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AMPULLARY METASTATIC NEUROENDOCRINE TUMOUR PRESENTING AS ACUTE LIVER FAILURE – A RARE OBSERVATION

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ABSTRACT

Neuroendocrine tumours (NETs) are a heterogeneous group of neoplasms made of cells with both neural and endocrinal properties. Gastrointestinal NETs are very rare, and among them, duodenal NETs are exceedingly rare. Though duodenal NETs frequently metastasize to the liver, will not cause severe functional disturbance. This case is a very rare presentation of a 49 year old female in Acute liver failure caused by liver metastasis of a poorly differentiated ampullary NET.

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INTRODUCTION

Neuroendocrinal tumours can arise from the diffuse neuroendocrine system in the central nervous system, respiratory tract, thyroid, skin, urogenital system, pancreas and the Gastrointestinal tract. Though they are rare to occur their prevalence is increasing because of better diagnostic modalities. In the Gastro intestinal tract NETs occur most commonly in the colon and rectum (69%), followed by small intestine (36%), stomach (10%), duodenum (5-8%) appendix (5%) and esophagus (0.4–2%) [(1)].

CASE STUDY

A 49-year-old female without any comorbidities presented with 30 days history of dull aching right hypochondrium pain, progressive jaundice, and loss of appetite. There was no history of toxin/drug exposure. On examination she has Icterus, tender hepatomegaly which is hard in consistency. Her Haemoglobin (11.6 gm/dl), leucocytosis (12,600 cells/mm3), Platelet count (2.09 lakhs/mm3), Total Bilirubin (16.95 mg/dl), Direct Bilirubin (9.04 mg/dl), aspartate aminotransferase (AST) (385 U/l), alanine aminotransferase (ALT) (44 U/L), alkaline phosphatase (129 U/L), Albumin (3.5gm/dl), Globulin (3.6gm/dl), international normalized ratio (INR) (1.6) . Renal function was normal, viral markers (HBsAg, HCV, IgM HAV, IgM HEV) were negative, serum ceruloplasmin was normal, CMV and EBV serology were not done. Ultrasound abdomen showed increased echotexture of liver and hepatomegaly. Contrast enhanced Computed tomography abdomen is done which showed hepatomegaly with multiple ring enhancing lesions noted in both lobes of liver which shows washout in venous phase; the differentials of metastasis with unknown primary and lymphoma were considered. Tumour markers (AFP, CEA, CA 125, CA 19.9) were within normal limits.

Upper GI endoscopy was done to rule out primary gastric/duodenal tumour, which showed a 1.5cm proliferative growth in the periampullary region FIG2. Biopsy was taken from the growth and sent for Histopathological examination.

Contrast enhanced MRI abdomen was done for better delineation of biliary anatomy and to rule out possible biliary obstruction secondary to tumour, as the patient was having worsening jaundice. MRI showed no biliary obstruction with normal common hepatic and common bile duct calibre FIG1.

Biopsy showed features suggestive of poorly differentiated neuroendocrinal tumour. During hospital stay patient developed overt

