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**CARBIMAZOLE-INDUCED PANCREATITIS AT THE AGA KHAN UNIVERSITY HOSPITAL, NAIROBI: A CASE REPORT**

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**ABSTRACT**

**Acute pancreatitis has many causes, with alcohol and gall bladder stones being the most common. Drug related pancreatitis occurs rarely and usually presents as mild disease. The diagnosis is by exclusion and relies on a thorough history and relevant investigations. Management includes withdrawing the drug and managing the pancreatitis as per protocol.**

**CASE REPORT**

This is a case of a thirty-eight-year-old hyperthyroid male patient who had been on carbimazole for two weeks. He has been on follow-up at the endocrinology unit with sub-acute thyroiditis. Currently he was admitted with epigastric pain radiating to the back associated with vomiting. There was no history of alcohol intake. On general examination, he had no icterus, and the vital signs of significance was a tachycardia of 116 beats per minute. Abdominal exam revealed epigastric tenderness with no signs of peritoneal irritation. Murphy's sign was negative.

Laboratory work up revealed an elevated serum lipase of 1090 U/L and a neutrophil leucocytosis of 12.5. Liver function tests showed a cholestatic picture. Thyroid function tests had an elevated T4 levels. On imaging, a hepato-biliary ultrasound ruled out gallstone disease. No other cause of

acute pancreatitis was apparent. The carbimazole was discontinued and standard management of pancreatitis was instituted with good clinical progress, and after four days of hospital stay, he was discharged on alternative therapy for hyperthyroidism, propylthiouracil.

**DISCUSSION**

Acute pancreatitis is a common surgical condition mostly presenting with mild disease. 23% of patients presenting with pancreatitis at our institution get admitted to the critical care units with moderate and severe disease with majority of cases being secondary to alcohol use(1). Diagnosis requires fulfilment of at least two of the following ; abdominal pain consistent with acute pancreatitis, elevated lipase or amylase levels at least three times the upper level of normal and characteristic signs on imaging(2).Severity assessment is done at

admission to determine patients who will require more aggressive treatment and subsequent admission to critical units..

The commonest cause of pancreatitis in the western literature is gallstone disease. On the contrary, alcohol ingestion accounts for the majority of cases in Africa (1)(3). Other uncommon causes of pancreatitis including metabolic conditions like hypertriglyceridemia, infections, traumatic pancreatic duct disruption, post ERCP, autoimmune and drug related causes.

Drug induced pancreatitis is rare, accounting for up to 2% of all cases (4). Patients usually present with mild disease however, severe cases have been reported (5, 6). Drugs as a potential cause are most often overlooked, therefore a high index of suspicion coupled with good history taking is key in identifying and withdrawing the offending agent.

Several mechanisms have been postulated to explain drug induced pancreatitis including duct obstruction, sphincter of oddi dysfunction, direct cytotoxic injury, immunological injury and indirectly via metabolic causes like hypertriglyceridemia and hypercalcemia(7). These can result from effects of the drug and or of its metabolites.

Irrespective of the mechanism, the common pathway leads to premature inactivation of pancreatic enzymes that cause damage to the pancreatic acinar. Following this damage there is production of local inflammatory mediators that cause endothelial dysfunction and increased vascular permeability. Fluid extravasation and interstitial oedema follows as a result.

If the insult persists, the mediators enter the blood stream and evoke a systemic inflammatory response syndrome that causes other organ dysfunction. The cycle perpetuates itself and leads to further compromised blood flow to the pancreas as the body shunts blood to vital organs leading to ischemia and subsequent pancreatic necrosis.

Drugs are classified as class 1 to 4 based on weight of evidence and clinical presentation in terms of latency period from time of initiation of drug to presentation of symptoms and recurrence of symptoms with re-challenge of the drug(5).

Class 1 drugs are those with one case report that describes recurrence of symptoms with re-challenge of the drug. Examples of these are commonly used drugs like carbimazole, codeine, metronidazole and isoniazid. Class 2 drugs like acetaminophen have consistent latency in 75% or more of reported cases. Class 3 drugs have two or more case reports with no re-challenge or consistent latent period while class 4 drugs have one reported case report with no data on re-challenge or consistent latency period.(5)

Thioamides have been associated with severe adverse effects such as agranulocytosis, hepatotoxicity and reactive vasculitis. It is theorized that they cause pancreatitis via an immune mechanism (8, 9). The sulfhydryl moiety of this group of drugs is implicated as a cause of this reaction. Interestingly, amongst the thioamides, pancreatitis following propylthiouracil use has not been described. The patient in this case report did not have recurrence of symptoms during follow-up. Time from initiation of the drug to presentation of symptoms differ following thioamide use. Marazuela et al described a patient on carbimazole for Graves' disease, who presented with symptoms after a latency period of 30 days. Re-challenge with a single dose led to development of acute pancreatitis(8). Chng et al described a case of a 70-year-old patient who developed pancreatitis following a latency period of 14 days. Methimazole has been implicated in a case report of a 51 year old lady who developed symptoms three weeks after initiation of the drug(10).

This case may possibly be an index report for Carbimazole-induced pancreatitis in the

region. The patient presented with mild acute pancreatitis that was solely attributable to carbimazole. Other similarities include latency period of two weeks that falls between the described duration and improvement in symptoms after drug discontinuation.

### CONCLUSION

Carbimazole is a rare cause of acute pancreatitis. It usually presents as mild disease with typical latency period of between 14 to 30 days. Symptoms presentation is dose independent and management includes supportive treatment and withdrawal of the drug. Substitution with Propylthiouracil is acceptable to manage the hyperthyroid state.

### REFERENCES:

1. M M. Acute Pancreatitis at the Aga Khan University Hospital, Nairobi; a two year audit. *The Annals of African Surgery*. 2007;1:60-2.
2. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. 2013;62(1):102-11.
3. Anderson F, Thomson SR, Clarke DL, Loots E. Acute pancreatitis: demographics, aetiological factors and outcomes in a regional hospital in South Africa. *South African journal of surgery Suid-Afrikaanse tydskrif vir chirurgie*. 2008;46(3):83-6.
4. Balani AR, Grendell JH. Drug-induced pancreatitis : incidence, management and prevention. *Drug safety*. 2008;31(10):823-37.
5. Badalov N, Baradarian R, Iswara K, Li J, Steinberg W, Tenner S. Drug-induced acute pancreatitis: an evidence-based review. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. 2007;5(6):648-61; quiz 4.
6. Książczyńska D. Drug-induced acute pancreatitis related to medications commonly used in gastroenterology. *European Journal of Internal Medicine*. 2011;22(1):20-5.
7. Hung WY, Abreu Lanfranco O. Contemporary review of drug-induced pancreatitis: A different perspective. *World journal of gastrointestinal pathophysiology*. 2014;5(4):405-15.
8. Marazuela M, Oacute, Nica, Paco GS, Aacute, de N, et al. Acute Pancreatitis, Hepatic Cholestasis, and Erythema Nodosum Induced by Carbimazole Treatment for Graves' Disease. *Endocrine Journal*. 2002;49(3):315-8.
9. Chng CL, Kek PC, Khoo DH. Carbimazole-induced acute pancreatitis and cholestatic hepatitis. *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*. 2011;17(6):960-1.
10. Agito K, Manni A. Acute Pancreatitis Induced by Methimazole in a Patient With Subclinical Hyperthyroidism. *Journal of Investigative Medicine High Impact Case Reports*. 2015;3(2):2324709615592229.