

Case Report

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Recurrent Neuroglycopenia: Do Not Forget Non-islet Cell Induced Tumor Hypoglycemia

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Abstract

Non-islet cell tumor hypoglycemia (NICTH) is an exceedingly rare paraneoplastic condition and often its commonest presenting symptom is hypoglycaemia. Most cases of NICTH are associated with underlying mesenchymal or epithelial neoplasm. However our case is unique as NICTH was associated with well differentiated liposarcoma, which has never been described before. Most of the reported cases of NICTH were diagnosed on the basis of biochemical tests. However NICTH can also be a diagnosis of exclusion as highlighted by our case report. This case also highlights both the diagnostic dilemma and the surgical challenges in the management of such cases. The elderly lady presented with repeated episodes of loss of unconsciousness for which she was hospitalised twice. Her symptoms closely resembled that of a cerebrovascular accident patient. However CT brain did not reveal any brain lesion. However she also had spontaneous episodes of hypoglycaemia which led to further investigations. Ultrasonography abdomen revealed presence of huge retroperitoneal mass on FNAB which was malignant. Subsequently, she was put on dextrose drip and thorough investigations ruled out metastatic disease. She underwent laparotomy and the mass was excised enbloc. Postoperative recovery was smooth and the hypoglycaemia resolved spontaneously. Final histopathologic examination was suggestive of well differentiated liposarcoma. At the 6-month follow-up, she was free from hypoglycemic episodes. This case highlights that NICTH can be a difficult diagnosis given its propensity to mimic several other benign conditions. NICTH can also be caused by liposarcomas. Diagnosis by excluding all other causes of hypoglycaemia is also an option where costly biochemical tests are unavailable. Surgical excision is the main stay of treatment.

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Case Report

A 76-year-old lady initially presented to a local hospital with symptoms of sudden loss of consciousness, generalized seizures,

and involuntary urination. She was managed conservatively and discharged in stable condition. A few days later, she was readmitted to the same hospital with a similar set of

symptoms. She received a provisional diagnosis of stroke for which she was treated. A subsequent computed tomography (CT) scan of the brain did not reveal any lesion. Routine blood glucose measurement showed random plasma glucose level of 34 mg/dl. She received a 25% dextrose injection and her condition dramatically improved. A routine ultrasonography revealed a large retroperitoneal mass. Fine needle aspiration cytology from the mass was suggestive of atypical lipomatous tumour. She was referred to our institution for further management. A complete metastatic workup was negative. A contrast enhanced CT scan of her abdomen showed a heterogeneous multilobulated retroperitoneal fat density that occupied the left part of her abdominal cavity. The mass displaced both the left kidney and the bowels across the midline (Figures 1, 2). Her blood biochemistry was within normal limits, with the exception of her plasma glucose levels that continuously fluctuated (range: 20 to 40 mg/dl) and led to recurrent hypoglycemic episodes. She was placed on a dextrose drip. A provisional diagnosis of NICTH was kept in mind. Her total plasma insulin level was 3.95 uIU/ml (normal value for adults: 0.7-9 uIU/ml). The C-peptide level was 0.79 ng/ml (normal: 0.7-1.9

ng/ml). Serum IGF 1 and 2 levels were not measured due to lack of availability in our hospital. Her cortisol and growth hormone levels were within normal limits. She underwent exploratory laparotomy followed by enbloc excision of the retroperitoneal mass under general anesthesia (Figures 3 and 4). The histopathologic examination was consistent with an atypical lipomatous tumour. Her postoperative recovery was not eventful. The plasma glucose level stabilized after the third postoperative day and she was discharged in stable condition. At the 6-month follow up she had no recurrence and was free from hypoglycemic episodes.

Discussion

Non-islet cell tumor hypoglycemia may be much more common than reported. More than 100 cases have been described in the literature since it was first reported in 1929 in a patient diagnosed with hepatocellular carcinoma. The causes of paraneoplastic hypoglycemia vary and include production of non-suppressible insulin-like growth factor 1 and insulin like growth factor 2; hypermetabolism of glucose; production of substances that stimulate ectopic insulin release; production of hepatic glucose inhibitor; insulin



Figure 1. CECT (Contrast enhanced computed tomography) images of abdomen showing a heterogenous retroperitoneal mass present in the left iliac fossa.

