Refractory hypoglycemia as a rare cause of initial presentation in previously undiagnosed hepatocellular carcinoma

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Introduction

Hypoglycemia presenting as the initial and sole presentation in a previously undiagnosed hepatocellular carcinoma (HCC) is extremely rare. We report of such a case who was successfully treated with resection.

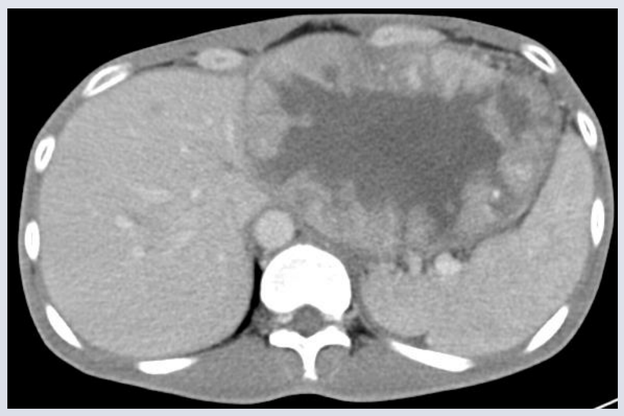
Methodology

Literature review was performed using on line public bibliographic database i.e. Pub Med and MedlinePlus. A search was made to include English Language articles which reported on hepatocellular carcinoma with hypoglycemia ; it's incidence, pathology, presentation and treatment. The literature was then appraised and discussed.

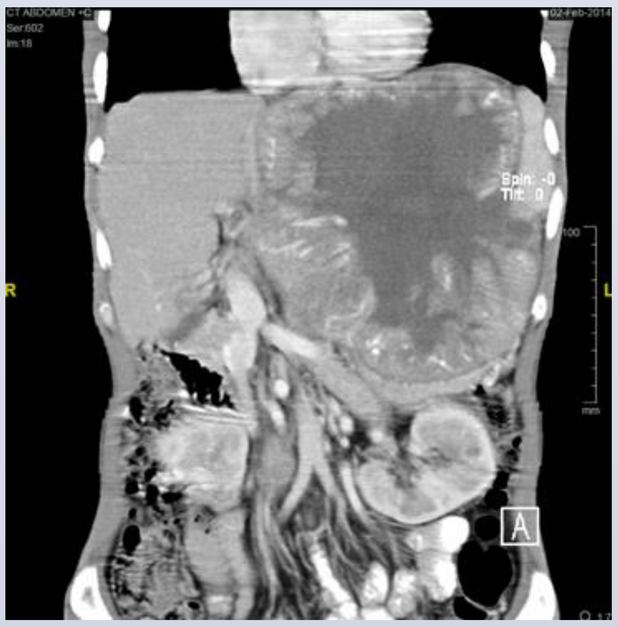
Case Report

A 29 years old male presented to us with loss of consciousness and blood glucose level was detected at 1.3 mmol/L. On further questioning, there was vague abdominal discomfort with weight loss. Abdominal examination revealed a palpable mass over the left liver lobe. Contrast enhanced computed tomography demonstrated a left lateral lobe HCC measuring 17 x 11 x 18 cm. Patient was also found to be Hepatitis B positive and serum alpha feto protein was 79 257 IU/ml. There were no evidence of metastatic disease.

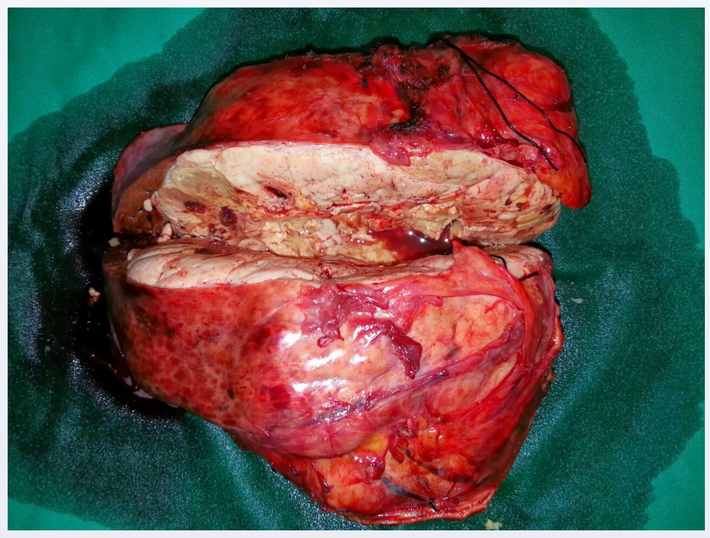
Hypoglycemia persisted despite continuous dextrose infusion. Serum insulin and IGF-1 level sent was low at 0.4 Mu/L and 42 ng/ml respectively. Emergency left lateral hepatectomy was performed with a segment 6 wedge resection for a lesion discovered on intra operative ultrasound. Histopathological examination revealed a moderately differentiated HCC. Post operative was uneventful and hypoglycemia episodes resolved. He was discharged well.



Axial View of the computed tomography image of the tumour confined to the left lateral lobe as evident by it's position lateral to the left hepatic vein



Coronal View of the large HCC. The portal vein, although compressed were not thrombosed.



The resected left lateral lobe with the large tumour bivalved.

DISCUSSION

Hypoglycemia induced by hepatocellular carcinoma is not a new phenomenon. Beers and Morton in 1935,in the American Journal of Cancer Research called it Nadler, Wolfer-Elliot Syndrome, aptly named after the physicians who first described the association between HCC and hypoglycemia.[1]

The incidence of hepatocellular carcinoma presenting as the initial presentation is extremely rare [2, 3]. Hypoglycemia may even be the sole presentation in a HCC patient, as reported by Jayaprasad N [4], similar to our patient who presented acutely with hypoglycemic attack. Hypoglycemia usually occurs late as part of a paraneoplastic phenomenon in HCC, which include hypercholesterolaemia, hypoglycaemia, hypercalcaemia and erythrocytosis.[5] The severity of the hypoglycemia have been reported to cause hypoglycemic encephalopathy [3] and even sudden death [6].

There are 2 known mechanism which HCC could cause hypoglycemia. The tumor could be so large and rapidly growing that the liver, being replaced by the tumour, is unable to satisfy the glucose demand for the tumour and other tissues. This is not the case for our patient the tumor is affecting the left lateral lobe and his right lobe is normal and not cirrhotic. The possible mechanism of his hypoglycemia could be due to the tumor secreting IGF (Insulin-like Growth Factor) 2 , which stimulates IGF 1 and insulin receptors [2,7]. This is proven by his low serum insulin and IGF 1 levels. Yonei Y et al. in an autopsy reported significantly higher IGF 2 levels in the plasma and the tumour tissue of HCC patients.[8] Unfortunately, we were not able to test for the IGF 2 levels in the plasma nor the resected specimen.

The treatment in most cases reported are palliation with symptomatic control as they usually present with advance disease. Thipaporn and colleagues have successfully achieved symptom control with the administration of high carbohydrate intake and corticosteroids [9]. Steroid stimulates gluconeogenesis therefore reducing risk of hypoglycemia. Percutaneous ethanol injection [10] and transarterial chemo-embolisation (TACE) have been used to achieve symptom control by cytoreduction.[11] Very few cases have been successfully treated by resection [2]. We are glad to report he was normoglycemic and symptom free after the resection.

CONCLUSION

IGF 2 induced hypoglycemia in HCC are rare with only few reported in literature and even fewer treated successfully by resection. The above case illustrated that hypoglycemia can be a presentation in HCC albeit rare. Early and appropriate management is crucial to ensure good overall outcome.

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