

Hypoglycemia Due To Fibrosarcoma

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Abstract

We report a patient with pleural fibrosarcoma recurrent after twelve years post resection, presenting with recurrent falls and loss of consciousness secondary to hypoglycaemia which was never present previously. Her symptoms improved after being treated with diazoxide, an antihypertensive.

CASE REPORT

A 76 year old lady was admitted with few months' history of recurrent falls at home. The capillary glucose (BM) after the fall at home was 1.4. There was a history of macular degeneration, osteoarthritis and a histologically confirmed pleural fibro sarcoma, removed 12 years ago. No hypoglycaemic symptoms occurred before or after the surgery. She smoked a cigarette, every day.

Clinical examination showed only reduced breath sounds and dullness at the right lung base. In hospital she suffered from recurrent symptomatic hypoglycaemic episodes and received continuous IV dextrose infusion.

The CXR showed an opacity in the lower half of right hemi thorax which was then confirmed on CT chest as pleural in origin, occupying lower half of right chest with extensions into posterior costophrenic & azygo oesophageal recesses. A provisional diagnosis of "non islet cell tumour hypoglycaemia" was made since there were low C peptide level 107(140-1390), and IGF-2 to IGF-1 ratio of 16.8 (n <10); Insulin level was 3.7, IGF-1 5.4 (n 6-36) and IGF-2 was 90.6. She was given a trial treatment of Diazoxide, based on previous reports, which markedly improved blood glucose. Hypoglycaemic symptoms disappeared completely and dextrose infusion was stopped. She was referred to oncologist /palliative care team for subsequent management.

DISCUSSION

Fibro sarcoma is a tumour of mesenchymal cell origin consisting of malignant fibroblasts. It can be primary or secondary. The secondary lesions can arise from pre-existing lesions or after radiotherapy. It constitutes 10% of musculoskeletal sarcomas and usually present in adults aged 30-60.

Hypoglycaemia from malignant tumours is rare.

Mesenchymal tumours of non pancreatic origin are the most common of the tumours to be associated with hypoglycaemia (cancer 1979). Hypoglycaemia secondary to mesenchymal tumours account for 64% of the cases with hepatomas, adrenal carcinomas, and gastrointestinal malignancies accounting for others (Odell et al (1978), Blackman et al (1978). In order to understand the pathophysiology of recurrent hypoglycaemia in patients with non islet cell tumour, it is essential to understand the biochemistry of insulin like growth factor (IGF). The IGF system comprises of ligands (insulin, IGF-I and IGF-II), receptors (insulin receptors, IR and the IGF-1 receptor, IGF-IR as well as non enzymatic IGF-2 receptors) (Le Roith et al). Although Insulin, IGF-I and IGF-II have their specific receptors, the ligands which share 50% amino acid homology bind non specifically to each others' receptors with varying affinity.

Seventy–80% of circulating IGF is normally bound to insulin-like growth factor binding protein-3 (IGFBP-3) and a protein called acid labile subunit to form an inactive complex which prevents hypoglycaemia. Some tumours like non islet cell tumours may over produce "big IGF-II" which normally represents 10-15% of total circulating IGF. The big IGF-II does not bind well to the IGFBP-3 and stimulates muscle glucose uptake and inhibits adipose tissue gluconeogenesis and lypolysis (Le Roith D (1997), Skarin A (2000). Diagnosis of "non-islet cell tumour hypoglycaemia" can be confirmed by demonstrating low serum insulin levels, C peptide and growth hormone concentrations in the setting of hypoglycaemia, along with elevated "big" IGF-II levels. A total IGF-II/IGF-I ratio of greater than 10 is thought to be diagnostic. (Teale JD et al (1990).

Our patient had a previously resected fibro sarcoma which recurred and presented as a paraneoplastic syndrome with hypoglycaemia over a decade after removal. The management of paraneoplastic hypoglycaemia involves glucose infusion to stabilise the patient and removal of the tumour.

The use of supraphysiological doses of growth hormone or somatostatin analogues (octreotide) have been documented, however large doses of growth hormone may cause fluid overload and maximal dose of octreotide may fail to suppress “big” IGF-II (Perros P et al(1996).

Our patient had refused any surgical input and was initially considered for diazoxide, which is known for its hyperglycaemic action described when used as an antihypertensive. It is useful in patients with unresectable disease, and owes its potent hyperglycaemic properties to two effects (Fajans SS et al (1968). Diazoxide directly inhibits release of insulin by β cells through stimulation of β -adrenergic receptors. Diazoxide also has an extra pancreatic hyperglycaemic effect, probably by inhibiting cyclic adenosine monophosphate (AMP) phosphodiesterase,

resulting in higher plasma levels of cyclic AMP and enhanced glycogenolysis.

References

- r-0. Blackman, N.R., Rosen, S.W, and Weintraub, B.D: Ectopic Hormones Adv. Intern. Med. 23: 85-113, 1978
- r-1. Fajans SS, Floyd JC, Jr., Thiffault CA, Knopf RF, Harrison TS, Conn JW. Further studies on diazoxide suppression of insulin release from abnormal and normal islet tissue in man. Ann N Y Acad Sci 1968; 150(2. 261-280
- r-2. Le Roith D.Seminars in medicine of Beth Israel Deaconess Medical Centre. Insulin-like growth factors.N Engl J Med 336:633-40, 1997
- r-3. Mesenchymal tumour associated with Hypoglycaemia. Cancer 44:785-790, 1979
- r-4. Odell, W.D., Wolfsen, A. R. Humoral Syndromes associated with cancer, Ann Rev. Med 29:379-406, 1978
- r-5. Perros P, Simpson J, Innes JA, Teale JD, McKnight JA. Non-islet cell tumour-associated hypoglycaemia: 111 In-octreotide imaging and efficacy of octreotide, growth hormone and glucocorticosteroids. Clin Endocrinol (Oxf) 1996; 44:727-31.
- r-6. Skarin A.Diagnosis in oncology. Small round cell tumours. Case of hypoglycaemic syncope due to peripheral neuroectodermal tumour. J Clin Oncol 18:1594-1597, 2000
- r-7. Teale JD, Marks V. Inappropriately elevated plasma insulin-like growth factor II in relation to suppressed insulin-like growth factor I in the diagnosis of non-islet cell tumour hypoglycaemia. Clin Endocrinol (Oxf); 33:87-98. 1990

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