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Case Report
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Elevated Liver Enzymes: An Atypical Presentation of Otherwise Asymptomatic Multiple Myeloma

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Abstract

Gastrointestinal system involvement is a rare presentation of Multiple Myeloma (MM) and is associated with poor prognosis and short-lasting remissions despite aggressive treatment. We present a patient with asymptomatic elevation of liver tests, found to have multiple myeloma involvement of the liver.

Introduction

Clinicians often encounter elevated liver chemistry test results in practice. The most common liver chemistries ordered are serum Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (AP) and bilirubin. Due to the widespread use of these tests either to screen asymptomatic patients during routine checkup or evaluate patients who are symptomatic and/or referred for elevation of abnormal test results, such abnormalities require a rational approach to interpretation and further work up, guided by the clinical presentation and the degree of elevation. Multiple Myeloma (MM) is a bone marrow based multi-focal, malignant disease characterized by autonomous proliferation of neoplastic plasma cells that rarely infiltrate the gastrointestinal system. We present a case of an elderly man with asymptomatic elevation of liver tests, found to have multiple myeloma involvement of the liver.

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Case Presentation

A 71-year-old white man with history of obesity, hypertension, hyperlipidemia, and hypothyroidism was referred to our clinic for evaluation of asymptomatic elevated liver enzymes noted on routine evaluation and had been present for about four years. He denied using alcohol, illicit drugs, herbal supplements, new medications, or recent travels. He has negative family history for liver disease. Medications included aspirin, fish oil, Lisinopril, Simvastatin, niacin, levothyroxine and coenzyme Q-10. Initial physical exam was unremarkable.

Laboratory results from 2013 showed ALT: 49 U/L (0 U/L to 45 U/L), AST: 43 U/L (0 U/L to 50 U/L) and Hgb: 14.8 g/dL. Laboratory tests in our clinic (2017) showed ALT: 60 U/L, AST: 59 U/L, AP: 60 U/L, Total bilirubin: 1.3 mg/dL, albumin: 4.6 g/dL, total protein: 8.5 g/dL (6.4 to 8.4), creatinine: 0.9 mg/dl, WBC: 4.5, Hgb: 14.1 g/dL and normal platelet count. Chronic liver diseases work-up (including ANA, AMA, ASMA, ceruloplasmin, iron, ferritin, TTG, IgA and hepatitis panel) were all negative/normal. Serum protein electrophoresis revealed IgG-kappa monoclonal protein of 2.6 g/dl. Beta-2-microglobulin was 3.9 mg/L (0.6 to 2.4), IgG 3093.9 mg/dl (694 to 1618), IgA <40 mg/dl (68 to 378) and IgM <25 mg/dl (60 to 263). Liver ultrasound revealed hepatomegaly, coarsened liver echotexture with no focal lesions.

It was suspected the patient had NASH, but there was no improvement of ALT/AST levels despite patient's life style changes for 3 months, and a liver biopsy was performed. This biopsy showed chronic hepatitis with grade 1 inflammation, mild peri-portal and peri-sinusoidal fibrosis (stage 1) and minimal macrovesicular steatosis. Prussian blue stain did not show increase stainable iron. Lobular and peri-portal inflammation was lymphocytes and plasma cells predominant (Figure 1). In-situ hybridization stains for kappa and lambda light chains showed kappa light chain predominance in mainly plasma cells and lymphocytes in peri-sinusoidal and peri-portal regions, consistent with a B-cell lymphoproliferative disorder. Peripheral blood smear showed pancytopenia without dysplastic changes, anemia with no rouleaux, immature granulocytes or plasma cells.

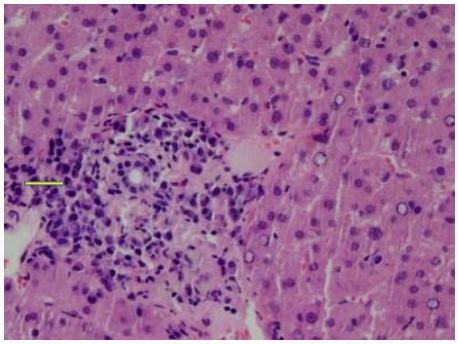

Figure 1: Liver biopsy (400x). Plasma cells infiltrate in the portal area.

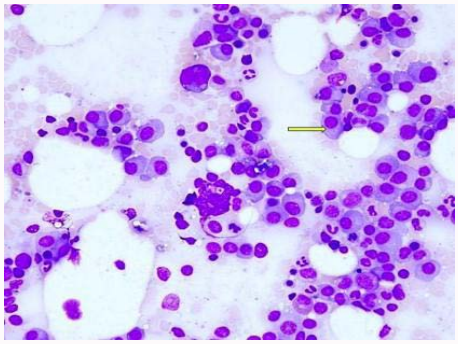

Figure 2: Bone marrow biopsy (400x) with wright giemsa stain showing multiple plasma cells.

