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A Case Report on Lamivudine Induced Pancreatitis.

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ABSTRACT

An 18 years old male patient with history of RVD (+ve) on ART reported generalized weakness, body pains, head ache, and loose motions 3 episodes since one week. Acute pancreatitis due to anti-retro viral therapy was diagnosed. Lamivudine was most probable causal agent. Pancreatitis was confirmed by ultra sound scan of abdomen.

Keywords: Lamivudine, Pancreatitis, Anti-retro viral therapy, Patient care.

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INTRODUCTION

Drug-induced acute pancreatitis is a rare entity that often is challenging for clinicians. Although more than 100 drugs have been implicated in causing acute pancreatitis, many case reports suffer from a combination of inadequate criteria for the diagnosis of acute pancreatitis, failure to rule out more common causes, and a lack of a rechallenge with the medication. Potential mechanisms for drug-induced acute pancreatitis include pancreatic duct constriction, cytotoxic and metabolic effects, accumulation of a toxic metabolite or intermediary, and hypersensitivity reactions.

Classification System of Drug-Induced Acute Pancreatitis:

Class Ia drugs

Hypertriglyceridemia, gallstones, and other drugs.

Class Ib drugs

At least 1 case report with positive rechallenge; however, other causes, such as alcohol, hypertriglyceridemia, gallstones, and other drugs were not ruled out.

Class II drugs

At least 4 cases in the literature Consistent latency (_75% of cases).

Class III drugs

At least 2 cases in the literature No consistent latency among cases No rechallenge.

Class IV drugs

Drugs not fitting into the earlier-described classes, single case report published in medical literature, without rechallenge.

Summary of Drug-Induced Acute Pancreatitis Based on Drug Class:

Class Ia	Class Ib	Class II	Class III	Class IV
Methyldopa	All-trans-retinoic acid	Acetaminophen	Aledronate	Ampicillin
Azodisalicylate	Amiodarone	Chlorthiazide	Atorvostatin	Bendroflumethiazide
Bezafibrate	Azathioprine	Clozapine	Carbamazepine	Benzapril
Cannabis	Clomiphene	DDI	Captopril	Betamethazone
Carbimazole	Dexamethasone	Erythromycin	Ceftriaxone	Capecytabine
Codeine	Ifosfamide	Estrogen	Chlorothalidone	Cisplatin
Cytosine	Lamivudine	L-asparaginase	Cimetidine	Colchicine
Arabinoside	Losartan	Pegasparagase	Clarithromycin	Cyclophosphamide
Dapsone	Lynesterol/methoxyethinylestradiol	Propofol	Cyclosporin	Cyproheptidine
Enalapril	6- MP	Tamoxifen	Gold	Danazol
Furosemide	Meglumine		Hydrochlorothiazide	Diazoxide
Isoniazid	Methimazole		Indomethacin	Diclofenac
Mesalamine	Nelfinavir		Interferon/ribavirin	Difenoxylate
Metronidazole	Norethindronate/mestranol		Irbesartan	Doxorubicin
Pentamidine	Omeprazole		Isotretinoin	Ethacrinic acid
Pravastatin	Premarin		Ketorolac	Famciclovir

Procainamide Pyritonol Simvastatin Stibogluconate Sulfamethoxazole Sulindac Tetracycline Valproic acid	Sulfamethazole Trimethoprimsulfamethazole		Lisinopril Metalozone Metformin Minocycline Mirtazapine Naproxen Paclitaxel Prednisone Prednisolone	Finasteride 5-fluorouracil Fluvastatin Gemfibrozil Interleukin-2 Ketoprofen Lovastatin Mefanamic acid Nitrofurantoin

The following case lamivudine induced pancreatitis comes under class –I b. Side effects associated with lamivudine therapy are rarely described. Gastrointestinal symptoms, such as nausea, vomiting, diarrhoea, and abdominal pain have been described, though more severe conditions can occur, such as rhabdomyolysis and severe anaemia. These side effects are most commonly described in patients with HIV infection than in those with chronic hepatitis B. Lamivudine is an oral nucleoside analog that inhibits HBV replication and markedly normalizes alanine transaminase levels. This effect is directly associated with improvement in liver inflammation and necrosis activity.[1]

Potential mechanisms for drug-induced acute pancreatitis include pancreatic duct constriction, cytotoxic and metabolic effects, accumulation of a toxic metabolite or intermediary, and hypersensitivity reactions.

