ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 12 | December - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MEN 1 SYNDROME WITH RARE PRESENTATION

General Medicine

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ABSTRACT

Background: Multiple Endocrine Neoplasias(MEN) are defined as the tumors involving two or more endocrine glands.MEN syndromes can be categorized into four types- MEN1,MEN2A, MEN2B, MEN4, each with an autosomal dominant inheritanceMEN1 or Wermer's syndrome is characterized by the triad of tumors of parathyroid (90-95%),pancreatic islets cells(30-70%),anterior pituitary gland (30-40%) and Early recognition of signs and symptoms complex of MEN syndromes is of paramount importance. This has a direct effect on patient's survival(5years)
Objective -To Present a case of MEN 1 syndrome with rare presentation
Case study-We hereby report a case of a 25 years old male, who presented to us with recurrent diarrhea(diagnosed as noninfective diarrhea) and upon detailed evaluation was found out to be a case of Wermer's syndrome
Conclusion-Early diagnosis of MEN 1 syndrome can have better outcome

KEYWORDS

MEN1,Insulinoma, Pitutary microdenoma,Wermer syndrome

INTRODUCTION:

Multiple Endocrine Neoplasias(MEN) are defined as the tumors involving two or more endocrine glands[1].MEN syndromes can be categorized into four types- MEN1,MEN2A, MEN2B, MEN4, each with an autosomal dominant inheritance[2] MEN1 or Wermer's syndrome is characterized by the triad of tumors of parathyroid (90-95%),pancreatic islets cells(30-70%),anterior pituitary gland (30-40%).[2] In addition to above tumor MEN-1 also consist of adrenal cortex tumor(40%),lipomas(30%), neuroendocrine tumors(2-10%),angiofibromas(85%) and meningiomas(1%)[3,4]. MEN-1 affect all age groups with reported age group is between 5 to 81 years,clinical symptoms along with biochemical manifestation of MEN 1 syndrome most commonly observed before fifth decade of life.[3,4,5] Earlier the presentation, worse is the prognosis. It has a sporadic prevalence of 8-14 %. We hereby report a case of a 25 years old male, who presented to us with recurrent diarrhea(diagnosed as noninfective diarrhea) and upon detailed evaluation was found out to be a case of Wermer's syndrome.

Case History

A 25 years old male presented to casualty with history multiple episodes of loose motions for 5 days, with no symptoms of pain in abdomen, fever or vomiting. He had visited outpatient department on multiple occasions with similar episodes in past 3 months. Each time given the symptomatic treatment and sent home. In the present visit, the patient was evaluated thoroughly which revealed the past history of insulinoma enucleation in 2014. The patient had presented with hypoglycemic episodes and neuroglycopenic symptoms. He was not evaluated for the underlying pathology at that time. Much to his fortune, he became asymptomatic and led an absolutely healthy life for the next 6 years till Feb 2020, when he started experiencing recurrent diarrhoeal episodes and a weight gain of 9 kgs with abdominal obesity. None of his first degree relatives had similar symptoms. He was a normal built young male, with moon facies, cushingoid habitus. His general examination revealed normal vital signs. Abdominal wall showed purple striae.Other systemic examination was unremarkable. The stool examination and complete hemogram showed normal parameters, pointing towards the non infective nature of diarrhea. He was treated symptomatically with fluid replacement, diet restriction, and antimotility agents with which his diarrhea improved. A battery of investigations was ordered to rule out multiple endocrine glands involvement which showed following results:

