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A case of adrenocorticotropic hormone producing pancreatic neuroendocrine tumor -A case report

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ABSTRACT
Neuroendocrine tumors are specialized tumors arising from enterochromaffin cells that are lining the entire gastrointestinal tract and has the ability to produce and secrete amines and also a wide range of hormones. Herewith, we are reporting a case of adrenocorticotropic hormone secreting pancreatic neuroendocrine tumor. A 52 year old female patient presented with abdomen pain over the right and left lumbar region for the past four months, indigestion, loss of weight and loss of appetite for the past three months, and difficulty in using both lower limbs for the past two days. On admission, the patient was drowsy and severely dehydrated, with an initial blood pressure of BP- 180/110 mm hg and random blood sugars of 440 mg/ dl, and urine acetone was negative. Abdomen examination revealed tenderness over the right and left lumbar region without any obvious mass. Laboratory examination revealed dysglycemia, hypernatremia, hypokalemia, metabolic alkalosis, and increased urinary sodium and potassium excretion. Ultrasound abdomen revealed multiple hyperechoic lesions in both lobes of liver. Contrast enhanced computed tomography of the abdomen showed hepatic metastasis largest in segment 2 of liver. Upper gastrointestinal scopy showed grade 3 esophageal candidiasis and colonoscopy was normal. In view of persistent hypernatremia, hypokalemia, and metabolic alkalosis an endocrine disorder was suspected. Direct Renin = 20.8 µIU / ml (4.4 – 46.1), Plasma aldosterone = 14.7 ng / dl (2.21 -35.3 ng / dl), aldosterone / direct renin ratio = 0.1 (< 2.36), baseline Sr. Cortisol 8 AM = > 63.4 µg / dl, 24 hour urinary cortisol was elevated (10872 µg/dl), overnight dexamethasone suppression test = 157.3 µg/dl, Plasma ACTH = 189.4 pg/ ml (< 46), high dose dexamethasone suppression test showed no suppression (169. 4 µg/ dl), magnetic resonance imaging of brain was normal. Hence, a diagnosis of ectopic Cushing syndrome was made. To localize the primary tumor, 18 fluorodeoxyglucose positron emission tomography of whole body revealed a metabolically active pancreatic mass lesion of 3 * 2 cms involving distal body and tail with metabolically active bipolar hepatic parenchymal lesions and bilaterally enlarged adrenals with normal attenuation values. Retroperitoneal lymph nodes were enlarged. Biopsy of the liver metastasis and pancreatic mass lesion showed features suggestive of a neuroendocrine tumor with synaptophysin, chromogranin, and CA 19-9 positivity. Hence, a final diagnosis of Stage 4 adrenocorticotropic hormone producing pancreatic neuroendocrine tumor was made. The patient was started on Tablet. Amiloride to correct the underlying metabolic abnormality, and Tumor board protocol from our institute suggested starting on Tablet. Cyclophosphamide 50 mg. The patient succumbed to the illness after fifty days.

KEYWORDS: Neuroendocrine tumor, ectopic Cushing syndrome, hypernatremia, hypokalemia, metabolic alkalosis, diabetes mellitus.

I. INTRODUCTION:

Neuroendocrine tumors are specialized tumors arising from enterochromaffin cells that are lining the entire gastrointestinal tract. They have subsequently been reported in a wide range of organs, but they most commonly involve the lungs and gastrointestinal tract. When neuroendocrine tumors cause clinical symptoms from secreted hormones, they are termed as functioning. The most common syndromes associated with functioning neuroendocrine tumors are insulinoma, and Zollinger- Ellison syndrome. Less common syndromes include Glucaganoma, Somatostatinoma, ACTHoma, etc. The diagnosis can be made based on molecular genetics, tumor biology, histopathology, biochemistry, and localization. Since most tumors are malignant at the time of clinical presentation surgical care is seldom required. Medical management includes somatostatin analogs, chemotherapy, and external irradiation. Herewith, we report a case of adrenocorticotropic hormone producing pancreatic neuroendocrine tumor.

