Case Report

Insulinoma with seizures – a rare presentation of a rare tumour

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Abstract

Insulinoma is a rare pancreatic endocrine tumour with an incidence of 4 per million population per year and is typically sporadic, solitary and less than 2 cms in diameter. Fewer than 5% of insulinomas are larger than 3 cms and are more likely to be malignant. Here we report a case of insulinoma in a female patient aged 57 years with a rare presentation of recurrent attacks of seizures, syncope and sweating along with episodes of hypoglycemia since 5 years. CT scan localized the tumour to the head of the pancreas and histopathology proved the diagnosis.

Keywords: Insulinoma, Whipple's triad, Seizures, Hypoglycemia.

Introduction

An insulinoma is a functionally active and commonly benign endocrine tumour of the pancreas with evidence of B-cell differentiation and clinical symptoms of hypoglycemia due to inappropriate secretion of insulin [1]. Pancreatic endocrine tumors are very rare lesions with an incidence of 4 per million population per year. Of these rare lesions, insulinomas are the most common. The majority of patients diagnosed with an insulinoma are between 30 and 60 years of age, with women accounting for 59% [2]. Diagnosis of this pathology relies on clinical features along with laboratory tests, imaging investigations to aid in localization and confirmation by histopathological evaluation [3]. An early successful diagnosis and excision of insulinoma will profoundly affect a patient's life [2].

Case Report

We present a 57 year old female patient who presented with recurrent episodes of syncope, sweating, seizures since 5 years. These episodes were associated with hypoglycemia which resolved with glucose administration. The seizures were of complex partial type for which she received anti-epileptic treatment. She also gives a history of weight gain, was diagnosed of hypothyroidism 2 years back and is on medication for the same. The other routine blood investigations were normal. Ultrasound abdomen showed moderate fatty liver changes. CT scan of the abdomen revealed a well defined moderately enhancing lesion measuring 13x11mm in the head of the pancreas. Rest of the pancreas appeared normal. A provisional diagnosis of Insulinoma was suggested. The lesion was excised and sent for histopathology.

Gross examination of the fibrofatty lesion measuring 2.5x2x1.5cms revealed a well circumscribed yellow brown area measuring 1 cm on the cut surface.

On microscopic examination, an encapsulated tumour composed of pleomorphic cells with finely granular cytoplasm and ill-defined cytoplasmic borders was noted. The tumour cells were seen arranged in trabecular and glandular pattern separated by vascular stroma. The nuclei were highly pleomorphic, vesicular with 1-2 nucleoli. (Fig 1, 2). Sparse mitosis with few apoptotic bodies were seen. The normal pancreatic tissue was seen at the edge of the tumour. A histological

Manuscript received 12th October 2016
Reviewed: 25th October 2016
Author Corrected: 10th November 2016
Accepted for Publication 22nd November 2016

diagnosis of pancreatic endocrine tumour (Insulinoma) was made. Since there was no unequivocal evidence of malignancy in the form of cellular anaplasia or infiltration of adjacent organs, long clinical follow up even after surgical excision was advised.

Discussion

Insulinomas account for 60% of islet cell tumors and are typically hypervascular, solitary, small tumors, 90% of which measure less than 2 cm and 30% measure less than 1 cm in diameter. Almost all insulinomas are located within the pancreas, even though aberrant cases have been described in the duodenum, ileum, lung and cervix. Approximately 10% are multiple, 10% are malignant and 4-7% are associated with MEN 1. Insulinomas are diagnosed over a wide age group range, but rarely before the age of 15. The peak incidence is found between 40 and 60 years [4].

The etiology and pathogenesis of insulinomas are unknown. No risk factors have been associated with these tumors. Embryologically, pancreatic tumors arise from similar precursor cells as pancreatic islet cells which are derived from the endoderm [2].

The tumour is characterized by endogenous hypersecretion of insulin and the subsequent development of symptoms. Symptoms of hypoglycemia include both neurogenic symptoms from adrenergic as well as cholinergic stimulation and neuroglycopenic symptoms as a direct result of a decrease in brain substrate. Signs and symptoms include diaphoresis, warmth, hunger, weakness, tingling sensations, paresthesia, difficulty in thinking, confusion, tremulousness, tiredness, drowsiness, palpitations, tachycardia, dizziness, nervousness, anxiety, blurred vision, stupor or coma [5]. The Whipple triad includes: symptoms of hypoglycemia, plasma glucose levels < 3 mmol / litre and relief of symptoms with administration of glucose [2].

