Case Study of the Month

Retroperitoneal Malignant Solitary Fibrous Tumor of the Small Pelvis Causing Recurrent Hypoglycemia by Secretion of Insulin-like Growth Factor 2

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1. Case report

A 28-yr-old patient suffered left flank pain, with grade 2 ectasia of the left kidney. The presumptive diagnosis of an extragonadal testicular tumor was established after a radiologic examination (abdominal computed tomography [CT] and positron emission tomography [PET] scan) (Fig. 1).

Because the testicular tumor markers were negative, we performed a biopsy of the retroperitoneal mass, which was suggestive of a mesenchymal tumor. Immunohistochemical studies were strongly positive for vimentin; positive for factor 8 expression in capillary vessels but negative in tumor cells; positive for clone MIB-1 in only 2–3% of cells; and negative for calretinin, CD21, CD34, S100, epithelial membrane antigen (EMA), desmin, smooth muscle actin (SMA), myogenin, pancytokeratin, and CD117. The patient had episodes of severe hypoglycemia caused by insulin-like growth factors (IGFs) produced by this tumor.

Because of the presumptive diagnosis of a hemangiopericytoma after biopsy of the retroperitoneal mass, our initial therapeutic approach was...
an intravenous infusion of two cycles of bevacizumab (Avastin: Genentech, San Francisco, CA, USA). After treatment, there was no evidence of any reduction in the tumor mass, so we performed a surgical resection (Fig. 2).

The definitive histologic report described a 1660 g tumor, measuring 18 × 15 × 11 cm, with a homogenous cut surface and relatively homogenous white, red, and brown markings (Figs. 3 and 4), well encapsulated without evidence of invasion of surrounding structures.
surrounding structures. The pathologist diagnosed the tumor as a malignant solitary fibrous tumor (SFT) with R0 resection. Immunohistochemistry demonstrated diffuse membranous expression of CD99, cytoplasmatic expression of Bcl2, and expression of CD34 but no expression of EMA, CD31, HMB45, desmin, or SMA (Fig. 5).

2. Discussion

Malignant SFTs, described in the literature as the Doege-Potter syndrome, are often associated with hypoglycemia [1]. SFTs are rare tumors with a 12–13% rate of malignancy. Hypoglycemia is seen in <5% of cases. The associated tumors are large, with a high mitotic rate. The hypoglycemia is related to IGF 2 (IGF2) produced by the tumor [2,3]. The downstream oncogenic pathways of IGF2, however, are not clear. SFT cells secrete IGF2 and proliferate in serum-free medium, consistent with an IGF2/insulin receptor (IR) autocrine loop. The etiologic relevance of IGF2 is supported by expression of IR A (IRA), the isoform with high affinity for IGF2, in all SFTs.

IR activation plays an oncogenic role in SFTs [3]. The most frequently described locations for these tumors are the pleura, lung, pancreas, intestine, greater omentum, and uterus [4–8]. The differential diagnosis for SFT includes hemangiopericytoma, gastrointestinal stromal tumors (GIST), malignant mesothelioma, synovial sarcoma, leiomyomatous tumors, and granulosa-cell tumors.

Immunohistochemical studies revealed reactivity for CD34, CD99, and Bcl2 but no staining for desmin, EMA, HMB45, SMA, S100, or CD31, thus confirming the diagnosis of SFT. After surgical resection of the tumor, high-molecular-weight IGF2 was not detected in the serum, and the hypoglycemia resolved. Immunohistochemically, IGF2 was localized to the Golgi area of the tumor cells. These findings suggest that hypoglycemia in this patient was caused by the overexpression of IGF2 by the SFT cells. Although SFT is typically associated with a favorable prognosis, a close follow-up is recommended because of limited information on its long-term behavior.

Conflicts of interest: The authors have nothing to disclose.

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Question:

What were the reasons for hypoglycemia in this patient?

A. Paraneoplastic syndrome.
B. High levels of circulated insulin-like growth factor 2 (IGF2).
C. High mitotic rate of spindle cells.
D. Expression of CD34 by tumor cells.
References