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"ISONIAZID INDUCED NECROTISING PANCREATITIS."

Paediatrics

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ABSTRACT

Isoniazid is one of the first-line anti-tubercular drug. Total incidence of adverse effect is 5.4%, notable side effects of isoniazid include hepatotoxicity, peripheral neuropathy, and less commonly hypersensitivity reactions. (1) Isoniazid is a rare cause of acute pancreatitis. (2) We are reporting a case of severe acute malnutrition with a clinically diagnosed case of tuberculosis (Mantoux test positive) that was started on ATT. Later developed pain abdomen and abdominal distention. Investigations showed significantly elevated pancreatic enzymes, and imaging suggested necrotizing pancreatitis. ATT were stopped.

KEYWORDS

anti-tubercular therapy, Necrotizing pancreatitis, Isoniazid.

INTRODUCTION

Isoniazid is the first-line drug in Anti tubercular therapy. It is active only against Mycobacterium Tuberculosis. It is a bactericidal act by inhibiting mycolic acid synthesis of bacterial cell wall.it is the fastest acting drug with maximum CSF penetration. Total incidence of isoniazid induced adverse effect is 5.4%. Notable side effects include hepatotoxicity, peripheral neuropathy and hypersensitivity reactions.[3] The incidence of drug induced pancreatitis is 0.1-2%.[4] isoniazid is a rare cause of drug induced pancreatitis. We are reporting a case of necrotizing pancreatitis in a child who developed after 2 months of ATT Therapy.

Case Report

A 4-year-old male child born of third-degree consanguineous marriage, immunized till date, presented with pain abdomen and abdominal distension for 4 weeks. On examination, he was dull, poorly nourished with moderate pallor, pedal edema (pitting type), and Tachypnea, present. Per abdomen soft, distended, umbilicus everted, epigastric &periumbilical tenderness present, liver 2cm from right costal margin, other systemic examination was normal.

No h/o fever, yellowish discoloration of eyes, passing clay-colored stools, blood in stool, high-colored urine and altered sensorium. No h/o recurrent respiratory tract infection, No h/o trauma. Before hospitalization, child was clinically diagnosed with pulmonary tuberculosis and started on ATT. His work up for pain abdomen and distension revealed, S.Amylase:1767IU/L, Slipase:720IU/L, hypoalbuminemia, iron deficiency anemia. Since pancreatic enzymes were significantly elevated, possibility of pancreatitis was considered.

The differential diagnosis included: pancreatitis secondary to trauma, infections (most common mumps and others.), cystic fibrosis, autoimmune pancreatitis, drug induced pancreatitis, protein losing enteropathy. On detailed history, examination, and investigations possibility of drug induced pancreatitis were considered. ATT were stopped.

Lab Investigations

	Tests	Results
1	CBC	Hb/Hct:7.3/25, TLC:14,000 (P:73, L:19, E:1, M:5), Plt:4.5lakh
2	Peripheral smear	Anisocytosis, Poikilocytosis, microcytic hypochromic anemia.
3	Retic count	0.5% (1-1.5%), DCT-Negative
4	RBC indices	MCV:76, MCH:21, MCHC:28
5	CRP	45 (0-6mg/dl)
6	RBS	156
7	LFT	SGOT/SGPT:34/18, TB:0.3 T PR/Alb:4.3/2.3, ALP:118
8	RFT	BUN:14, S Creat:0.9
9	S electrolytes	Na:138, K:4.6, Cl:107
10	TFT	FT4:7, T3:122, TSH:1.4
11	Coagulation profile	PT:17, APTT:43, INR:1.1
12	Lipid profile	S cholesterol:61, S. triglyglycerides:59
13	Urine R/M, c/s	PH:1.03, Sugar/Albumin: nil, No growth
14	Stool R/M, C/S	Acidic, no ova cysts &parasites. No growth.
15	PFT	S Amylae:1767, S Lipase:720
16	Blood C/S	No growth
17	ESR	25mm/hr
18	Viral markers	HAV/HBS Ag/HCV/HEV/HIV ELISA: negative
19	S Cal/Phos	8.4/3.36
20	Sickling test	Negative
21	ANA IgG	Negative
22	HBA1c	4.5
23	LDH	1083
24	ABG	PH:7.38, Pco2:22, po2:111, Hco3:13
	DCT: direct Coombs test ABG: arterial blood gas analysis	CBC: complete blood count, LFT: liver function test, TFT: thyroid function test, RFT: renal function test, PFT: Pancreatic function test.