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II. CASE REPORT:

A 52 year old female patient with no known co-morbidities presented with complaints of abdomen pain over the right and left lumbar region for the past four months. Indigestion, loss of weight, and loss of appetite for the past three months, and difficulty in using both lower limbs for the past two days. She is married with two children and attained menopause two years back. On admission, the patient was drowsy and severely dehydrated, had petechial spots over the lower limb and upper limb, and had features of hirsutism. Oral candidiasis was present. The patient had an initial blood pressure of 180/110 mm hg, random blood sugars of 440 mg/ dl, and urine acetone was negative. Abdomen examination revealed tenderness over the right and left lumbar region without any obvious mass. Laboratory examination revealed total count – 19900 cells/ µL, hemoglobin – 13 g/dl, platelet count – 69000 cells/ µL, random blood sugar – 440 mg/ dl, liver function test - normal, Urea/creatinine – 26 / 0.7 mg/dl, serum sodium – 149 meq / L, serum potassium - 2.7 meq / L, urine acetone – negative, serum osmolality – 380 mosm / kg, PH - 7.48, Hco3- 28 meq/ L, serum magnesium = 2.4 mg /dl, serum calcium = 8.8 mg / dl, serum phosphorous = 3.8 mg / dl, thyroid function test was normal, viral markers were negative, cultures were negative. Urine sodium =70 meq / L, urine potassium = 36.8 meq / L, urine calcium = 5.4 meq / L, urine creatinine = 18.4 mg / dl suggesting renal loss of electrolytes. In view of persistent hypernatremia, hypokalemia and metabolic alkalosis an endocrine disorder was suspected. Direct Renin = 20.8 µIU / ml (4.4 – 46.1), Plasma aldosterone = 14.7 ng / dl (2.21 - 35.3 ng / dl), aldosterone / direct renin ratio = 0.1 (< 2.36), baseline Sr. Cortisol 8 AM = > 63.4 µg / dl, 24 hour urinary cortisol was elevated (10872 µg/dl), overnight dexamethasone suppression test = 157.3 µg/dl, Plasma adrenocorticotropic hormone = 189.4 pg/ ml (< 46), high dose dexamethasone suppression test showed no suppression (169. 4 µg/ dl) suggesting ectopic adrenocorticotropic hormone syndrome. Upper gastrointestinal scopy showed grade 3 esophageal candidiasis and colonoscopy was normal. Ultrasound abdomen showed a hyperechoic lesion in both lobes of liver. Contrast enhanced computed tomography of the abdomen showed hepatic metastasis largest in segment 2 ofthe liver. 18 fluorodeoxyglucose positron emission tomography of the whole body revealed a metabolically active pancreatic mass lesion of 3 * 2 cms involving the distal body and tail with metabolically active bipolar hepatic parenchymal lesions and bilaterally enlarged adrenals with normal attenuation values. Retroperitoneal lymph nodes were enlarged. Biopsy of liver metastasis and pancreatic mass lesion showed features suggestive of neuroendocrine tumor with synaptophysin, chromogranin, and CA 19-9 positivity. Hence, a final diagnosis of Stage 4 Adrenocorticotropic hormone producing pancreatic neuroendocrine tumor was made. The patient was started on Tablet. Amiloride to correct the underlying metabolic abnormality, and the tumor board protocol from our institute suggested starting on Tablet Cyclophosphamide 50 mg. The patient succumbed to the illness after fifty days.

III. DISCUSSION:

Pancreatic neuroendocrine tumors are rare tumors. The presence of hypertension, severe hypokalemia, weight loss, and hypercortisolemia should raise suspicion towards ectopic Cushing syndrome. They are difficult to treat because of their aggressive nature. According to a study published by Ji Wu et al, ACTHoma was more common in women (66.4%), and the mean age was 44.7 years. Tumors were generally large, and the mean tumor size was 4.43 cm. The incidence of clinical manifestations was: hypokalemia, 69.3%; diabetes, 63.2%; weakness, 60.1%, hypertension, 56.4%; moon face 41.1%; and edema, 37.4%. These tumors were more commonly found in the tail of pancreas, and the most frequent site of metastasis was the liver. Our patient had hypertension, diabetes, hypokalemia, and a tumor of 3 * 2 cm lesion at the distal body and tail of pancreas with liver metastasis. The patient was diagnosed as stage 4 Adrenocorticotropic hormone producing pancreatic neuroendocrine tumor. The patient succumbed to the illness after fifty days.

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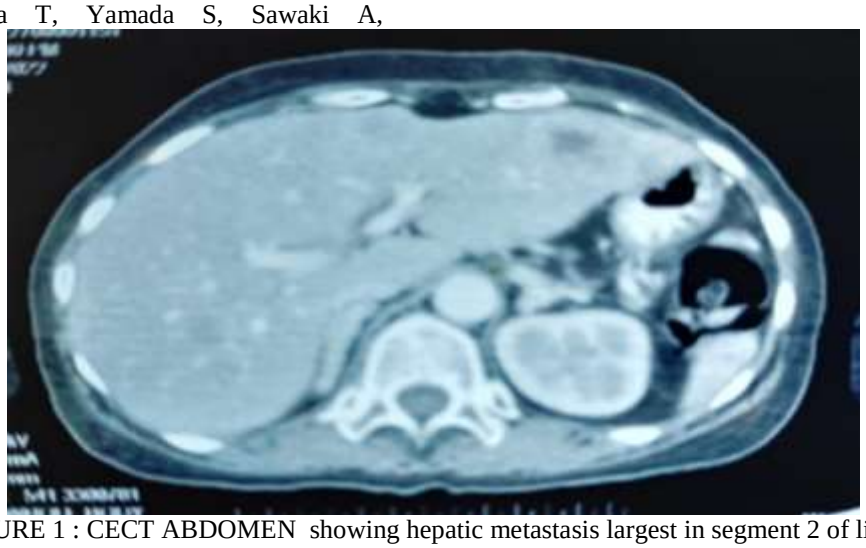