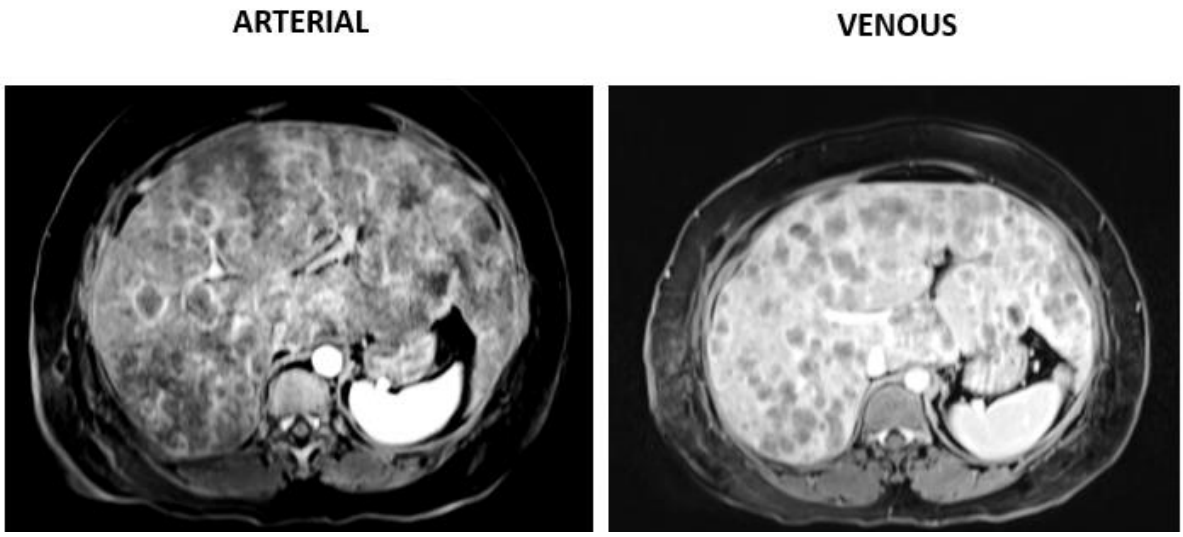

FIG 1 – Contrast MRI- Multiple small well-defined lesions, T1 isotense/ T2 hyperintense with surrounding hypointense rim, peripheral enhancement on arterial and venous phase with relative washout on delayed phase

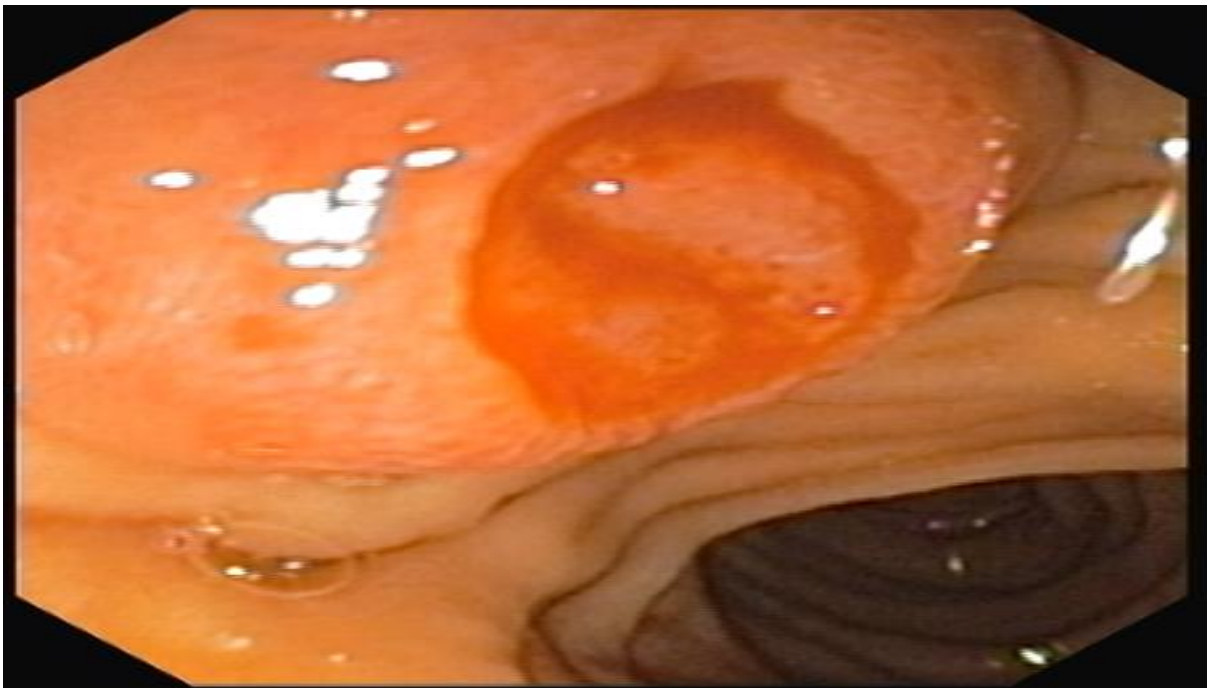

FIG 2 – upper GI endoscopy - 1.5cm proliferative growth in the periampullary region with friable overlying mucosa

