An urological cause of hypoglycaemia: A case report of the Doege-Potter syndrome

Nuno Ramos 1, Rodrigo Ramos 2, Celso Marialva 2, Eduardo Silva 2

1 Urology Department, Garcia de Orta Hospital, Almada, Portugal; 2 Urology Department, Portuguese Institute of Oncology, Lisbon, Portugal.

Summary The Doege-Potter syndrome is a rare paraneoplastic syndrome presenting with hypoglycaemia due to ectopic secretion of insulin-like growth factor II (IGF-II) from a solitary fibrous tumor. The underlying tumor can be benign or malignant and rarely present in extrapleural sites. We describe the case of a 83-year-old male diagnosed with a Doege-Potter syndrome due to a kidney tumor.

Keywords: Hypoglycaemia; Insulin-like growth factor; Solitary fibrous tumor.

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Introduction Solitary fibrous tumor (SFT) was first reported by Klemperer and Rabin in 1931 as a lesion that originated in the pleura (1, 2). Nevertheless, SFTs are rare mesenchymal tumors, found in various anatomic locations, with approximately 20% in extrapleural locations like liver, orbit, lung and gastrointestinal tract. These tumors occur mainly in adults, with a peak age of 60-80 years and are equally distributed between genders (3). SFTs are rarely symptomatic and the vast majority are incidentally found. However, these tumors may also potentially cause symptoms, such as refractory hypoglycaemia, due to the production of insulin-like growth factor (IGF-II). When hypoglycaemia is associated with an SFT, it is referred as the Doege-Potter syndrome, a potentially life-threatening condition (2, 4). Majority of the tumors are benign, but 10%-20% can be malignant. Malignancy is determined by invasive growth with an unclear boundary, high cell density, mitoses, pleomorphism and the presence of bleeding or necrosis (5). Benign SFTs can be cured by complete surgical resection. The role of chemotherapy and radiotherapy is still unclear. We describe the case of an 83-year-old man, who underwent a surgical resection for a SFT, associated with refractory hypoglycaemia.

Case Report

A male 83 years old male patient was referred to our hospital due to a progressive increase of abdominal volume, in association with frequent episodes of syncope, as a result of hypoglycaemia. The patient had a history of arterial hypertension and was medicated with lisinopril. Physical examination revealed the presence of a palpable mass in the left flank. On admission, his blood glucose level was 33 mg/dl (normal range 70-109 mg/dl), being administrated continuous glucose infusion and glucocorticoid. The hypothesis of insulinoma was ruled out by serum insulin level of 12.3 µU/mL (normal < 28.0 µU/mL) and serum C-peptide level of 3.6 ng/ml (normal range 0.9-7.1 ng/ml). Plasma IGF-I and IGF-II levels were measured being respectively 29.00 ng/mL (normal: 55-166 ng/mL) and 458 ng/mL (normal: 288-736 ng/mL). The ratio IGF-II/IGF-I was higher than 10, suggestive of hypoglycaemia caused by non-islet cell tumor, the Doege-Potter syndrome. Computed tomography (CT) demonstrated a large renal exophytic mass in the left kidney of 19 x 17 x 18.7 cm, heterogeneous, with little contrast-enhancement, without signs of renal vein invasion neither areas of necrosis (Figure 1). Open left radical nephrectomy was performed. The postoperative course was uneventful, and hypoglycemic symptoms disappeared immediately after surgery.

Histopathological analysis revealed a tumor composed of spindle cells without atypia neither mitoses or areas of necroses. Immunohistochemical staining revealed a tumor positive for activators of transcription 6 (STAT6), CD34 and IGF-II, and negative for MDM2, AE1/AE3,EMA, S-100, SMA, and desmin (Figure 1). Based on the histological and immunohistochemical findings, a diagnosis of SFT of the kidney was made. The tumor secreted IGF II, which caused hypoglycaemia, but did not present malignant potential. On the first year of follow-up, the patient was observed in consultation every 3 months, remaining tumor-free based on CT scan at 6 and 12 months. Patient reported no episodes of hypoglycaemia during this period. Due to the rarity of this tumor, there are no specific guidelines available to monitor these patients. Therefore, we have used the European Association of Urology (EAU) guidelines for Renal Cell Carcinoma for subsequent follow-up.

Conclusions SFTs can arise from a wide range of anatomic sites, both intrapleural or extrapleural, as the retroperitoneum. Refractory hypoglycaemia may occur in 4% of SFT and is reported as Doege-Potter syndrome (6). It is caused by the inappropriate secretion of a high molecular-weight form of IGF-II (HMW IGF-II). This molecule is an incompletely processed molecule of IGF-II, derived from the tumor, which fails to form a complex with IGF-binding protein-
Radiotherapy has limited value, although it has been tried as an adjuvant treatment in case of incomplete surgical resection (3, 12). Symptomatic medical treatment of hypoglycaemia has been tried with some success for patients unfit for surgery (8). In conclusion, hypoglycaemia caused by SFTs are benign, 20% may present local recurrence and metastases (9, 10). Malignant criteria include: high IGF-II (8). CT scan and magnetic resonance imaging (MRI) are effective tools for identifying SFT, determining the invasion of the surrounding structures, revealing information on distant metastasis and for follow-up. CT imaging typically shows a smooth, well circumscribed, homogeneous mass with or without necrosis or calcifications (2). MRI presents as a tumor with high signal intensity on T2-weighted images and iso-intensity or low intensity on T1-weighted images (6). Fluorodeoxyglucose positron emission tomography (FDG-PET) can also offer benefit in the diagnosis of SFT. PET and update review on the Doege-Potter syndrome. J Cardiothorac Surg. 2009; 4:45.

3. This leads to higher bioavailability compared to mature IGF-II, with activation of insulin receptors, inhibiting hepatic gluconeogenesis and increasing peripheral glucose uptake which results in hypoglycaemia (7). The detection of HMW IGF-II requires immunoblot analysis, not available at our institute. The patients with Doege-Potter syndrome, usually presents suppressed serum insulin, C peptide and low IGF-1 against normal or elevated levels of IGF-II (8). CT scan and magnetic resonance imaging (MRI) are effective tools for identifying SFT, determining the invasion of the surrounding structures, revealing information on distant metastasis and for follow-up. CT imaging typically shows a smooth, well circumscribed, homogeneous mass with or without necrosis or calcifications (2). MRI presents as a tumor with high signal intensity on T2-weighted images and iso-intensity or low intensity on T1-weighted images (6). Fluorodeoxyglucose positron emission tomography (FDG-PET) can also offer benefit in the diagnosis of SFT. PET and update review on the Doege-Potter syndrome. J Cardiothorac Surg. 2009; 4:45.

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Correspondence
Nuno Ramos, MD (Corresponding Author)
nuno.ramos@hgo.min-saude.pt
Garcia de Ota Hospital, Av. Torrado da Silva, 2801-951, Almada (Portugal)
Rodrigo Ramos, MD
Celso Marialva, MD
Eduardo Silva, MD
Urology Department, Portuguese Institute of Oncology, Lisbon (Portugal)