Highly Active Antiretroviral Therapy

Human immunodeficiency virus (HIV) infection is a proposed mechanism for acute pancreatitis because HIV directly causes inflammation of the pancreas. Highly active antiretroviral therapy may also be involved in the development of acute pancreatitis because the antiretroviral therapy could potentially cause a toxic effect directly to the pancreas or induce negative effects associated with acute pancreatitis. Protease inhibitors (PIs) can cause metabolic disturbances, including development of insulin resistance, hyperglycaemia, hypercholesterolemia, and hypertriglyceridemia. However, triglyceride levels need not be elevated, as cases have been reported in which levels were normal. According to several studies, no significant increase of acute pancreatitis risk occurs after the introduction of PIs to treatment.[2]

CASE REPORT:

Here we report case of pancreatitis following 8 years of lamivudine therapy.

A 18-year-old man with a history of eight years of RVD (+ve) on ART. Initial treatment with 30 mg stavudine, 150 mg lamivudine and 200 mg nevirapine on 2008. Patient was admitted with chief complaints of head ache, body pains, and generalized weakness since one week. History of 3

episodes of loose motions. On examination patient was conscious/irritable, febrile.Pulse rate was found to be 108 bpm. Blood pressure was 110/70 mm of Hg. Per abdomen was soft, no organomegaly was found.

He was investigated for complete blood picture, complete urine examination, thyroid test, liver function test, random blood sugar, blood urea, serum creatinine, CT brain, ECG and ultra sound scan of abdomen.

Complete blood picture shows leucopoenia, anaemia and hypochromic. In CUE pus cells and epithelial cells were very high (pus cells: 4-5/ hpf and epithelial cells: 6-7/ hpf). CT brain shows hyper dense area with multiple hypodensitise involving both caudated nucleus and lentiform nucleus. ECG shows suspected right ventricular hypertrophy and short PR interval negative T - wave. Ultra sound scan of abdomen revealed multiple necrotic lymph nodes in pre pancreatic and para- aortic region in largest measure 14*8 mm in left para- aortic region. Remaining investigations were in normal range.

Diagnosis of pancreatitis is based on patient ultra sound scan of abdomen report.

Upon admission (24/7/2016) patient was treated with

1. Inj. Eptoin 300 mg in 100 ml NS / IV/ TID (Phenytoin).
2. Inj. Acyclovir 500 mg in 100 ml NS/IV/ TID.
3. Tab. PCM 500 mg/ PO/TID (Paracetamol).
4. Inj. Monocef 2 gm / IV/BD (Ceftriaxone).
5. IV Fluids 2 pint NS and 2 pint RL.

On day 2 (25/7/2016) Tab. Naproxen 250 mg and Inj. Mannitol 20% 100 ml/ IV/ OD was added. Patent was suggested to continue the ART. On day 4 (27/7/16) Tab. Fluconazole 200 mg/ PO/ BD was added.

DISSCUSSION:

Lamivudine should be used with caution in patient with a history of pancreatitis or other significant risk factors for the development of pancreatitis. Treatment with lamivudine should be stopped immediately if clinical manifestation or laboratory abnormalities suggestive of pancreatitis occurred.[3]

There are only two previous publications indicating that lamivudine induces pancreatitis. Patient referred to ART centre to change medication to prevent elevated complication. We also suggest careful monitoring of amylase levels during treatment with lamivudine.

Andhra Pradesh is one of the rare life threatening complications of the ART (4% - 22%). The risk of AP in HIV- infected populations is 35 – 800 times higher than in the general population. The risk increase with the progression of HIV infection and worsening of CD4count.[4]

CONCLUSION:

Pancreatitis is a serious condition with significant potential morbidity and mortality. Although drug induced acute pancreatitis is relatively rare, a firm understanding of the drugs associated with the condition should alert the clinician to appropriately diagnose and treat patients. Caution should be taken while prescribing lamivudine in patient with pancreatitis or in HIV patients.

ABBREVATIONS:

1. ART- Anti retro viral therapy.
2. BD- Bis die (twice daily).
3. CT- Computerized tomography.
4. CUE- Complete urine picture.
5. ECG- Electrocardiography.
6. HBV- Hepatitis B virus.
7. HIV- Human immunodeficiency virus
8. IV- Intravenous.
9. Inj- Injection.
10. OD- Omni die (once daily).
11. PO- Per oral.
12. USG- Ultrasonography.

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