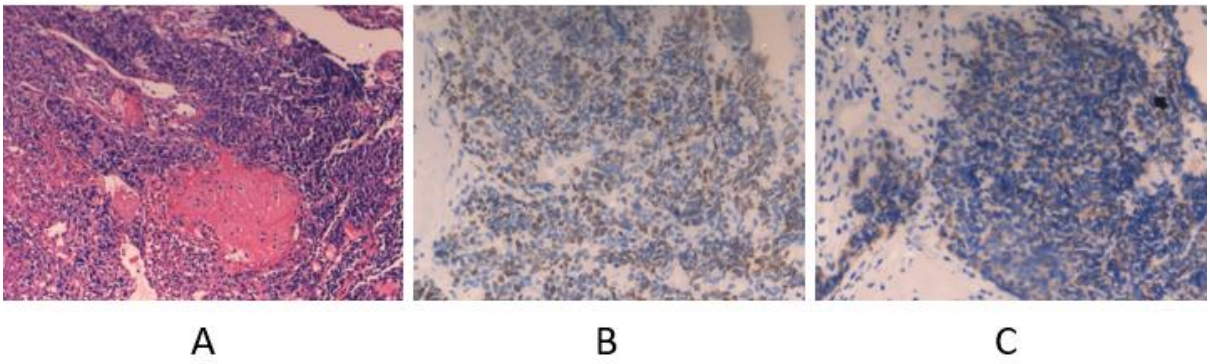

FIG 3 - Infiltrating tumour, arranged in syncytial and focal nested pattern with vague glandular differentiation, with focal areas of necrosis (FIG3A). Immunohistochemistry was done to know about tumour characteristics Ki 67 labelling index was 40% (FIG3B) synaptophysin (FIG3C), was weakly positive, chromogranin was negative, CDX2 was negative

encephalopathy along with worsening jaundice, coagulopathy, intermittent hypoglycaemia. Thus, the final diagnosis of Poorly differentiated non-functional periampullary neuroendocrine carcinoma with hepatic metastasis causing Acute liver failure was made. Patient was given supportive care in the form of anti-encephalopathy measures, fluid replacement, and blood sugar monitoring. Due to personal reasons patients was taken home against medical advice. A Telephonic follow up was done and was found that she died shortly after discharge.

DISCUSSION

Acute liver failure is a severe acute liver injury with impaired synthetic function (INR ≥1.5) and encephalopathy in a patient without pre-existing liver disease or cirrhosis [(2)]. Liver metastases are a rare cause of acute liver failure with only 0.44% of total cases occurring due to malignant infiltration and Non-Hodgkin's lymphoma is the predominant aetiology causing infiltration [(3)]. Malignancy causes ALF by widespread hypoxic hepatocellular necrosis secondary to (a) massive sinusoidal infiltration: hepatic vessels obliteration by tumour cells and (b) cytokine release by the tumour cells : bile duct injury, leukocytes and sinusoidal cells activation impeding the sinusoidal microcirculation [(4)]. In Acute liver failure due to malignant infiltration there can be predominant elevation of AST as seen in this case [(4)].

Duodenal-Neuro Endocrine Tumours(D-NET) are by themself exceedingly rare with an overall incidence of 0.19/100000 and accounts for 5%-8% of all GI-NETs [(5)]. Majority of D-NETs (90%) are non-functional and D-NETs

of ampulla of Vater or the periampullary region are Poorly differentiated, have More advanced stage of the disease, Usually present with lymph node metastasis or liver metastasis, and Have an overall poor survival [6]. The combination of D-NET with liver metastasis causing acute liver failure is an exceedingly rare with no known case documented in literature, although One case of metastatic NET with unknown primary causing ALF is known [7]. Though Various treatment options available for patients with hepatic metastases from NET: systemic, locoregional and surgical [8] , because of the advanced nature of the disease and paucity of time none of the therapies could be attempted.

CONCLUSION

Acute liver failure is a life-threatening illness and universally fatal if not appropriately managed. Early etiological diagnosis is needed for proper treatment. Metastasis is unlikely to cause acute liver failure, but in rare instances like in our case, metastatic NETs can present with an acute liver failure. Physicians must have a high index of suspicion to consider such aetiology of ALF.

Conflict of interest statement:

Authors declare that there are no financial, personal or any other conflicts of interest that may affect the objectivity of this work.

Authors' contributions

All authors made contributions to the article

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