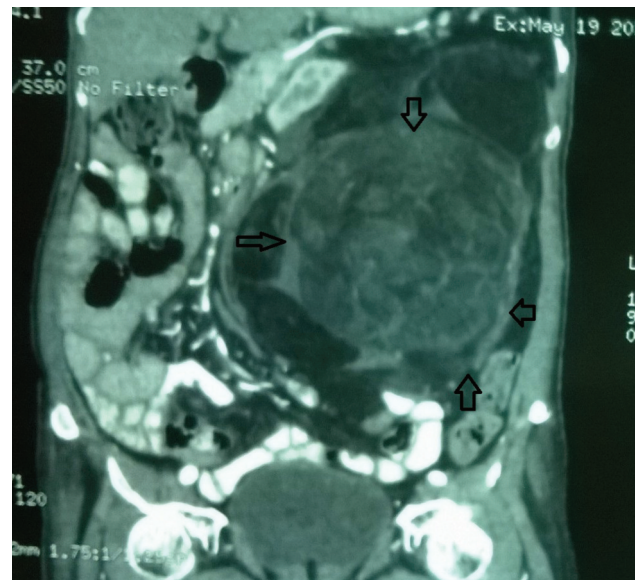


Figure 2. Contrast enhanced computed tomography [CECT] (coronal cut) images of abdomen showing a multilobulated retroperitoneal mass extending from the pelvis up to the diaphragm. The mass has pushed the bowels off the midline.

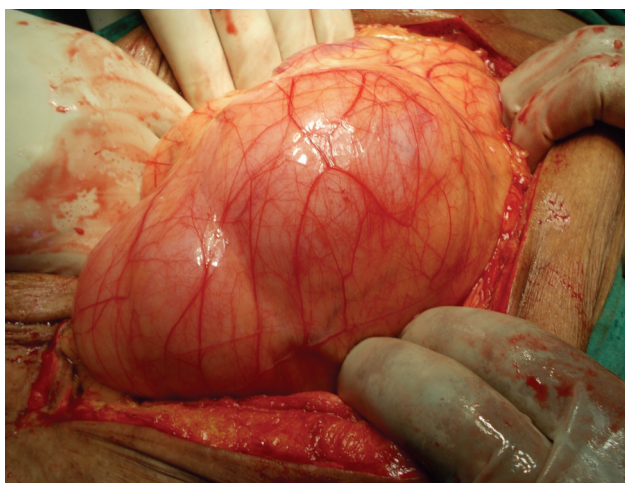


Figure 3. Globular mass visible upon entry into the abdomen.

binding by a monoclonal protein; insulin receptor proliferation; or, rarely, ectopic insulin production.⁵⁻⁸ Patients with NICTH have hypoinsulinemic hypoglycemia and low GH and beta-hydroxybutyrate. The C-peptide level is usually low. Total IGF2 may be either increased, decreased, or within the normal range. However, an inappropriately reduced IGF1 level in a patient with hypoinsulinemic hypoglycemia is a strong indicator of NICTH. Increased ratio between total IGF2 and IGF1 >10 is a useful additional marker

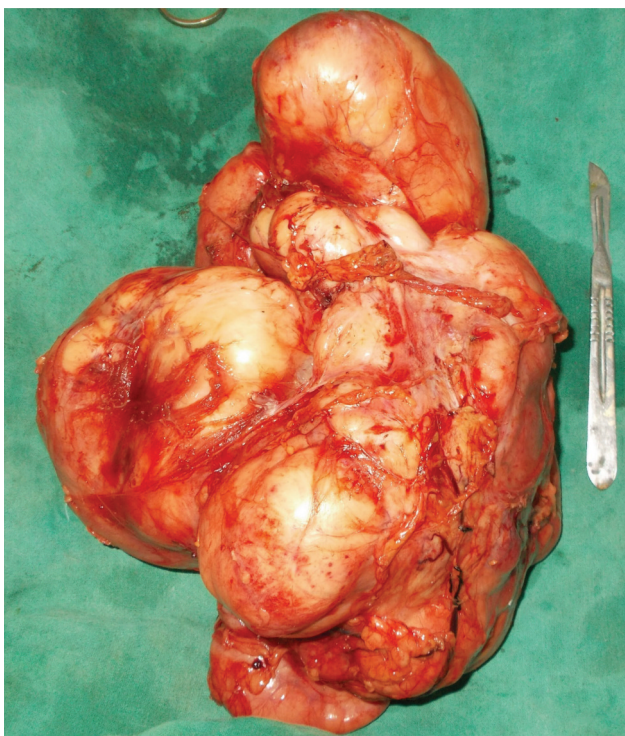


Figure 4. The excised retroperitoneal mass measured 27×21×10 cm.

when the facility for measuring big (pro) IGF2 is not available.⁹ However, in clinical practice, such biochemical tests may not be readily available. The usefulness of such costly tests is also questionable as often the diagnosis is not obvious initially in a patient who only presents with hypoglycemia. Our case has highlighted the fact that NICTH could often be a diagnosis of exclusion. Resolution of symptoms after surgery was an indirect proof of tumor induced hypoglycemia in the current case. A variety of pharmacological agents that include diazoxide, corticosteroids, and recombinant growth hormone have been used to manage hypoglycemia.¹⁰ However, they often lead to partial resolution of symptoms and are costly. Our experience with this case has shown that 25% dextrose, which is easily available, can be an alternative solution for peri- and intra-operative management of hypoglycemia. Surgical resection remains the most rapid, cost-effective therapy to normalize glucose metabolism in most cases of NICTH and should be the preferable option when indicated. Aggressive tumor debulking can also lead to good palliation of symptoms.

Conflicts of Interest

None declared.

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