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Isolated AST elevation due to macro-AST: A case report

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Abstract
Aspartate aminotransferase (AST) is a transaminase enzyme found in the liver, heart, skeletal muscle and various other tissues. A sustained isolated increase in AST levels, without accompanying clinical symptoms, liver disease, is uncommon and can be attributed to macro-AST mainly a benign high molecular weight complex. A 33-year-old female patient presented with symptoms of fatigue, body aches and mild abdominal discomfort. Her liver function tests indicated persistently elevated AST levels, which ranged from 412 to 730 U/L, while other liver enzymes and imaging results were unremarkable. Further investigations uncovered anaemia with haemoglobin levels between 5.9 and 9.3 g/dL, low levels of Vitamin D3 and absence of autoimmune or viral markers. A liver biopsy demonstrated normal histology. To assess the macro-AST, polyethylene glycol (PEG) precipitation was conducted and PEG AST level showed 171 U/L, thereby confirming the presence of macro-AST. The patient was clinically stable and showed no abnormal symptoms. In situations where there is isolated AST elevation without a clear cause, macro-AST should be considered. The PEG precipitation method serves as a straightforward and efficient diagnostic tool. Recognizing macro-AST can prevent unnecessary interventions and alleviate patient anxiety related to persistent abnormal test results.

Keywords: Polyethylene glycol (PEG) precipitation method, macro-aspartate aminotransferase (AST), ultrasound-guided liver biopsy

Introduction
Aspartate aminotransferase (AST) is a pyridoxal phosphate-dependent enzyme that catalyzes the reversible transfer of an alpha-amino group between the amino acids aspartate and glutamate [1]. It is present in various tissues, including the liver, myocardial cells, kidneys, brain, skeletal muscle and red blood cells [2].

Macro AST is high molecular weight complex formed by plasma enzymes and immunoglobulins like IgG, IgA, or IgM and are rarely observed in the general healthy population [3]. Sometimes, increased enzyme activities in plasma can be linked to the existence of macro enzymes, leading to diminished plasma clearance and an extended half-life [4].

Macro-AST has been mentioned in several case reports and it is considered as rare, benign cause of isolated increases in AST levels and its prevalence seems to be less than that of other macro-enzymes [5]. Various methods have been proposed for diagnosing macro-AST includes protein electrophoresis, ultracentrifugation, gel filtration chromatography (GFC), immunofixation electrophoresis (IE) and assays involving polyethylene glycol (PEG) precipitation method [6].

Here, we describe an isolated AST elevation caused by the macro-AST, a macro enzyme, detected using PEG precipitation method.

Case report
A 33-year-old female patient presented with complaints of body aches, exertional shortness of breath and occasional pain in the lower left quadrant of the abdomen. She had previously visited another hospital where isolated elevation of Aspartate Aminotransferase (AST) was noted in her liver function tests, several other investigations, like direct coombs test, complete blood profile with peripheral smear, CPK/CPK-MB and Fibroscan were suggested.

Her medical history includes grade 2 corrosive ingestion. There is no history of jaundice or any other indications of liver disease. On examination, the laboratory results indicated AST 412 U/L, Ceruloplasmin 1.11 g/L and thyroid stimulating hormone 0.86 µIU/mL, with a 24-hour urine copper level of 4.79 mcg. On other day, the AST was recorded as 614U/L, creatine phosphokinase 78 U/L, lactate dehydrogenase198 U/L, Vitamin D3 4.7 ng/mL and B12 was 605 pg/mL. The complete blood count showed Hemoglobin 5.9 g/dL, WBC 6100, platelets were 3Lakhs and the Antinuclear antibody test using the IFA method showed a negative result. The patient came again for a follow-up visit to our hospital with the complaints of itching, chest discomfort and shortness of breath. Laboratory tests revealed an elevated AST level of 708 U/L and the doctors recommended Tocotrienol 400 mg (oral, once daily, 10 days), Alegra 120 mg (twice daily, 10 days), Tab. Lafutidine and domperidone 10 mg + 30 mg (oral, once daily, 10 days). Liver function tests of the patient's father and siblings were within normal limits. During another follow-up, she presented with complaints of itching and dyspepsia and there was a recent history of abortion (due to genetic factors?). Patients showed no interest in genetic testing, hence it was not conducted. Once again, the AST level was recorded as 730 U/L and a complete blood profile showing a hemoglobin level of 9.3 g/dL, white blood cell counts 6900 and platelet count of 2.9L. Patient was recommended to use Tab. Lafutidine and domperidone 10 mg+30 mg (oral, twice daily, 10 days), Docosahexaenoic Acid 160 mg (oral, once daily, 10 days), Eicosapentaenoic Acid 240 mg (oral, once daily, 10days) and started Tab. Ursodeoxycholic acid 300 mg (oral, twice daily, 10 days). An ultrasound-guided liver biopsy was performed on the right lobe of the liver and the sample was sent for histopathological examination. During microscopic analysis, several fragmented liver cores containing approximately nine portal tracts were observed and a normal liver was reported. