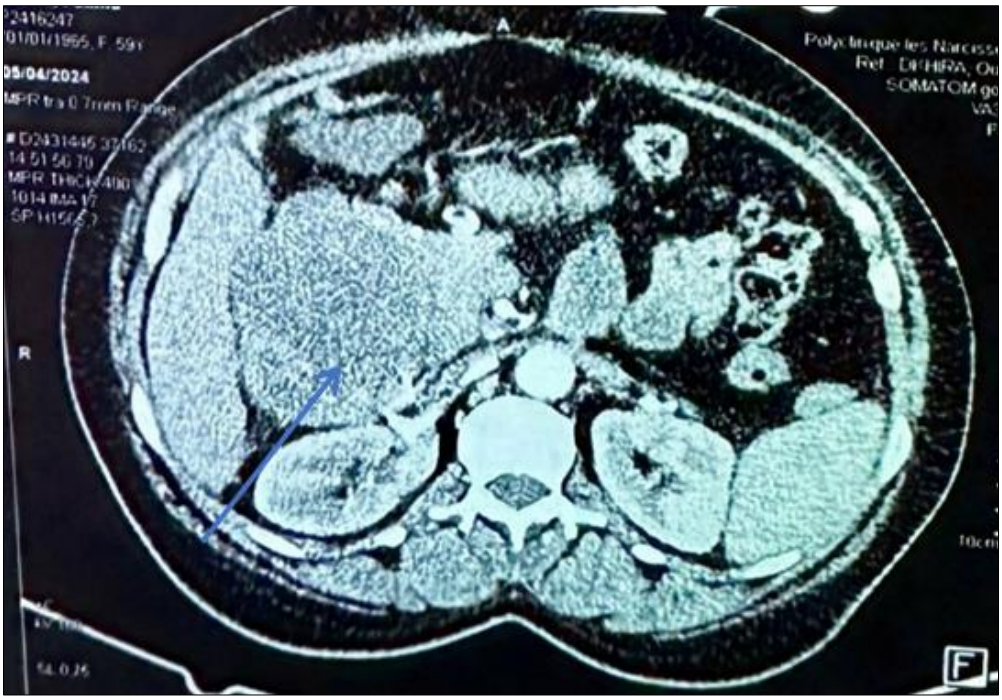

Figure 1: Axial CT section: exophytic duodeno-pancreatic mass, well limited and heterogeneously enhanced after injection of contrast medium.

Glycemia was stabilized by meal splitting and the introduction of corticosteroids, and the patient underwent tumor resection. The surgical procedure consisted of cephalic duodeno-pancreatectomy combined with pyloric and jejunal resection.

