Original Research Paper

Volume - 12 | Issue - 02 | February - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Internal Medicine

HYPOGLYCEMIA: PARANEOPLASTIC MANIFESTATION OF HEPATOCELLULAR CARCINOMA IN PATIENT OF DIABETES WITH LIVER CIRRHOSIS – A CASE REPORT

Dr Meet Shah* M.D Medicine With Fellowship In Diabetes Consultant Physician And Diabetologist. *Corresponding Author

Dr Nidhi Modi M.B.B.S

ABSTRACT Hepatocellular Carcinoma (HCC) can present with plenty of paraneoplastic manifestation out of which hypoglycemia has prevalence of 4-27%. Here we present a case of 54 years old male patient having diabetes with liver cirrhosis who presented with hypoglycemia but eventually diagnosed as case of hepatocellular carcinoma. As we all know that hypoglycemia is frequent complication of diabetes and Liver cirrhosis and it easily gets treated by primary care physician but this case represents that we must not forget the possibility of hypoglycemia being paraneoplastic manifestation of underlying hepatocellular malignancy.

KEYWORDS : Hypoglycemia , Paraneoplastic manifestations

Case Report :

54 years old male patient was presented to our medical department with history of giddiness followed by unconsciousness since last 15 minutes. As informed by the close relatives of the patient, he had complained of blurring of vision, sweating along with giddiness followed by unconsciousness. There was no history of fever, trauma or convulsions. On Physical examination his pulse was 88 bpm with blood pressure of 138/90 mm Hg. He had gross ascites with pitting oedema in both legs along with jaundice. Rest all findings were within normal limits. His blood sugar on glucometer was found to be 48 mg/dl. Patient was treated with inj. Dextrose 25%. Patient quickly responded to our treatment. As it was a case of severe hypoglycemia, we decided to go for detailed work up for the same.

Patient was already known case of diabetes with cirrhosis of liver since last 4 months. On first visit to author's clinic, his HbA1c was 7.8%. At that time, he was also diagnosed as a case of compensated cirrhosis of liver. As Patient was nonalcoholic, we explained for further workup regarding etiology of liver cirrhosis which was declined by the patient due to financial constrain. He was prescribed Metformin 1000 mg, Dapagliflozin 10 mg and Propranolol 40 mg by the author. After this patient never came back in our follow up and presented with hypoglycemia along with ascites in current visit.

As per Gastro consultation, patient was treated with inj. Albumin 20 gm iv OD infusion and inj. Terlipresin 0.5 mg iv 6 hourly for 5 days with other supportive treatment. On 2nd day also, there was recurrent hypoglycemia on six hourly sugar charting. Many times patient required intermittent dextrose injection to correct severe hypoglycemia. His current HbA1c was found to be 4.2%. On 5th day onwards there were no further episodes of hypoglycemia and his sugars became quite stable. Patient's lab parameters improved gradually (Table 1) and patient responded to our treatment very well.

On further evaluation, he was found to be Hepatitis C reactive with alpha feto protein of 2000 ng/ml(Table 2).CT Abdomen revealed multiple tumors of variable size in liver largest of 6 cm in size invading main branch of portal vein with regional lymph node metastasis as well as pulmonary metastasis(T4N1M1). Patient was diagnosed as case of decompensated cirrhosis of liver (Hep C reactive) with hepatorenal syndrome and hepatocellular carcinoma (Child pugh score -C and MELD score 22).

Patient was discharged on T. Rifaximin 550 BID, T. Propranolol 40 mg OD , Liq. Lactulose 2 tsf HS and T.Urodeoxycholic acid 150 mg BID. No antidiabetic medicines were prescribed. Patient was explained to check their sugar two times a day. He was also advised to go for oncologist opinion for further management of HCC.

In Follow up after 10 days, his sugars were within normal limits. Patient remained euglycemic thereafter. He was on palliative care for HCC.

After 3 months unfortunately patient succumbed to death due to sepsis.

Lab parameters (Table 1):

	Reference Range	On 1st day (At admission)	On 3rd day	On 6th day (At discharge)
Hb (gm%)	12-16	8.6	8.5	8.9
WBC (/cumm)	4000-10000	5500	6200	6500
Platelet (/cumm)	1,50,000 – 4,50,000	1,34,000	1,15,000	1,20,000
SGPT (U/L)	<40	250	180	120
SGOT (U/L)	<30	188	130	90
T. Biilirubin (mg/dl)	<1.0	9.0	7.5	6.0
D. Billirubin (mg/dl)	<0.25	7.2	6.5	4.5
S. creatinine (mg/dl)	0.6-1.2	2.4	1.8	1.5
S. Protein (gm/dl)	6.4-8.3	7		
S. Albumin (gm/dl)	3.5-5.5	3.4		
PT INR	<1	1.4	1.51	1.4
RBS charting(mg/dl)	70-140	4 Episodes of Hypoglycemia in a day	2 episodes of hypoglycemia in a day	No episodes of Hypoglycemia