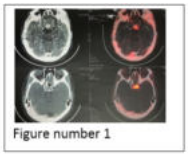
INVESTIGATIONS :Blood parameters

Parameters	Patient values (Normal range)	Disease associated with Increased values	Disease associated with Decreased values
Serum prolactin	**797**(3-18.6ng/ml)	Prolactinoma Pitutary adenoma	Drugs like levodopa Dopamine
Serum C peptide (Fasting)	**2.79 on** 23/5/2014 **8.92**(0.78-5.19ng/ml) on 1/6/2020	Insulinomas Liver cirrhosis	Insulin dependent diabetes
Serum gastrin (PPI stopped 10 days before sample withdrawal)	**2539**(13-115pg/ml)	Achlorhydria Gastrinoma Forgut carcinoid tumors	
Serum chromogranin A (proton pump inhibitors(PPI) and H2 receptors antagonist stopped 10 day before sample withdrawal)	**2920**(<108 mg/dl)	Gastrinoma Pheochromocytoma Carcinoid tumor Medullary carcinoma of thyroid	
Intact parathyroid hormone	**4.3**(15-68.3pg/ml) 1/6/2020 **140**(15-68.3mg/dl) 27/8/2020	Hyperparathyroidism Medullary thyroid carcinoma	Hyperthyrodism Autoimmune hypoparathyrodism
Serum cortisol (8am)	**14.89**(5-23ug/dl) 3/7/2020 **0.960**(3-21ug/dl) 19/8/2020	Cushing syndrome Adrenal adenoma/carcinoma Pituitary adenoma and carcinoma Hypoglycemia	Congenital adrenal hyperplasia Pituitary insufficiency Addisons disease

Serum Insulin(Fasting)	**41**(2-25uIU/ml) 23/5/2014 2.6(2-25uIU/ml) 03/7/2020	Insulinoma Insulin autoimmune syndrome Factious hypoglycemia Corticosteroid use	Diabetes mellitus Pituitary tumors Cystic fibrosis of pancreas
Metanephrine free plasma	18.8 (<65pg/ml)	Phaeochromocytoma	
Nor-Metanephrin free plasma	42.3 (<196pg/ml)	Phaeochromocytoma	
IGF-1 (Somatomedin C)	238(88-537ng/ml)	Gigantism Acromegaly	Hypopitutarism
Serum calcitonin(Thyro calcitonine)	1.66(0-10.2pg/dl)	Medullary carcinoma of thyroid Hyperparathyrodism Chronic inflammatory condtions	
Serum Calcium	**11**(8.8-10mg/dl)	Bone tumors Hyperparathyrodism	Hypoparathyrodism Renal failure ,Rickets
Serum phosphorus	4(2.5-4.5mg/dl)		
Serum alkaline phosphatase	120(38-126U/L)		
Thyroid profile	TSH-1.17(2.77-5.27) FT3-3.22(0.8-1.9) FT4-1.17(0.4-4.68)		

Radiological parameters

Pet scan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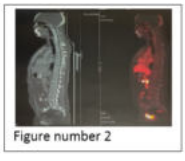
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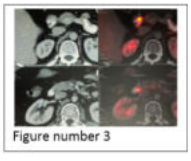
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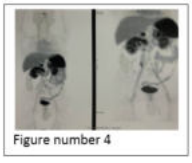
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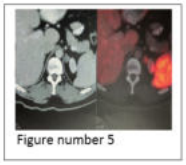
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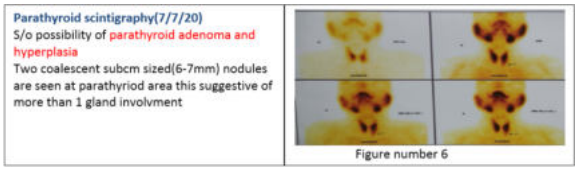
PET scan(Figure 1 -5)(Date-7/7/2020)
Foci of increased dotanoc tracer uptake are seen pancreatico duodenal groove and duodenal papilla

Few peripancreatic lymph nodes with increased dotanoc tracer uptake are seen largest measuring 14*11mm .The largest of peripancreatic node is is abutting junction of neck and body of pancrease all above finding suggestive of somatostatin receptors expressing disease in pancreato duodenal groove and duodenal papilla and metastatic peripancreatic lymph node