FIGURE 1 : CECT ABDOMEN showing hepatic metastasis largest in segment 2 of liver.

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FIGURE 2 : MRI BRAIN showing normal study

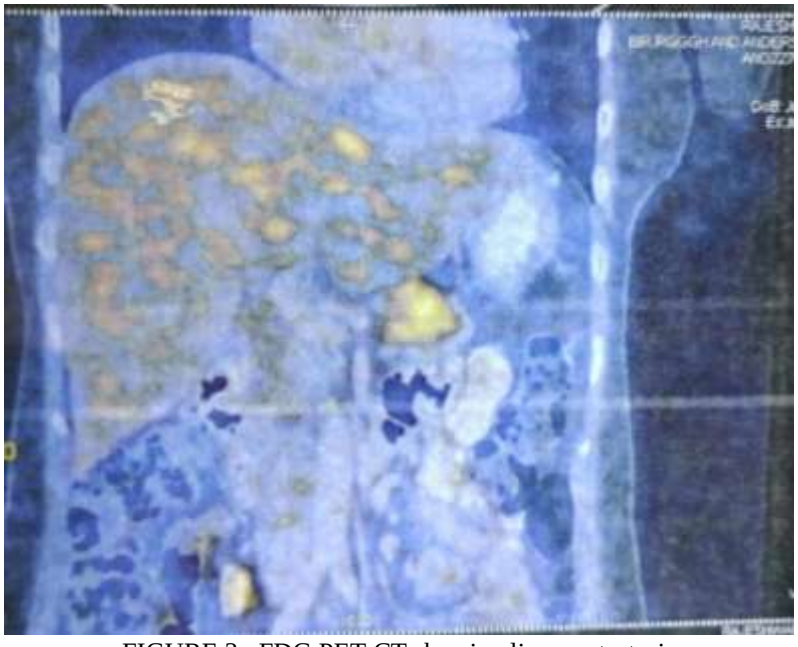
FIGURE 3 : FDG PET CT showing liver metastasis

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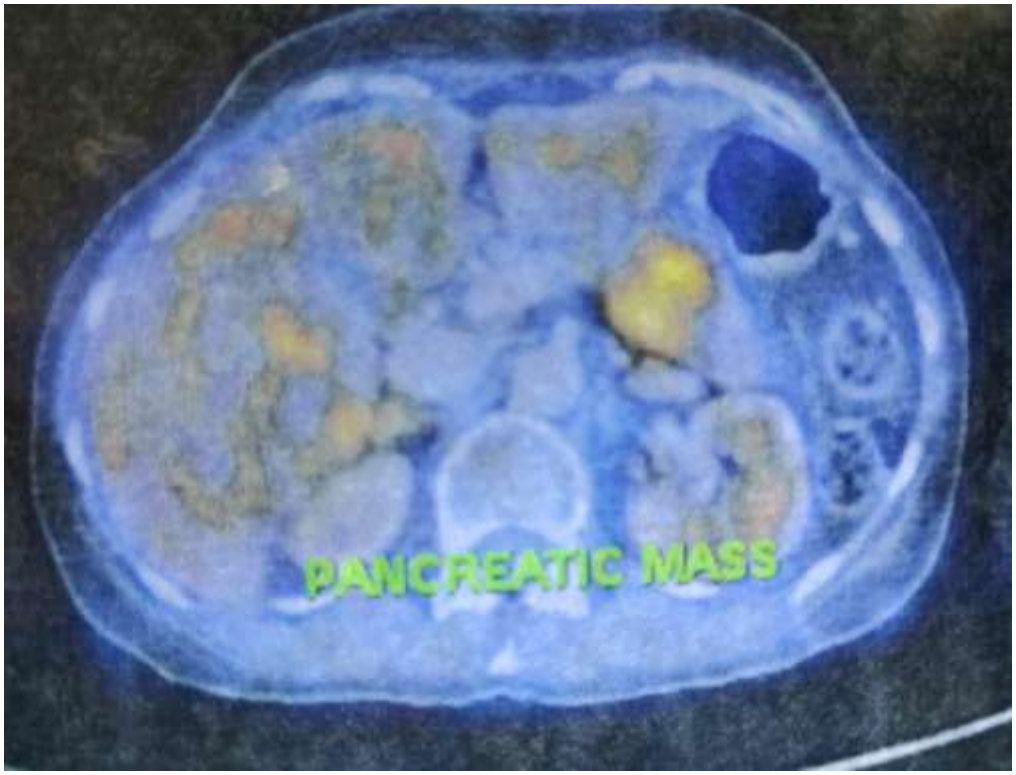