Ascitic Fluid Analysis

PH	1.003
Protein	1.428
Sugar	122mg/dl
Albumin	1.1
SAAG ratio	1.2
Amylase	1974U/L
Lipase	628U/L
ADA	8.5U/L(0-40)
LDH	599
CBNAAT	M TB not detected
Culture sensitivity	No growth

SAAG- serum ascites albumin gradient, ADA: adenosine deaminase, CBNAAT: cartridge based nucleic acid amplification test LDH: lactate dehydrogenase

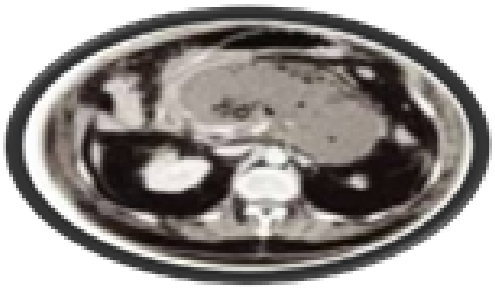

Fig (a): CECT image of necrotizing pancreatitis.

Radiological Studies:
USG ABDOMEN & PELVIS :
liver &spleen normal size with normal echotexture with gross ascites pancreas obscured by bowel shadow. ERCP-disrupted pancreatic duct.

Abdomen Doppler: Normal study.

USG-KUB-Normal, 2D-ECHO-Normal, USG Neck-No cervical lymphadenopathy, Thyroid gland size & echotexture normal.

Upper Gi Endoscopy-Normal.

CECT Abdomen And Pelvis-
Liver, spleen no focal lesion in the parenchyma. Pancreas multiple hypodense non enhancing areas. Noted in body, head, tail of pancreas with evidence of peripherally enhancing hypodense collection with hyperdense areas within noted adjacent to tail of the pancreas is extending superiorly into lesser sac pushing stomach anteriorly likely 'Acute necrotizing pancreatitis with walled off necrosis' 'modified CT severity index score -10/10. (severe)

Child was kept NPO, oxygen support given and abdominal girth was monitored. A Gastro-enterologist's opinion was taken. since child was tachypneic and had gross ascites, therapeutic ascitic fluid drainage was advised. tapping done & sent for analysis.in view of symptomatic anemia packed red blood cell transfusion and for hypoalbuminemia, albumin transfusion was considered. meanwhile child was started on nutritional supplements: fat soluble vitamins (Vit A, D, E, and K) and oral medium chain triglycerides. Gradually Pancreatic enzyme (tab pan lipase 25,000IU/kg) was started for pancreatic insufficiency. Over the period of hospital stay, repeat pancreatic enzymes showed a decreasing trend. Intermittent hypoalbuminemia occurred, hence albumin transfusion considered.

DISCUSSION

Annual incidence of acute pancreatitis in children is around 1 in 10,000[5]. Drug induced pancreatitis was more frequently associated with aggressive course with systemic involvement [6]. serious complications following isoniazid induced pancreatitis are necrosis at the tail of the pancreas and peripancreatic stranding. [7] Necrotizing pancreatitis includes both pancreatic gland necrosis and peripancreatic fat necrosis. Over a period of 4 weeks or longer, the collection becomes more liquid and becomes encapsulated by a visible wall. At this point, the process is termed walled-off pancreatic necrosis.

The development of fever, leukocytosis, an elevated procalcitonin level and increasing abdominal pain suggests infection of the necrotic tissue. [8]A CT scan may reveal evidence of air bubbles in the necrotic cavity. Abdominal pain was suggestive of pancreatitis, which is one of the diagnostic criteria for pancreatitis. [9] The latency period for isoniazid-induced pancreatitis is 12-45 days. In this case the child developed symptoms within 15 days.

Persistent abdominal pain, one should consider screening for acute pancreatitis by measuring pancreatic enzymes in patients undergoing anti-TB therapy. Both isoniazid and rifampicin are associated with acute pancreatitis.

Since drug-induced acute pancreatitis is potentially reversible and mandates permanent avoidance of isoniazid, so drug withdrawal is necessary [10]. The exact mechanism for development of acute pancreatitis remains unclear. Hepatitis and pancreatitis can be completely recovered if the drug is withdrawn early. A high index of suspicion and early withdrawal of isoniazid is the key to avoid hazardous consequences.

CONCLUSION:

The pharmacological intervention and resolution of pancreatitis after discontinuation of isoniazid confirms the cause of pancreatitis among all other anti-TB drugs.

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