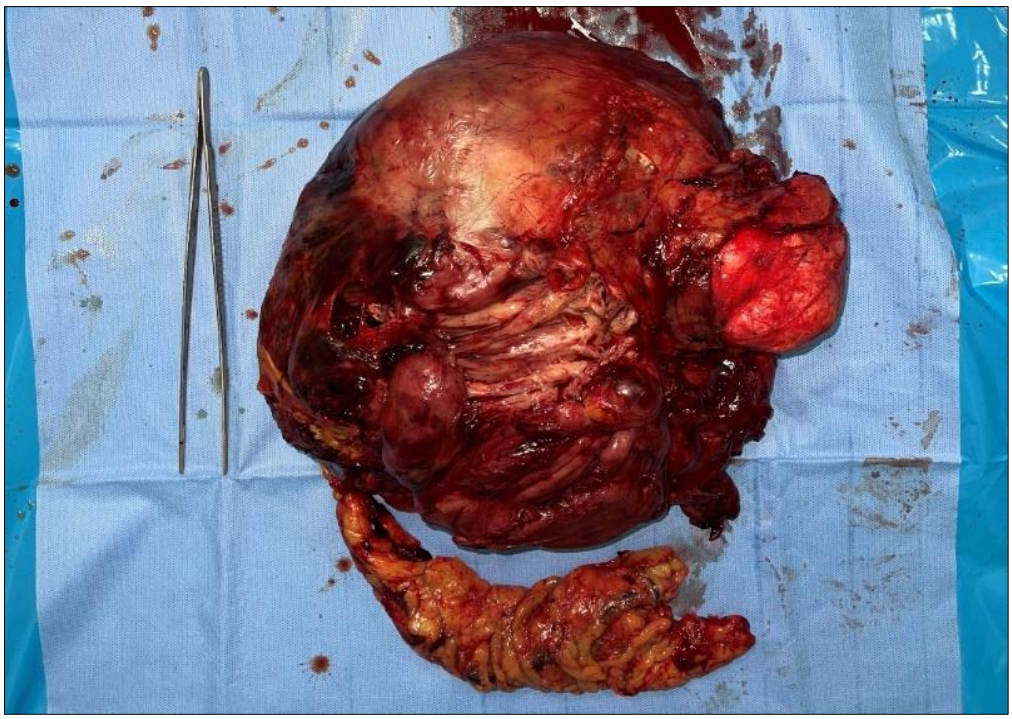

Figure 2: Tumor mass measuring 30 cm ×40 cm

Pathological study showed malignant tumor proliferation, expressing vimentin, anti-CD34 antibodies and anti-STAT6 antibodies with a Ki67 of 25%, initially suggestive of a dedifferentiated solitary fibrous tumor of the pancreas. After tumor resection, the patient showed no further hypoglycemia; the course was unfavorable. She died one month later following septic shock.