Bone marrow biopsy showed mildly decreased myeloid/erythroid ratio and adequate trilineage maturation, normal stainable iron and plasmocytosis (38%) with mostly mature forms compatible with plasma cell myeloma (Figure 2). Flow cytometric immunophenotyping showed atypical monotypic plasma cell population (kappa light chain restricted), expressing CD56 without CD19 or lambda chain. Congo red stain did not show characteristic apple-green birefringence under polarized. Cytogenetic profile showed 46, XY, normal male karyotype. Multiple Myeloma FISH panel showed nuclei positive for Trisomy 9, 11 and 15, consistent with Multiple Myeloma apparent hyperdiploid related clone. PET/CT scan showed no abnormal metabolic activity but increased mottled activity in T- and L-spine. Subsequently spine MRI was negative for lytic lesions. This patient met diagnostic criteria for MM and received lenalidomide.

Discussion

Liver chemistries are indirect markers of hepatobiliary disease. Though commonly referred to as liver function tests, they are not true measures of hepatic function and thus, are best referred to as liver chemistries or liver tests. There is an accumulating set of data demonstrating that elevation in liver chemistries correlate with morbidity and mortality in certain populations [1]. A true healthy normal ALT level in prospectively studied populations without identifiable risk factors for liver disease ranges from 29 IU/l to 33 IU/l for males and 19 IU/l to 25 IU/l for females, and levels above this should be assessed by physicians [2]. This is the first case report, to our knowledge, in the literature of an asymptomatic patient, diagnosed with multiple myeloma after presenting with mild elevation of liver enzymes.

Multiple myeloma is a bone marrow based multi-focal, malignant disease characterized by autonomous proliferation of neoplastic plasma cells, accompanied by the secretion of monoclonal immunoglobulins detectable in the serum or urine [3,4]. MM classically affects the elderly with a median age at time of diagnosis of approximately 70 years, with <5% under 40 years [5]. Male to female ratio is nearly 1:1 [3,6]. Besides environmental risk factors, recent studies have indicated that dietary factor and obesity may be risk factors possibly contributing to an upward trend in MM incidence in recent decades [7,8]. The increasing incidence of MM combined with aging population make some authors to anticipate that the incidence of MM in older adults may reach 77% by 2030 [9].

Myeloma is classified as asymptomatic or symptomatic. The most common clinical features or laboratory findings are: anemia (73%), bone pain (58%), renal impairment (20% to 40%), hypercalcemia (28%), fatigue or weakness (32%), and weight loss (24%) [10].

Usually, extramedullary presentations of MM are incidentally found in the late stage of the disease by imaging studies or at autopsy. Gastrointestinal system involvement is a rare extramedullary presentation of MM and is probably associated with poor prognosis and short-lasting remissions despite aggressive treatment [11]. Previous studies have shown that liver involvement by MM is mainly secondary to diffuse plasma cell infiltration (portal, sinusoidal or mixed) or myeloid metaplasia, and the clinical manifestations reported were hepatomegaly, jaundice, ascites, or fulminant liver failure [12,13]. Thomas et al. showed plasma cell infiltration of the liver and abnormalities of the liver enzymes as part of necropsy results of 64 patients with MM. However, this study could not conclude that the laboratory abnormalities were specifically due to MM involvement of the liver since many others abnormalities (fatty infiltration, hepatocellular necrosis, hemosiderosis and amyloidosis) were observed. In our patient, the elevation of liver enzymes was specifically due to plasma cell infiltration of the liver.

Minimal elevations in liver enzymes may be approached by a history and examination, discontinuation of hepatotoxic medicines and all alcohol consumption, in addition to rational evaluation for hemochromatosis, fatty liver, viral hepatitis, autoimmune liver disease, Wilson's disease, and alpha-1antitrypsin deficiency and imaging to rule out obstruction and/or mass lesion. NAFLD is a diagnosis of exclusion.

Though transient elastography is being increasingly used to assess fibrosis and steatosis non-invasively, and has been shown to be accurate in predicting the degree of fibrosis, in atypical cases or in cases where the results do not support the clinical diagnosis, a liver biopsy should strongly be considered for diagnostic confirmation and rule out any "rare" conditions like lymphoma, myeloma etc., allowing an early diagnosis and treatment.

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