

CASE REPORT

Mildly Elevated Alkaline Phosphatase (ALP) - a Liver Tumour Hint Not to Be Missed

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ABSTRACT

Healthcare providers are responsible for performing medical check-ups, analyse and interpret patient's laboratory results. It is common for an initially asymptomatic patient to receive abnormal results including liver enzymes such as alkaline phosphatase (ALP). The concern in these patients is the cut-off value for mildly elevated levels that requires intervention. This paper reports a case of liver malignancy in a 32-year-old man who presented with a mild elevation of ALP level less than five times the upper limit of normal. The patient had no clinical symptoms. Early ultrasound liver assessment showed dilated common bile duct, which led to an urgent CT scan of the liver that revealed supportive features of fibrolamellar carcinoma. The patient was managed successfully with early partial hepatectomy that has saved him from morbidity and mortality of liver malignancy. Indeed, liver malignancy can be detected early in a health clinic from a further assessment of trivial elevation of ALP.

Keywords: Liver tumour, Alkaline Phosphatase, Hepatocellular Carcinoma

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INTRODUCTION

A liver function test (LFT) is commonly arranged for patients with a follow-up for underlying chronic disease, especially those with risk factors for metabolic syndrome (1). Mildly raised liver enzymes mostly signify benign lesions in which further monitoring of the increment trend is usually satisfactory. Up to one-third of these patients do not present any associated liver disorders (2-4). The serum levels mostly return to the normal level spontaneously during follow-up (2, 3). At a primary care level, regardless of the increment from the normal value, a patient with abnormal LFT requires further assessment from adequate history taking and clinical examination. Subsequent testing is done based on this information. The characteristic of LFT results could suggest the underlying pathology such as disproportionate elevation in serum aminotransferases compared with alkaline phosphatase (ALP) would signify hepatocellular causes. While, disproportionate elevation in ALP compared with

serum aminotransferases indicate cholestatic in origin (4) as illustrated in Figures 1. In the clinical setting, these two conditions are difficult to be distinguished hence, close monitoring on the trends of these enzymes are preferred among the clinicians. However, raised liver enzymes may reflect underlying tumour especially when other causes from detailed history have been ruled out and the levels remain persistently high. Focal nodular hyperplasia (FNH) and fibrolamellar carcinoma (FLC) are among the malignant liver tumours that mainly affect women in the reproductive age group compared to men (5). It is usually undetectable unless further imaging study such as ultrasound is performed, which then could save the patient. These tumours if detected and managed early could prevent further complications and reduce mortality. Nevertheless, in view of its benign nature, mildly elevated liver enzymes are usually due to inflammation, infection or metabolic disorder, rather than carcinoma. An isolated mild elevation of ALP level of less than five times the upper limit of normal (ULN) is not a common manifestation of liver malignancy (3). Hence, other differential diagnoses need to be considered in an asymptomatic patient during the initial visit at a primary health care clinic.

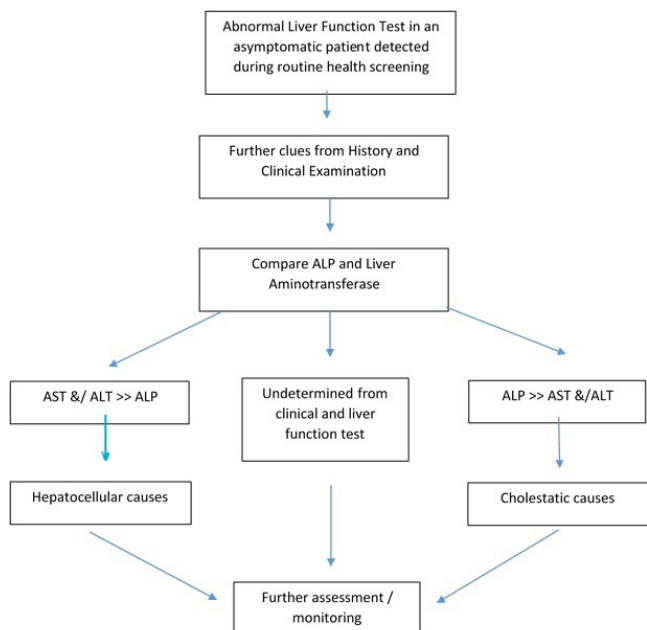


Figure 1: Algorithm of Approach in Abnormal Liver Function Test

CASE REPORT

A 32-year-old man with underlying intermittent gouty arthritis came to the clinic for a routine medical check-up. The patient was asymptomatic without any recent acute gout. Clinically, the patient had an ideal body mass index and was normotensive without peripheral features of chronic illness and had no joint abnormalities. The only significant finding from the systemic examination was a palpable liver just below the right subcoastal margin, which was soft, non-tender with a well-defined edge. In view of his age and underlying gouty arthritis with a history of taking non-steroidal anti-inflammatory drugs intermittently, blood investigations were conducted for other chronic illnesses including renal function and LFT.