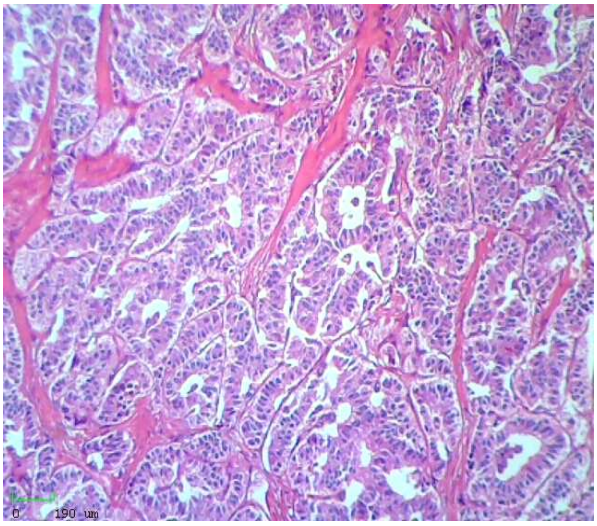

Figure-1: Photomicrograph showing tumour cells arranged in trabecular and glandular pattern separated by stroma (10x)

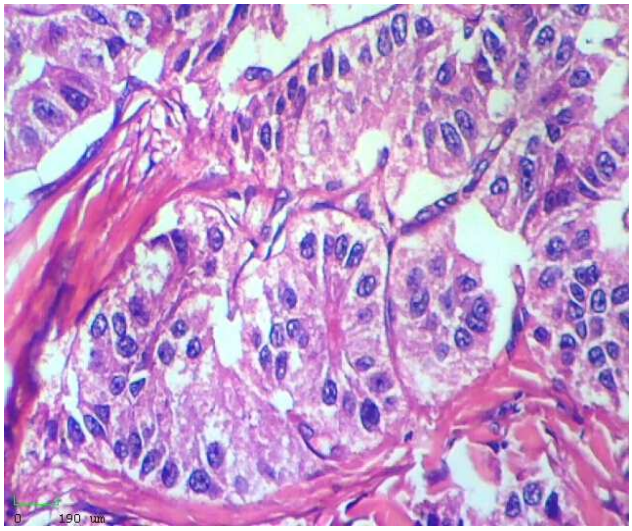

Figure-2: Photomicrograph showing tumour cells with finely granular cytoplasm and pleomorphic vesicular nuclei (40x)

The diagnosis of insulinoma is suggested by endogenous hyperinsulinemia in the presence of hypoglycemia and reversal of the symptoms by the administration of glucose [5]. In patients with insulinoma, there is continued secretion of insulin despite a lower glucose level. Insulin is synthesized as a single chain precursor, proinsulin - which is cleaved into a C-peptide and insulin, both of which are secreted in equimolar concentrations [6].

Once the biochemical diagnosis of a probable insulinoma has been established, localization investigations can greatly aid management decisions. Non invasive methods such as abdominal ultrasound, CT scanning and MRI have the advantage of being simple and quick to perform [7].

The majorities of insulinomas is located in the pancreas or are directly attached to it. Compiled data indicate that insulinomas are equally distributed between the head, body and tail of the pancreas with a slight predominance in the head and tail region [8]. Grossly, insulinomas are well circumscribed, softer than the surrounding pancreatic parenchyma and have red brown cut surface. Insulinomas are frequently discovered while still small with 75% of the tumors measuring 0.5-2 cm in diameter and less than 2 g in weight. The reported diameter ranges from 0.5 – 11 cm. Tumour size is unrelated to severity of symptoms. Malignant insulinomas may show gross local invasion of peripancreatic fatty tissue and / or adjacent organs such as the duodenum or the spleen. The first metastases are usually found in the regional lymph nodes (peripancreatic, celiac, periaortic) and the liver. Spread to other distant sites is unusual [2]. Microscopically, insulinomas exhibit four main histological patterns - solid, trabecular, gland-like tumour growth and mixed forms. Larger tumors are encapsulated but the capsule is usually incomplete. Smaller tumors and microadenomas are rarely encapsulated. Tumor cells frequently exhibit a bland cytology and cells with large, pleomorphic nuclei are rare. If present, these features are not predictive of malignant behavior. A relatively uncommon, but characteristic finding in insulinoma is the deposition of amyloid [9]. Almost all insulinomas exhibit immunoreactivity for insulin and proinsulin. The intensity and extent of this immunoreactivity does not correlate with circulating insulin levels [2].

Conclusion

Insulinoma is reported to be the most common cause of hypoglycemia in patients who are well without systemic illness, once factitious hypoglycemia has been excluded [10]. Early diagnosis and confirmation by histopathology is essential to prevent lethal hypoglycemia [3].

Funding: Nil, Conflict of interest: None.
Permission of IRB: Yes

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How to cite this article?

Samartha V, Hegde S, Philipose T.R.Insulinoma with seizures – a rare presentation of a rare tumour.*Int J Med Res Rev* 2016;4(11):1975-1977.doi:10.17511/ijmrr. 2016.i11.12.

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