Correspondence

Low Gradient Severe Aortic Stenosis with Normal Ejection Fraction

Sir,

Low gradient severe aortic stenosis (LGSAS) with normal or preserved left ventricular ejection fraction (LVEF) is still not very well understood and a debatable entity. The data put forward by the retrospective studies has shown that this subset of patients carry a very poor prognosis.1,2

Currently this entity is defined by a mean gradient of ≤40 mm Hg (peak velocity ≤4 m/s) across the stenotic valve and a valve area of <1cm² on echocardiography. The various clinical settings in which this can occur is systemic hypertension, a smaller LV size as per body surface area of the patient leading to a lower stroke volume, mildly lower LVEF of 50%, underestimation of valve area by Doppler because of underestimation of left ventricular outflow tract diameter (LVOT) and misalignment of Doppler sample volume. Also there has been an internal inconsistency in defining severe aortic stenosis by current guidelines relating to cut offs of valve area in relation to gradient and jet velocity.3 The presence of hypertrophy as a result of aortic stenosis or hypertension or both surely adds to the angina and heart failure and changes the course and outcome of the disease process. Another important thing to consider that a valve area of <1cm² is a broad term; more critical stenosis and hypertrophy decrease the systemic arterial compliance leading to poor prognosis.

This has lead to authors to study the intrinsic myocardial dysfunction by speckle tracking showing a decreased longitudinal strain in presence of normal LVEF proving that the LVEF is not truly normal in these cases. Valve calcification on transesophageal echocardiography (TEE) and brain natriuretic peptide (BNP) levels may be helpful in decision making. So, with this ongoing unsettled debate, one expects to see changes and further refinement of the current guidelines in near future.

References


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Wilson’s Disease Unmasked by Antitubercular Therapy Induced Liver Injury

Sir,

An 18 year old female patient was diagnosed to have tubercular cervical lymphadenopathy and started on antitubercular therapy (ATT).

The lymphadenopathy regressed, however, after four months of ATT, patient developed jaundice, abdominal distension and swelling of bilateral lower limbs. She had no bleeding manifestation or altered behaviour. She had no history of jaundice in the past, history of alcohol consumption or family history of liver disease.

On physical examination, patient had pallor, icterus and bilateral pitting-type pedal edema. She had abdominal distension with shifting dullness. There was no hepatosplenomegaly. Investigations revealed a hemoglobin of 9.6 gm/dl; white cell count was 5,600/cm³ (71 % neutrophils); platelet count was 1,74,000/cm³. Coagulation profile was deranged: Prothrombin time (PT) 42.3 seconds, international normalized ratio (INR) 2.76, activated partial-thromboplastin time (aPTT) showed no clot formation. Biochemistry findings showed 0.6 mg/dL serum creatinine, 2.5 g/dL albumin, 354 IU/L alkaline phosphatase (35 to 104 IU/L), 73 IU/L alanine aminotransferase (5 to 40 IU/L), 137 IU/L aspartate aminotransferase (5 to 37 IU/L), 22.5 mg/dL total serum bilirubin (normal value < 1), 14.2 mg/dL direct bilirubin (< 0.25 mg/dL).

Tests for hepatitis C virus antibody, hepatitis B, and hepatitis A were negative, as were tests for human immunodeficiency virus (HIV) types 1 and 2, anti-nuclear (ANA) and anti-mitochondrial (AMA) antibodies. Alpha-fetoprotein levels were unremarkable. Ascitic fluid examination revealed a transudative picture with total protein 0.3 gm/dL and 190 cells (mainly mononuclear).

ATT induced drug induced liver injury (DILI) was diagnosed by exclusion and all the drugs omitted. Patient was continually observed in-patient. There was no improvement in liver biochemistry following ATT withdrawal. Patient was worked up for other causes of liver injury.

Ultrasound abdomen revealed coarse echotexture of the liver, small liver, with nodular surface (suggestive of chronic liver disease), with moderate ascites. Contrast-enhanced computed tomography of the abdomen was suggestive of chronic liver disease.

Patient underwent evaluation for Wilson’s disease. Slit-lamp examination revealed bilateral Kayser-Fleischer rings in superior and inferior region. Serum ceruloplasmin levels were 21.5mg/dL (normal 22-58) and 24 hour urine copper was 269 microgram/day (normal < 60).

A diagnosis of Wilson’s disease was made. Biopsy could not be done due to coagulopathy. MRI of the brain was done to support the diagnosis, which showed hyperintensities in bilateral globus pallidus suggestive of mineral deposits.

Patient most likely had ATT induced acute decompensation of underlying Wilson’s disease. Because of patient’s nonaffordability for liver transplantation, she was started on medical therapy with...
a combination of zinc and trientine. Patient showed gradual signs of improvement.

In our knowledge this is the first case of ATT induced decompensation of otherwise asymptomatic Wilson’s disease.

**Discussion**

Drug-induced liver injury (DILI) is a significant problem and has been a long-standing concern in the treatment of tuberculosis (TB) infection. The risk of TB-DILI ranges from 5% to as high as 33%. DILI is ultimately a clinical diagnosis of exclusion. Usually, the time of onset to acute injury is within months (2-6) of initiating therapy. Treatment should be interrupted and, generally, a modified or alternative regimen used.

Wilson’s disease is a rare cause of liver disorder due to a failure of biliary copper excretion, in which clinical manifestations range from increased levels of aminotransferase and bilirubin, decreased serum ceruloplasmin, and detectable Kayser-Fleischer rings, to fulminant hepatic failure. It can also present with neurologic, hematologic and renal dysfunction, and affects young subjects between five and 40 years of age. This typical presentation represents only 50 percent of patients ultimately diagnosed with Wilson’s disease. The factors that dictate disease tempo in any particular patient remain unknown. It is possible that in some patients a hepatic injury unrelated to the metabolic abnormalities of Wilson’s disease may be the primary process that triggers acute decompensation of Wilson’s disease. To our knowledge, an association between ATT induced hepatic dysfunction and Wilson’s disease has not been reported.

This case highlights the need for increased awareness of asymptomatic chronic liver diseases in patients presenting with apparent drug-induced hepatitis, when the withdrawal of implicated drug does not result in improvement of liver function. The deterioration of our patient’s clinical condition and the biochemical findings strongly point to an underlying disease that was not obvious at the initial presentation. Since other causes of hepatocellular failure including viral or immunologic disease were excluded, the diagnosis of Wilson’s disease underlying DILI appeared more likely. Drug toxicity superimposed onto the underlying Wilson’s disease may have caused the release of free copper and progressively more severe liver damage. Diagnosis was established on the basis of age < 35 years, Kayser-Fleischer rings, low-normal serum ceruloplasmin and 24-hour urinary copper in excess of 40 mcg.

In summary, the clinician should suspect an underlying chronic disease process in case of DILI showing no improvement following drug withdrawal. The unexplained deterioration of hepatic function in a young person should alert the clinician to the presence of an underlying disorder, such as Wilson’s disease, the early detection of which is crucial to the prognosis. As the literature has no documented reports of ATT unmasking underlying Wilson’s disease, this case encourages further investigation.

**References**


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