Unexpected Elevated Levels of Serum Transaminases - A Rare Laboratory Finding

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Abstract

Estimation of serum transaminase levels are one of the commonest investigation performed in clinical laboratories. Liver enzymes alteration accompanying in patients with liver disease shows unexpected finding in the form of marked elevation and sudden fall. The pattern of enzyme abnormality, interpreted in the context of the patient's characteristics, can aid in directing the subsequent diagnostic work-up. This case report present a 300 fold rise in transaminases in a 53 year old patient admitted in emergency ward. Such serious elevations have been rarely reported in literature.

Keywords: Serum transaminase, Liver enzymes, Liver disease, Liver function test

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Introduction

The aminotransferases (formerly transaminases) are the most frequently utilized and specific indicators of hepatocellular necrosis. These enzymes- aspartate aminotransferase(AST, formerly serum glutamate oxaloacetic transaminase-SGOT) and alanine aminotransferase(ALT, formerly serum glutamic pyruvate transaminase-SGPT) catalyze the interconversion of amino-acids and oxoacids by transfer of amino group. Liver enzymes alteration may be either the accompanying biochemical picture in a patient with symptoms or signs suggestive of liver disease or an isolated, unexpected finding in a patient who has undergone a wide range of laboratory tests for a nonhepatic disease or for minor, vague complaints. The latter situation is a common clinical scenario today

because of the routine incorporation of hepatic tests in automated blood chemistry panels. [1] This case report presents a rare investigative finding in a patient with nonhepatic disease. We have taken prior informed and written consent from the patient attendant.

Case report:-

A 53-year-old male patient, a resident of Lucknow, Uttar Pradesh was admitted by the attendant in the emergency ward of King George's Medical University, Lucknow. At the time of admission patient was in altered sensorium with the complaint of difficulty in breathing from last 3 days. He was a known case of chronic obstructive pulmonary disease since 8 years and a known case of type 2 diabetes mellitus since 5 years on medication for both the conditions. No other relevant positive history was present. A chronic smoker since age of 18 (100-105 pack years) and an occasional alcoholic. The general physical examination of the patient was unrevealing. Chest auscultation revealed bilateral rhonchi; other system examination was unremarkable. Routine haematological laboratory investigations were performed as a part of the management. Biochemical parameters were estimated on Vitros 250 dry chemistry analyzer using Vitros kits. The patient's biochemical profile revealed, respiratory acidosis and deranged renal function at the time of admission. On day 3rd of admission liver function test (LFT) revealed a striking rise in the level of transaminases AST 15,500.0 IU/L and ALT 11,600.0 IU/L, the other liver enzymes i.e alkaline phosphatase and bilirubin being in the reference range. The AST/ALT ratio was 1.3 which ruled out the possibility of alcoholic hepatitis. After marked elevation next day LFT showed sudden fall in both transaminases, AST 5290.0 IU/L and ALT 6220.0 IU/L. Other investigations included lactate dehydrogenase (LDH) 11,750.0 IU/L, γ-glutamyl transpeptidase (GGT) which was not significantly elevated and hepatitis viral markers were negative. The ALT/LDH ratio was 0.5 while GGT/ALP ratio was 0.53. Follow up of liver enzymes on day 5th showed both transaminases falling to range of 1274.0 IU/L and 3105.0 IU/L while LDH was 2610.0 IU/L. Sputum was positive for Klebsiella culture after a week. Only symptomatic treatment like bronchodilators

and antibiotics were advised by the physician during early phase of management.