FIGURE 4 : PET CT showing liver metastasis and pancreatic mass

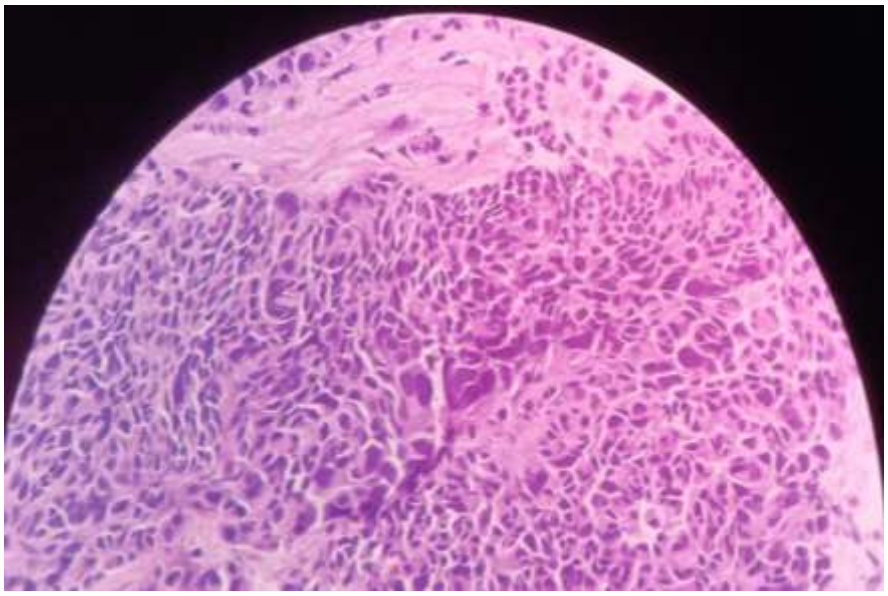

FIGURE 5 : Biopsy of liver metastasis showing neoplasm arranged in cords, nests, pseudo glandular sheets of round to oval cells with increased nuclear cytoplasmic ratio, moderate nuclear atypia. Stroma shows desmoplasia with lympho plasmacytic infiltrate.

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Table 1 : Laboratory values of patients

COMPLETE BLOOD COUNT	PATIENT VALUE	NORMAL VALUE
RBC COUNT (million cells/cu.mm)	4.98	3.5-5
WBC COUNT(Cells/cu.mm)	19900	4500-12000
HEMOGLOBIN(g/dl)	13	12-15
MCV (fl)	86	90±8
PCV (%)	36	40±6
PLATELET COUNT (lakh cells/cu.mm)	69000	1.5-4
COAGULATION PROFILE		
PROTHROMBIN TIME(seconds)	14	11-13.5
ACTIVATED PARTIAL THROMBOPLASTIN TIME(seconds)	28	25-35
INR	0.9	<1
LIVER FUNCTION TEST		
TOTAL BILIRUBIN (mg/dl)	0.8	0.3 – 1.3
DIRECT BILIRUBIN (mg/dl)	0.4	0.1-0.4
SGOT (IU/L)	72	12-38
SGPT (IU/L)	68	7-41
ALP (IU/L)	78	35-130
TOTAL PROTEIN (g/dl)	6.8	6.5-8
SERUM ALBUMIN (g/dl)	4.5	3.5-5
RENAL FUNCTION TEST		
BLOOD UREA (mg/dl)	26	15-40
SERUM CREATININE (mg/dl)	0.7	0.5-1.3
SERUM ELECTROLYTES		
SERUM SODIUM (meq/L)	149	135-145
SERUM POTASSIUM (meq/L)	2.7	3.5-5
SERUM MAGNESIUM (mg/dl)	2.4	1.7-2.2
SERUM CALCIUM	8.8	8.5-10.5
SERUM PHOSPHOROUS	2	1.5-2
THYROID FUNCTION TEST	Normal	
VIRAL MARKERS	NEGATIVE	
BLOOD CULTURE AND SENSITIVITY	Negative	
URINE CULTURE AND SENSITIVITY	Negative	
ECHOCARDIOGRAM	Normal	
CHEST X RAY	Normal	
P^H	Negative	
SERUM BICARBONATE(meq/L)	28	22-26