Increased somatostatin receptor expression is seen in 17x22mm sized nodules seen in medial limb of left adrenal gland and Increased somatostatin receptors expression seen in 18x22 sized mild enhancing nodules seen in sella turcica

In setting of MEN 1 syndrome finding suggestive of ADRENAL ADENOMA AND PITUTARY ADENOMA respectively



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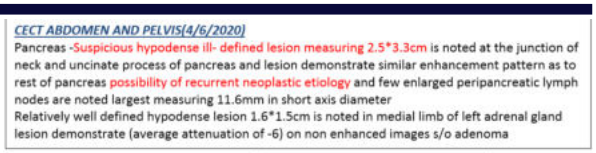

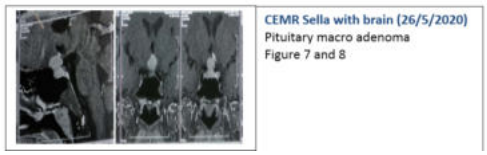

So the presence of MEN 1 syndrome was established based upon the involvement of parathyroid, pituitary and adrenal adenomas on parathyroid scintigraphy and PET SCAN in addition to metastatic pancreatic lymph nodes . The possibility of gastrinoma based upon many folds elevated chromogranin A and gastrin levels.

Retrieval of previous surgery related documents revealed following findings:

CECT abdomen and pelvis(26/5/2014) Pancreas -2.3*1.4cm sized well defined homogenous intensity enhancing mass is seen in the body of pancreas adjacent to lesser curvature of stomach it shows intense enhancement in arterial phase with decreasing enhancement in subsequent phase Impression -All above finding suggestive Insulinoma at pancreatic body
C peptide level (23/5/2014) 2.79(0.81-3.85ng/ml)
Serum Insulin(23/5/2014) **41**(2-25uIU/ml)

Course Of Treatment:

After establishment of the diagnosis, the patient was started on proton pump inhibitors, octreotide, cabergoline and pancreatic enzymes replacement. He showed much symptomatic improvement in gastrointestinal symptoms for next 3 months. In early September 2020, the patient again started experiencing the episodic hypoglycemia symptoms which indicated towards the recurrence of insulinoma. Addition of glucagon therapy did not prove much helpful, and the patient was electively planned for the tumor resection. Unfortunately the patient could not survive it and succumbed to intraoperative ventricular fibrillation due to sudden sympathetic surge.

DISCUSSION :

The clinical symptoms of MEN 1 syndrome depend on site of tumor and there secretions. Insulinoma may be the first manifestation of MEN 1 in 15% of patients[3,5] and approximately 4% of patients with insulinoma will have MEN 1.Parathyroid tumors which are most common tumor of MEN 1 clinically present as primary hyperparathyrodism.[6,7,8].Studies of MEN 1 related mortality showed that 30-46% of death which occurs in MEN 1 syndrome are results of malignant pancreatic tumors, gastrinomas and forgut carcinoid seen most commonly in young age group.[9]

In a patient younger than 40 years of age who presents with insulinoma, quest should be made to find out the existence of Wermer's syndrome unless proven otherwise..The presence of gastrinoma is rather common in age group of >30 years. The presenting symptoms of which are gastric peptic ulcers, recurrent diarrhea and steatorrhoea. Survival and surgical feasibility depends upon the tumor size of NET. NET >4CM , is less favourable for resection an has 50-70% chances of having hepatic metastasis at the time of diagnosis. NETs<2.5 cm have 100 % 15 year survival rate post surgery. Pituitary tumors are most commonly macroadenomas and warrant medical treatment based upon the type. Surgical resection is required if there are any pressure symptoms. Adrenal adenomas are however usually benign and are to be symptomatically managed. The risk of malignancy increases with tumor size > 4 cm. Emphasis should be laid out to rule out the presence of pheochromocytoma as early as possible. Early recognition of signs and symptoms complex of MEN syndromes is of paramount importance. This has a direct effect on patient's survival(5years)

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