Discussion:-

The findings of this particular case satisfy the diagnostic criteria for hypoxic hepatitis (HH).[2] By definition the rise in transaminases are required to be atleast 20 fold; however we report a nearly 300 fold rise in transaminase levels. The underlying etiology could be respiratory failure and sepsis aggravated by other comorbid conditions. There are various case series and retrospective studies that are available from around the globe but a few from India, hence the incidence of HH in this setup is yet not known. This patient a known diabetic and Chronic Obstructive Pulmonary Disease (COPD) presented with respiratory failure and altered sensorium. As the viral markers were negative, possibility of acute viral hepatitis was ruled out. The liver functions on the day 3rd of admission showed elevated transaminase levels and near normal bilirubin levels. The AST/ALT ratio of 1.3 and GGT ruled out the possibility of alcoholic hepatitis.[1] This unexpected elevated levels of transaminases was followed by a fall in the enzyme levels on next day, with ALT/LDH ratio <1.0 and thereon thus classically fitting the picture of HH. [1,2,3] Acetaminophen-induced hepatic damage causes 54% and 16% of the cases of acute liver failure in the United Kingdom and United States respectively. [4] The patient history may suggest drug- or toxin-induced liver damage, there are no specific serologic tests for either condition, except in the case of acetaminophen poisoning, in which plasma acetaminophen levels may also represent a helpful guide to therapy. In this case no history of acetaminophen overdose was available. The etiology of HH or more commonly known ischemic hepatitis is the clinical entity that satisfies the following criteria- [5]

1. A typical clinical setting of cardiac shock, respiratory failure, or circulatory shock
2. A massive but rapidly reversible increase in the serum transaminase levels (at least 20 times the upper limit of normal)
3. The exclusion of any other causes of liver damage.

This condition was first described in patients with cardiovascular disease who also had a marked rise in serum transaminase levels along with the morphologic evidence of centrilobular liver necrosis with no evidence of viral or drug injury. [6] HH is reportedly a common occurrence in intensive care patients with incidence of around 10% and is associated with a poor outcome. [7] The major factors leading to HH are passive congestion, ischemia, and arterial hypoxemia of the liver resulting from underlying co-morbid conditions like a low cardiac output associated with congestive heart failure, chronic respiratory failure, sepsis, profound anaemia, excessive bleeding etc.

Development of HH is usually the consequence of a multifactorial event of several distinct acute and chronic organ dysfunctions leading to centrilobular liver cell necrosis. The primary mechanism involves ischemia or hypoxia to liver leading to the loss of mitochondrial respiration, adenosine triphosphate (ATP) depletion and hindrance in the energy-dependent metabolic pathways and transport processes. The first hypoxic lesions are observed in the centrilobular areas approximately 2 h after ischemia begins. The early metabolic changes are fully reversible upon the restoration of normal blood supply. The injuries become irreversible after 3 h of normothermic ischemia. If hypoxia persists, mitochondrial electron transport becomes impaired and intracellular ATP levels fall. Membranous ion transport systems are damaged, the selective membrane permeability and the membrane potential cannot be sustained anymore, and cell-volume regulation is impaired. The K+ efflux into the extracellular space increases and Ca2+ accumulates within the cell. Cytosolic Ca2+ activates proteases and phospholipases which in turn perpetuate cell injury by damaging membranes and the cytoskeleton. An increased influx of extracellular water leads to cell and organelle swelling (ballooning). Vacuoles are formed and blebs detach from the cell membrane. Besides hepatocytes, sinusoidal endothelial cells and Kupffer cells are also affected by hypoxic liver damage. They are also activated and generate reactive oxygen species, chemokines, and proinflammatory cytokines perpetuating the damage. The ischemic phase

may also be followed by reperfusion injury. Patients with HH are frequently of advanced age: the median age was about 70 years and predominantly males. [8]

The typical clinical signs of liver injury are uncommon in patients with HH and jaundice has been observed only in 10–15% of all patients with HH and occurred mainly in the late course of the disease. [8] A case series of 118 admissions with HH had a significantly higher acute physiology score, a significantly longer stay in the intensive care unit and significantly increased intensive care unit mortality in comparison with all other admissions (n = 948) to the intensive care units during the 22-month observation period[9]. Multivariate regression analysis revealed that the presence of HH was a strong and independent risk factor for mortality in our collective of patients admitted to the intensive care unit: patients requiring vasopressor therapy and suffering from HH had an increased mortality risk nearly five times higher.[9] An early diagnosis of HH and proper management of the underlying cause are vital for the patients.

Conclusion:-

Hepatic injury and hypoxic hepatitis may be a common occurrence in the clinical setting however there are few reports of very high serum transaminases elevations. The rise was about 300 fold in this particular case. The exact reason behind such severe rise is not clear however we suspect the coexistent respiratory failure and sepsis in this case.

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