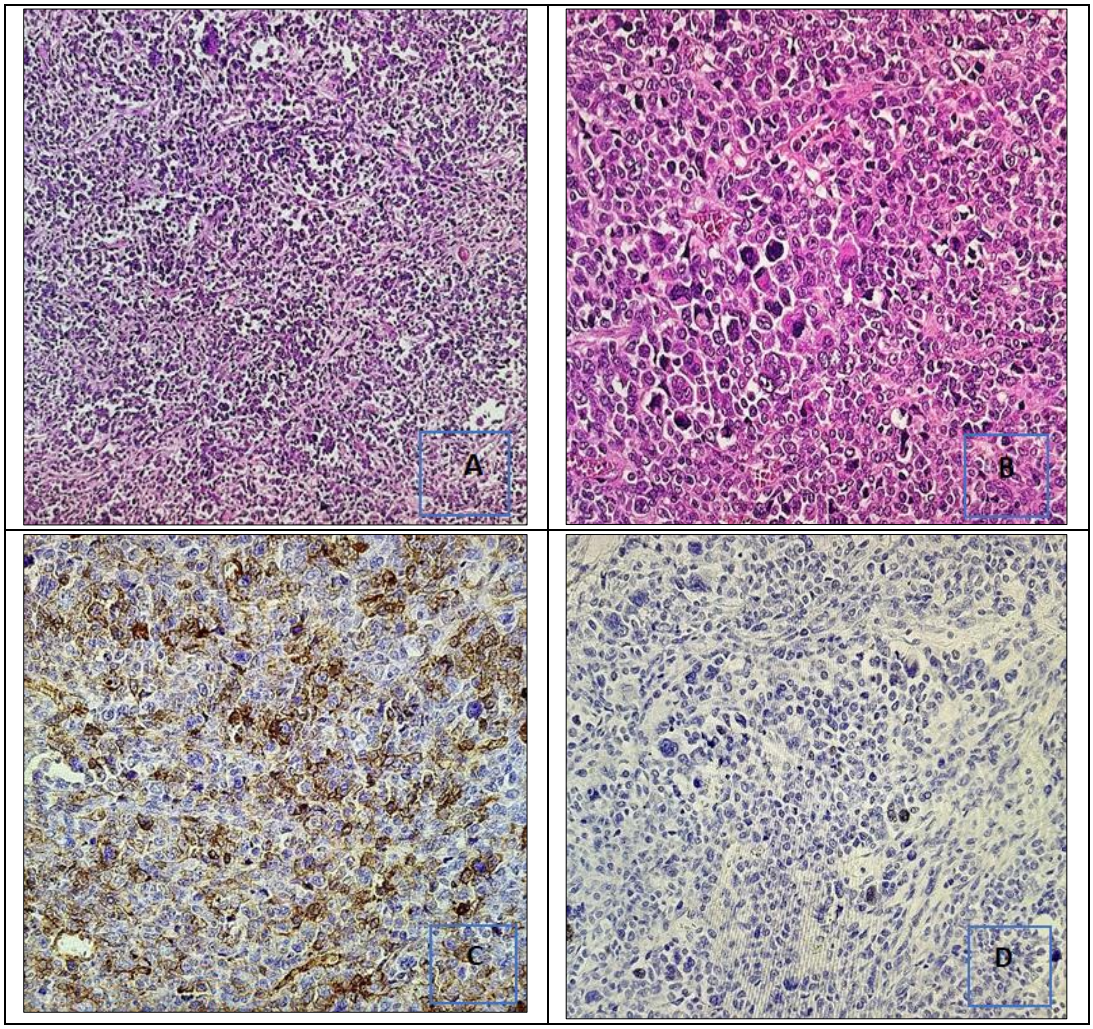

Figure 3: (A) HE (×20) proliferation is arranged in diffuse sheets and lobules, tumor cells are medium to large; sometimes round; sometimes strongly nucleolated spindle-shaped.

(B)HE (×40) Large tumor cells; with pleomorphic, multinucleated nuclei; irregularly contoured, densely chromatinized and nucleolated.

(C) IHC (×40) Membrane expression of anti CD34 antibody

(D) IHC (×40) Nuclear expression of antiSTAT6 antibody

DISCUSSION

Solitary fibrous tumors (SFTs) of the pancreas are extremely rare spindle cell neoplasms of mesenchymal origin [3]. They can occur at any age, without gender predominance [4]. Clinical presentation varies from the incidental discovery of a mass on radiological imaging, or following abdominal pain or comatogenic hypoglycaemia secondary to paraneoplastic secretion of insulin-like growth factors IGF2, as was the case in our patient [5, 6].

The IGF2 assay is more accessible than the Big-IGF2 assay, but may be normal, which does not rule out the diagnosis. The use of the IGF2/IGF1 ratio can serve as a diagnostic tool [7], a ratio greater than 10 being strongly suggestive of paraneoplastic secretion of Big-IGF-2. In our patient, this ratio was 39.48.

Imaging can be used to diagnose a pancreatic tissue mass and to assess its local and distant extension. However, it cannot be used to suggest the diagnosis of pancreatic TFS, as the lesions observed are not specific. On ultrasonography, TFS appears as a well-limited, rounded or oval, hypoechoic mass, often heterogeneous and associated with foci of haemorrhage or necrosis. A CT scan shows a well-limited, tissue-dense formation, intensely enhanced after contrast injection due to a large vascular contingent. MRI has the same morphological characteristics as CT [8, 9].

Anatomopathological study remains the key to the diagnosis of TFS. Macroscopically, it is a solid, smooth-surfaced tumor, often bulky, with foci of central necrosis, cystic areas or, more rarely, calcifications, elliptical to spindle-shaped tumor cells growing randomly, and a hemangiopericytic growth pattern due to vascular proliferation and perivascular sclerosis [9].

Immunohistochemical staining is positive for CD34 and vimentin and STAT6, which is more sensitive (98%) and specific (85%) for SFT [13], and negative for mesothelial cell-derived cytokeratin and epithelial membrane antigen. Staining is also negative for S-100, which is positive for neurogenic tumors, and negative for c-kit, which is positive for gastrointestinal stromal tumors.These features are useful for distinguishing SFT from other mesenchymal tumors [14].

Surgical resection of the SFT of the pancreas is the standard treatment. If excision is not possible, is contraindicated or incomplete, symptomatic treatment with glucocorticoids (prednisolone 30-60 mg/d), continuous pump infusion of glucagon (0.06-0.3 mg/h) [12], or recombinant GH (3-12 mg/d) may be suggested. Somatostatin analogues and diazoxide do not appear to be effective [11].

CONCLUSION

Paraneoplastic hypoglycemia secondary to IGF2 secretion by fibrous tumors is an extremely rare cause of organic hypoglycemia. The very high IGF2/IGF1 ratio confirms paraneoplastic IGF2 secretion. Management remains poorly codified. Tumor excision leads to resolution of hypoglycemia, while corticosteroid therapy and tyrosine kinase inhibitors may be effective therapeutic alternatives for hypoglycemia if the tumor cannot be removed.

Competing Interests: The authors declare that there are no competing interests regarding the publication of this paper

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