Recurrent Non-islet Cell Tumor Hypoglycemia Secondary to Recurrent Renal Sarcoma

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Key Words

Kidney neoplasms • Kidney tumor • Malignancy •
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Abstract

Introduction: Non-islet-cell tumor hypoglycemia (NICTH) is a rare paraneoplastic syndrome encountered in the setting of a wide variety of benign and malignant tumors. **Case presentation:** A 46 year old lady was referred to our unit, with a large left sided retroperitoneal mass found on surveillance imaging on a background of renal sarcoma 6 years previously, for which she had a left nephrectomy. She had initially presented with symptoms of hypoglycaemia which was a result of tumor secretion of insulin like growth factor 2. She was counselled regarding the recurrence and listed for excision. On the day of surgery she developed symptomatic hypoglycaemia. The tumour was completely resected from the nephrectomy bed. The tumour was histologically identical to the initial tumor. **Conclusion:** We report a rare case of recurrent non-islet cell hypoglycaemia in a lady with recurrent malignancy. Her hypoglycaemic episodes fully resolved on each occasion following resection. There have been reports of NICTH associated with recurrent retroperitoneal tumours and synchronous thyroid tumours and uterine leiomyomata. NICTH should be considered in patients with a known malignancy who present with recurrent hypoglycaemia. This is, to the best of our knowledge at the time of writing, the first case in the literature of recurrent NICTH secondary to recurrent renal sarcoma.

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Introduction

Non-islet cell tumor hypoglycemia (NICTH) is a rare paraneoplastic syndrome encountered in the setting of a wide variety of benign and malignant tumors. Patients can present initially with hypoglycemia or be diagnosed secondary to malignancy. Hypoglycemic episodes usually resolve following full surgical resection of the tumor. We report the first case of a lady with recurrent NICTH due to recurrent renal sarcoma.

Case Report

A 46 year old lady was referred to our unit, a tertiary referral centre, with a large left side retroperitoneal mass found on surveillance imaging on a background of renal sarcoma 6 years previously.

She initially presented with hypoglycemia and complained of dizzy spells and fainting episodes. Computed tomography at the time revealed an 11cm tumor of the left kidney. She underwent a left side radical nephrectomy— histology revealed a grade 2 sarcoma of the kidney. Biochemical analysis revealed her hypoglycemic episodes were a result of insulin-like growth factor 2 (IGF-2) secretion from the tumor. These episodes fully resolved after the nephrectomy [1].

Six years on from her initial presentation and treatment, annual surveillance imaging [magnetic resonance imaging (MRI) and positron emission tomography (PET)] revealed three abnormalities: a 1cm lesion within the thyroid gland which was subsequently diagnosed as a papillary carcinoma, a 2 cm leiomyoma within the uterus and a small area of uptake within the nephrectomy bed. MRI demonstrated a 9 × 11cm fluid filled mass with some solid elements within the nephrectomy bed (fig. 1); this prompted referral.

Fig. 1. Coronal and axial T2 weighted MRI demonstrating recurrence in left renal bed.

On presentation to our clinic, she was entirely asymptomatic. Abdominal examination revealed fullness in the left flank. Random blood glucose was 4.1 mmol/l. She was counselled regarding the recurrence and listed for excision. On the day of surgery she began to feel drowsy and on evaluation it was noted she was quite confused. Her capillary blood glucose at the time was 2.3 mmol/l. She was given 100ml of 20% dextrose following which her symptoms resolved and her blood glucose corrected to 8.2 mmol/l. The tumor was completely resected from the nephrectomy bed. She made an uneventful post-operative recovery and had no further hypoglycemic episodes.

Histology revealed an encapsulated tumour of homogenous, cream gelatinous tissue with areas of hemorrhage and necrosis measuring $9.2 \times 11.8 \times 7.8$ cm. Extensive immunohistochemistry was performed. The tumor was positive for BCL-2. Tumor cells were negative for AE1/AE3, SDSA, desmin, Vimentin, CD 31, 34, 56, chromogranin, synaptophysin, melanA, HMB45, S100, WT-1, TTF-1, CD45 and EMA. This tumor was morphologically identical to the original tumor which was diagnosed as sarcoma, grade 2 of 3 (fig. 2).

On review in clinic 6 weeks post operatively, she had returned to normal daily activities, had no further hypoglycemic episodes and random blood glucose level was 4.7 mmol/l. She will be followed up with surveillance cross sectional imaging and clinical review.

Discussion

We report a rare case of recurrent non-islet cell hypoglycemia in a lady with recurrent malignancy. Her hypoglycemic episodes fully resolved on each occasion following resection. There have been reports of NICTH associated with recurrent retroperitoneal tumors and synchronous thyroid tumors [2] and uterine leiomyomata [3] as was the case with our patient.

NICTH has been reported in genitourinary cancers in the form of renal cell carcinoma [4, 5] and prostate [6].

NICTH is a rare paraneoplastic syndrome encountered in the setting of a wide variety of benign and malignant tumors [7], due to tumor production of high molecular weight IGF-2. When a tumor is not previously known or readily apparent, cross sectional imaging of the chest, abdomen, and pelvis is likely to be high yield. Prompt and complete surgical resection is curative—as was seen in our case, while subtotal resection and other local modalities such as radiation therapy may be successful. When resection is not feasible or is delayed, initial management of hypoglycemia involves increased caloric intake and frequency and/or intravenous glucose or dextrose. When conservative measures fail, medical therapy can be effective in alleviating hypoglycemia, although the degree of success likely correlates with overall tumor burden and progression [8]. The tumors are usually large and slow growing. Although most patients with NICTH are known to have a tumor prior to the onset of hypoglycemia, there have been case reports of patients presenting with low blood glucose and then being found to have a sarcoma or benign mesenchymal tumors [8]. Tumors which cause hypoglycemia via NICTH over-express IGF-2 genes and secrete excessive amounts of partially processed precursors of IGF-2, named ‘big’ IGF-2. NICTH is 4 times less common than insulinoma [9]. Prostate cancer represents around 2% of the total incidence [6]. IGF-2 can be normal or high, as usual laboratory testing cannot differentiate between the different molecular weights in the serum [6].

Fig. 2. **a** Thick walled fibrous capsule infiltrated by tumour. (Hematoxylin and eosin, $\times 2$ magnification). **b** High power view of tumour cells, which have a moderate amount of pale eosinophilic cytoplasm, moderately pleomorphic spindled to ovoid nuclei, variably irregular nuclear membranes and a stippled chromatin pattern. (Hematoxylin and eosin, $\times 40$ magnification).

The tumors causing NICTH are usually very large. They are easily detected by conventional radiological imaging. Functional imaging like FDG-PET may lead to a false negative result due to accelerated uptake of FDG by skeletal and cardiac muscles as these tissues have a much higher expression of insulin receptor when compared with the tumour tissue. Therefore, FDG-PET is a poor method to evaluate relapse of the disease and metastasis in these patients [10].

This is, to the best of our knowledge at the time of writing, the first case in the literature of recurrent NICTH secondary to recurrent renal sarcoma.

Conclusion

We report a case of non-islet cell hypoglycaemia due to recurrent renal sarcoma which resolved on resection. NICTH should be considered in patients with a known malignancy who present with recurrent hypoglycemia.

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