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Liraglutide Induced Acute Pancreatitis and Jaundice in an Elderly Female – Case Report

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***Abstract*— Acute pancreatitis is common clinical entity which we come across in our day to day clinical practice, it is defined as acute inflammation of pancreatic gland caused by various etiologies like CBD stone impaction, biliary strictures, systemic disease, alcoholism, major stress like surgeries, trauma including medications (1). It has been classified as mild, moderate and severe pancreatitis depending on the clinical , bio chemical and radiological appearance.(2)**

We not so commonly encounter acute pancreatitis with few of common anti diabetic medications we prescribe in our clinics like sulphonylurease,DPP4 inhibitors (3,4,5,6). Liraglutide is one the most commonly prescribed medications in management of Type 2 diabetes during recent days. It is a derivative of a human incretin , glucagon-like peptide-1 (GLP-1) and it used as a long-acting glucagon-like peptide-1 receptor agonist.(7) Liraglutide binds to the same receptors as does the endogenousmetabolic hormone GLP-1 that stimulate insulin secretion. It acts with glucose dependent fashion specially post prandial high glucose levels it causes insulin secretion by incretin effect, delayed gastric emptying and decreases prandial glucagon secretion (8,9).

Liraglutide has also been used in the management of Obesity and also has shown beneficial cardio vascular effects during recent clinical trials.(10)

The most common reported adverse effects are nausea, vomiting, abdominal discomfort and there are also cases reported with medullary carcinoma of thyroid and few cases of acute pancreatitis.(11)

We Report a case of elderly lady DM2 with morbid obesity started on liraglutide developed Acute Pancreatitis and Cholestatic Jaundice , with symptoms resolving clinically as well as biochemically after stopping liraglutide.

***Index Terms*— Liraglutide, Glucagon like peptide 1, pancreatitis.**

I. Case Presentation

Highlight a A 64 year old female ,Obese known case of diabetes, hypertension and dyslipidemia on medications.

s/p cholecystectomy / Abdominal Hysterectomy with background Endometrial Carcinoma

Presented to Emergency department with history of Epigastric pain , Nausea, poor oral intake and generalized itching since 7 days and also experienced Yellow discoloration eyes

No fever/vomiting/loose stools/chest pain/constipation/cough/Shortness of breath Patient was Allergic to diclofenac medication.

Medication history

- Irbesartan – hydrochlorothiazide
- Gliclazide
- Metformin
- Insulin glargine
- Liraglutide
- Atorvastatin

On examination:

Afebrile

jaundiced

Cardio vascular and Respiratory system were unremarkable

Abdomen : soft , mild epigastric and right hypochondrium tenderness+, no hepato splenomegaly

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Lab investigations:

Labs investigations	Results Values	Normal range
WBC	10.80	4.00 - 10.00
HB%	12.3 gm%	12.0-15.0 gm/dl
Platelets	299	150- 400
INR	1.0	<1.5
Urea	9.00	2.7- 8.7 mmol/L
Creatinine	67	53-97 umol/L
Sodium	130	135-145 mmol/L
Potassium	3.8	3.5-5.1 mmol/L

Lab investigations continued

Investigations	Result values	Normal range
Bilirubin total	110.3	2.5 – 24 umol/lit
Bilirubin D	96.6	
ALK	500	45 - 129 U/lit
ALT	243	0- 30 U/lit
AST	92	0- 31 U/lit
Amylase	1636	13-53 U/lit
Lipase	>3000	13-60 U/lit

CRP	22	<5

Lab investigations continued:

Investigations	Values	Normal range
Beta hydroxybutyrate	0.2	0 - 0.6 mmol/l
ABG	No metabolic acidosis	
Thyroid profile	Well in Normal limits	
Viral serology	Negative	
Ca 19-9	250	0-27 U/ml
Ca 125	9.6	0-35 U/ml
CEA	2	

Ultrasound Abdomen :

- Status post cholecystectomy
- Prominent IHBR and CBD 8mm dilated - ? Post cholecystectomy sequelae.
- Mild fatty liver with fatty changes
- Paraumbilical hernia-incidental finding

Provisional diagnosis:

Acute pancreatitis ??

