Indian J Gastroenterol (September–October 2014) 33(5):476–477
DOI 10.1007/s12664-013-0440-0

LETTER

All that glitters is not gold: Elevated liver enzymes do not mean liver disease always

Jeyamani Ramachandran · K. G. Sajith

Received: 17 September 2013 / Accepted: 15 December 2013 / Published online: 14 January 2014

Dear Editor,

We wish to share a very important learning point with gastroenterologists and hepatologists who are called upon to comment on abnormal liver function tests (LFTs). While evaluating for elevated liver enzymes especially serum aspartate amino transferase (AST) and alanine aminotransferase (ALT), it is important to remember nonhepatic causes of the same. This can happen in many nonhepatic illnesses due to the location of these enzymes in different tissues. Though AST is mainly concentrated in the liver, it is present in high concentration in skeletal muscle, heart, kidneys, red cells, brain, and small bowel. ALT is seen in liver, muscle, and the kidneys. The common nonhepatic causes of elevated transaminases are muscle injury, myocardial infarction, congestive cardiac failure, renal injury, small bowel ischemia, hypothyroidism, and Addison's disease [1].

We encountered five children between the age of 3 and 9 years (with the eventual diagnosis of muscular dystrophy) who were extensively worked up for suspected liver disease up to liver biopsy when they presented with elevated AST and ALT. Except one patient in whom the diagnosis was made within 3 months of detection of abnormal transminases, the diagnosis of muscle dystrophy was delayed by many months in others. The table shows liver function tests of the five children. A closer look at the LFT revealed many interesting features. There was persistent AST and ALT elevation (at least ten times) over a period ranging from months to years without much waxing or waning. What was striking was that the abnormality was only restricted to transaminases and the rest of the liver function tests including bilirubin, albumin and alkaline phosphatase and GGT were normal (Table 1). So were the prothrombin time, ultrasonogram of the abdomen and etiological work up for acute or chronic liver disease. They had signs or no symptoms suggestive of liver disease. In view of these facts, we thought of a nonhepatic cause of this elevation. Though there were no obvious symptoms pertaining to muscular system, on repeated questioning, history suggestive of proximal muscle weakness in the form of difficulty in climbing stairs was evident. One child had a positive Gover's sign on examination. Two of them had history of delayed motor milestones. We checked for serum creatine phosphokinase (CPK) and true to our suspicion, the serum CPK was grossly elevated in all these patients in the range of 7,000–33,000 U/L. One patient who underwent muscle biopsy was diagnosed to have Becker's muscle dystrophy, and the other four were diagnosed to have Duchenne's disease.

Lack of awareness of muscular origin of elevated transaminases frequently results in delay in the diagnosis of muscle diseases and unwarranted anxiety regarding liver diseases. In one patient, the institution of anti-tuberculous therapy was delayed because of mistaken diagnosis of hepatitis. Interestingly, in patients with Duchenne's muscular dystrophy, ALT levels were shown to have a good correlation with CPK levels. In fact, raised transaminase has been shown as a sign of occult muscle dystrophy and should warrant screening for CPK [2]. A recent report by Wright et al. also suggests that these elevations are more prominent in the initial stages of muscle disease, and hence, the diagnosis of muscle disease is often overlooked [3]. The usual time delay for the diagnosis is between 3 and 12 months from the detection of elevated liver enzymes [4].

J. Ramachandran (✉) · K. G. Sajith
Department of Hepatology, Division of Gastrointestinal Sciences,
Christian Medical College, Vellore 632 004, India
e-mail: jeyamani@cmcvellore.ac.in

Table 1 Liver function tests and muscle enzymes of children with muscle dystrophy

	Case 1	Case 1 repeat	Case 2	Case 2 repeat	Case 3	Case 4	Case 5
Age	4.5 years	3 months later	2 months	8 months	8 years	6 years	4 years
Total bilirubin (mg/dL)	0.4	0.3	0.7	0.1	0.6	0.5	0.5
Direct bilirubin (mg/dL)	0.1	0.1	0.2	0.04	0.4	0.2	0.2
AST (IU/L)	785	486	697	938	532	445	473
ALT (IU/L)	526	420	640	932	544	487	491
ALP (IU/L)	77	110	400	161	200	101	178
Total protein (g/dL)	7.0	7.0	7.5	7.2	7.0	7.2	7.2
Albumin (g/dL	4.6	4.5	4.4	4.7	4.2	4.6	5.3
Serum CPK (u/L)		24,560		33,295	15,000	7,000	20,909
LDH (u/L)		2,700		2,898			4,107

AST aspartate amino transferase, *ALT* alanine aminotransferase, *ALP* alkaline phosphatase, *CPK* creatine phosphokinase, *LDH* lactate dehydrogenase

Muscular origin of elevated AST, ALT has also been reported in adults in the setting of extreme muscular exertion, rhabdomyolysis, following seizures, and in polymyositis in the absence of liver disease [5]. In fact, coexistent autoimmune hepatitis and polymyositis have been reported, and this can be diagnosed with certainty on observing elevation serum bilirubin, prothrombin time, and liver biopsy changes [6]. Typhoid fever is one such instance where AST, ALT elevation could occur due to myositis as well as hepatitis [7]. Persistent transaminase elevation seen in Dengue fever may also be muscular in origin [8]. Simultaneous serum CPK estimation will resolve the tissue of origin of transaminases in such clinical scenario.

We would like to stress on the importance of considering muscular diseases and estimating serum CPK while investigating for isolated transaminase elevation especially in children with no other evidence of liver disease. This not only steers us toward the correct diagnosis but also avoids unnecessary, invasive and expensive investigations for nonexistent liver disease.

References

1. Limdi JK, Hyde GM. Evaluation of abnormal liver function tests. Postgrad Med J. 2003;79:307–12.
2. Tay SK, Ong HT, Low PS. Transaminitis in Duchenne's muscular dystrophy. Ann Acad Med Singapore. 2000;29:719–22.
3. Wright MA, Yang ML, Parsons JA, Westfall JM, Yee AS. Consider muscle disease in children with elevated transaminase. J Am Board Fam Med. 2012;25:536–40.
4. Urganci N, Arapoğlu M, Serdaroğlu P, Nuhoğlu A. Incidental raised transaminases: a clue to muscle disease. Ann Trop Paediatr. 2006;26:345–8.
5. Nathwani RA, Pais S, Reynolds TB, Kaplowitz N. Serum alanine aminotransferase in skeletal muscle diseases. Hepatology. 2005;41:380–2.
6. Hounoki H, Shinoda K, Ogawa R, Taki H, Tsuneyama K, Tobe K. Simultaneously developed polymyositis and autoimmune hepatitis. BMJ Case Reports. 2011. doi:10.1136/bcr.09.2011.4763.
7. Mirsadraee M, Shirdel A, Roknee F. Typhoid myopathy or typhoid hepatitis: a matter of debate. Indian J Med Microbiol. 2007;25:351–3.
8. Lee LK, Gan VC, Lee VJ, Tan AS, Leo YS, Lye DC. Clinical relevance and discriminatory value of elevated liver aminotransferase levels for dengue severity. PLoS Negl Trop Dis. 2012;6:e1676.