The results revealed mildly elevated ALP, which was persistent in the range of 145 – 155 IU/L as shown in Table 1. On further questioning, the patient had no previous history of liver abscess or hepatitis. The patient also had no family history of malignancy or liver disorder, denied any high-risk behaviour and was not on any other new drugs. In view of the normal liver aminotransferases, gamma-glutamyl transferase level was measured, which revealed a high measurement value of 158 IU/L. This signalled for further investigation of an underlying obstructive lesion even with his normal level of alpha-fetoprotein (AFP). Therefore, an ultrasound assessment was carried out that confirmed the presence of common bile duct dilatation and obstruction with the presence of a hyperechoic mass within the region of the pancreatic head. The patient was referred urgently to the surgical team. Subsequent CT scan pancreatic protocol showed a large heterogeneous lobulated mass involving

Table 1: Patient’s Serial Blood Result

Parameter	First Result	Second week	Third week	Fourth week	Normal Value
Total protein (g/L)	74	72			64 - 85
Albumin (g/L)	43	42			34 - 50
Globulin (g/L)	31	30			20 - 39
Alkaline Phosphatase (U/L)	149	151			38 - 124
Aspartate Aminotransferase (U/L)	39	37			12 - 73
Alanine Aminotransferase (U/L)	18	17			12 - 78
Gamma-Glutamyl Transferase (U/L)	-	-	158		< 34
Total Bilirubin (µmol/L)	10	11			<22
Hepatitis B surface antigen and C		Non-reactive			
Hepatitis C virus antibody		Non-reactive			
Alpha-feto protein (ng/ml)				9	<20

segment II, III, IVA and IVB of the liver measuring 7.5cm x 13.3cm x 10.1cm (Figure 2). The patient was diagnosed with fibrolamellar hepatocellular carcinoma and was managed surgically by partial hepatectomy.



Figure 2: CT scan of Abdomen showed Large Heterogenous Lobulated Liver of segment II, III, IVA and IVB

DISCUSSION

LFT is commonly ordered in the primary care setting for those at risk of liver disease, for those with concomitant chronic illness, for high risk group patients, for monitoring malignancy and before initiating and monitoring hepatotoxic medications (1, 2, 4). However, the test is not recommended for mass screening of liver malignancy. Nevertheless, incidental findings of its abnormal value can give significant clues for further

assessment to rule out malignancy.

One of the significant parameters associated with cholestatic liver disease is ALP. Serum ALP originates mainly from the liver and bones, though it may be contributed by the kidneys, intestine or even bronchopulmonary carcinoma (3). However, the range of the serum level is variable according to age. It is expected to increase in infants and toddlers, pregnant women, adults with diabetes and could be idiopathic in benign familial cases (4). However, the value is expected to be lower in the middle age group, which is atypical in our case (2). The monitoring role in primary care is indeed important especially in the undetermined cases or in a healthy individual as it may be related to medications or fatty meals. However, the value is expected to return to the normal range in accordance with its half-life of seven days (4). Nevertheless, the value was persistently elevated in this patient on subsequent readings. The patient had benefited from a serum GGT level measurement, in which a hepatobiliary origin of the disorder was supported by a simultaneous elevation of its level (2). Nevertheless, GGT usefulness is limited by its lack of specificity (2). Typically, ALP is expected to rise up to fourfold the ULN of serum GGT level in significant obstructive liver disease (2, 3). However, the patient in this report showed a mildly raised value. This would further hide the possible clues of liver carcinoma. In this scenario, from the primary care point of testing, an ultrasound of the liver is the best initial imaging study to characterise the presence of cholestasis by looking for biliary tract obstruction to explain the mildly raised ALP (2, 5). It is useful to support the provisional diagnosis when looking for a compressing mass. Although imaging test is not accurate in distinguishing liver carcinoma from other solid tumours in the liver, it is widely available, non-invasive and commonly used for screening patients with liver tumours (5). Another atypical feature in this patient was the normal level of AFP. Nevertheless, serum tumour markers are not a diagnostic tool, but rather act as supportive parameters towards the diagnosis of malignancy. In addition, normal AFP levels are present in as many as 30% of patients at time of diagnosis and usually remain low, even with advanced hepatocellular carcinoma (2,4).

Liver carcinoma usually reflects the endpoint of a chronic liver disease spectrum. Although FLC and FNH can be present in a healthy patient, it may manifest with common upper gastrointestinal manifestations such as nausea and dyspepsia (5). However, these were absent in this patient. The patient also had no constitutional symptoms and did not present with specific symptoms related to liver pathology such as jaundice and itchiness. These observations suggest that liver carcinoma was the lowest possible differential diagnosis considering routine medical check-up revealed only mild elevation of ALP with normal results of other parameters. Furthermore, the patient showed no stigmata of chronic liver disease,

splenomegaly or ascites that are usually associated with hepatobiliary and pancreatic carcinoma. The palpable liver could be a normal finding in a thin body-built man as in this patient.

The only clue in this case was the suspicious mass at the pancreatic head region based on the ultrasound interpretation. The patient was referred directly to the surgical team based on these assessments for further management with an early CT scan. CT scan revealed a diagnosis of an atypical variant of hepatocellular carcinoma, specifically FLC based on the findings of a central scar. The patient was successfully managed with partial hepatectomy. The prognosis for this patient was good as he was diagnosed at an earlier stage that was curable with surgical resection (5).

CONCLUSION

A persistent elevation of serum ALP although mildly raised warrants further investigations to rule out malignancy. This case has indeed proven that a focused and proper history taking, appropriate physical examination with a strong index of suspicion as well as selected and supportive investigations that is commonly practised at a primary care level served significant roles in identifying unusual presentations of an uncommon variant of solid tumours.

ACKNOWLEDGEMENTS

The authors would like to thank the Director General of Health Malaysia for his permission to publish this article (NMRR-20-1728-56055.). We also would like to express our gratitude to the surgical department of Hospital Sultanah Zahirah, Kuala Terengganu for their excellent cooperation and involvement in this case. This report was funded by the International Islamic University of Malaysia Research Initiative Grant Scheme (Publication) P-RIGS18-034-0034.

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