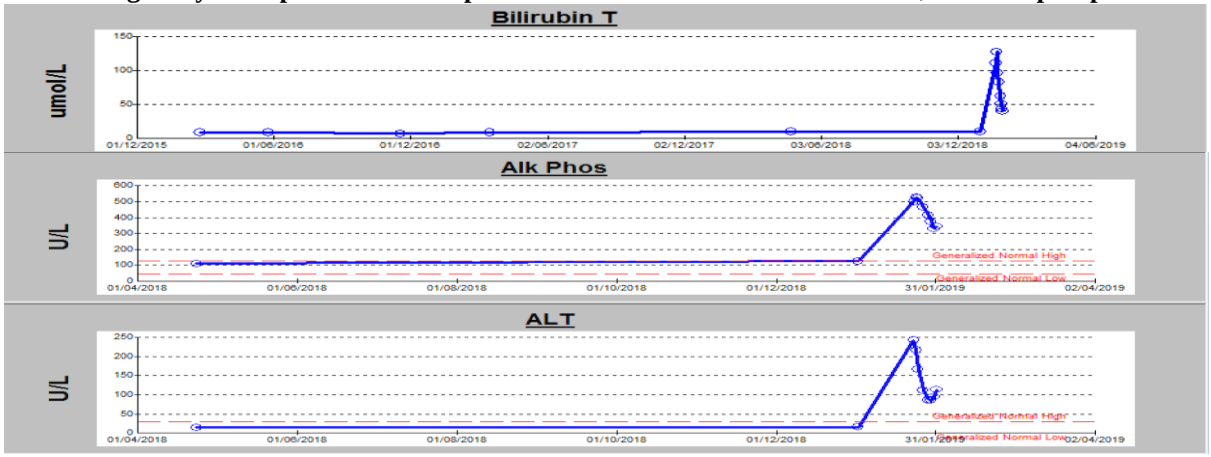
- ✓ **CBD stone/ sludge**
- ✓ **CBD strictures**
- ✓ **Metastasis**
- ✓ **Malignancy of ampulla of head of pancreas**
- ✓ **Drug Induced**

Further imaging:

- **MRI / MRCP Abdomen : no significant pathology or obstruction of Common bile duct**
- **Endoscopic Ultrasound EUS : normal**
- **Auto immune work up – ANA including Anti mitochondrial, Anti smooth muscle antibody, Anti liver kidney microsomal antibody – NEGATIVE**

After stopping Liraglutide:

Decline In Bilirubin, Alkaline phosphatase and ALT



II. DISCUSSION

Acute pancreatitis is common clinical entity which we come across in our day to day clinical practice, it is defined as acute inflammation of pancreatic gland caused by various etiologies like common bile duct (CBD) stone impaction, biliary strictures, systemic disease, alcoholism, major stress like surgeries, trauma including medications. (1,2,3)

Diabetes mellitus is the major cause of morbidity and mortality in the present days and management of diabetes is a complex involving oral medications to injectable insulins.

We not so commonly encounter acute pancreatitis with few of common anti diabetic medications we prescribe in our clinics like sulphonylurease,DPP4 inhibitors. (3,4)

Liraglutide is one the most commonly prescribed medications in management of Type 2 diabetes and obesity. It works in Glucose dependent fashion specially and causes insulin secretion by incretin effect, delayed gastric emptying and decreases prandial glucagon secretion.(7)

The adverse effects include most commonly nausea, vomiting, abdominal discomfort , reflux symptoms , rarely there are also cases reported with medullary carcinoma of thyroid.(11,12)

Few cases have also been reported of liraglutide induced pancreatitis ,the large majority of these reactions occur within the first 1–12 weeks of exposure to the drug and are believed to be due to idiosyncratic or allergic reactions.In contrast, there also cases reported with the patients receiving liraglutide for 6–18 months before the acute pancreatitis event occurred.(12). In the LEADER trial, 3.1% of liraglutide treated patients reported an acute event of gallbladder disease such as cholelithiasis or **cholecystitis** along with elevation of liver enzymes, **hyperbilirubinemia**, cholestasis, hepatitis.(11) Considering the patient co morbidities , advanced age initially malignancy was highly suspected causing obstruction of common bile duct, but all the imaging studies ruled out malignant and obstructive pathology.

Patient was started on liraglutide and was stopped 6 months back as she developed abdominal pain, nausea and vomiting but was not investigated further . Again patient was restarted on liraglutide for her poor diabetic control and within 4 weeks of starting the liraglutide she developed abdominal pain, nausea, poor oral intake and jaundice.

Patient was hospitalized with supportive management and liraglutide was stopped , in the next 3 days the liver functions started to decline and were normalized in 1 week.

Hereby we report this case of elderly female with multiple co morbidities as a case of Liraglutide induced acute pancreatitis and cholestasis.

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