Special investigations (Table 2):

Investigation	Result	Reference Range
HbA1c	4.4%	HbA1c <7%: well controlled
Ascitic Fluid R/M	Total protein <2 g/dl Fluid Albumin <1 g/dl WBC count-235/cumm RBC count -280 /cumm	<3: Transudative >3: Exudative
Anti HCV Ab	Reactive	-
HCV RNA Quantitative Viral load (Real Time PCR)	103 copies /ml	
HCV Genotype	3	-
HbsAg	Non reactive	-
HIV	Non reactive	-
Alpha Feto Protein	>2000	0.89-8.78 ng/ml
C peptide	2.46 ng/ml	0.92-3.73 ng/ml

DISCUSSION:

Hepatocellular carcinoma is considered to be the 5th most common malignancy worldwide with significant mortality.[1]

Classical presentation of HCC include malaise, weight loss , anorexia, abdominal pain while atypical presentation include paraneoplastic manifestation. There are plenty of paraneoplastic manifestations of HCC like hypoglycemia, hypercholesterolemia, hypercalcemia, erythrocytosis. Out of all, Hypoglycemia has prevalence of 4-27%.[1]

Hypoglycemia seen in HCC is divided into two categories [2]:

Type	Stage of disease	Mechanism
Type A	In advanced HCC	-Increased glucose demand by the rapidly growing tumor which is not compensated by the Liver. -Hypoglycemia triggers increased glucagon level and suppressed insulin and c peptide levels due to counter regulatory response.
Type B	In early stage	-Defective processing of pro IGF2 by the hepatocytes. -IGF2 being small particle, it gets transferred easily through capillary membranes and have more access to IGF1, IGF2, and insulin receptors, thereby causing increased glucose uptake.

In our case c peptide was normal which suggested non islet cell tumor. It was probably type A hypoglycemia in view of large size with rapid progression of tumor.

There are no definite treatment of hypoglycaemia irrespective of type. Primary modality of treatment is intravenous glucose infusion for immediate correction of low sugar. Those patients who are refractory to intravenous glucose infusion requires secondary modality of treatment which includes cytoreduction by ethanol injection, trans arterial chemo embolization(TACE). TACE can be the method of choice in unresected large HCC.

High carbohydrate diet with corticosteroids are also utilized whenever required.[3] Oral prednisolone can be tried on initial basis. Those patients not responding to oral prednisolone can be treated with long term therapy on dexamethasone 2 mg /day to maintain euglycemia[4].Other potential treatment options can be glucagon infusion , high dose of growth hormone , somatostatin analogue , diazoxide but their response can be transient[5]. Liver transplantation or complete surgical resection of tumour are of definite benefit.

HCC patients with paraneoplastic manifestations have overall decreased survival irrespective of tumor size and stage [6].

SUMMARY :

- Hypoglycemia can be paraneoplastic manifestation of underlying HCC. Regular surveillance of AFP in cirrhosis of Liver can help us in early identification of HCC.
- Hypoglycemia is also frequent complication seen in patients of cirrhosis of liver. Potential etiology behind this can be impaired hepatic glucose production, sepsis (esp. spontaneous bacterial peritonitis) , acute kidney injury (esp. hepatorenal syndrome) and multiple drug interactions affecting liver metabolism.
- Antidiabetic drugs need to be prescribed meticulously in patient of Liver cirrhosis with respect to their CTP or MELD score ,renal function test , risk of hypoglycemia and these patients should be kept in close follow up.

REFERENCES:

1) Schiff L, Schiff ER, Diseases of the Liver. 7th ed. Philadelphia, PA: Lippincott: 1993.
2) Hypoglycemia, the first presenting sign of hepatocellular carcinoma. Nikeghbalian S, Bananzadeh A, Yarmohammadi H Saudi Med J. 2006 Mar; 27(3):387-8.
3) Transarterial chemoembolization for palliation of paraneoplastic hypoglycemia in a patient with advanced hepatocellular carcinoma. Whitsett M, Lindenmeyer CC, Shaw CM, Civan JM, Fenkel JM J Vasc Interv Radiol. 2013 Dec; 24(12):1918-20.
4) Hepatocellular carcinoma with persistent hypoglycemia: successful treatment with corticosteroid and frequent high carbohydrate intake. Thipaporn T, Bubpha P, Varaphon V J Med Assoc Thai. 2005 Dec; 88(12):1941-6.
5) The role of glucagon administration in the diagnosis and treatment of patients with tumor hypoglycemia.Hoff AO, Vassilopoulou-Sellin R Cancer. 1998 Apr 15; 82(8):1585-92.
6) Prognostic role and significance of paraneoplastic syndromes in hepatocellular carcinoma. Qu Q, Wang S, Chen S, Zhou L, Rui JA Am Surg. 2014 Feb; 80(2):191-6.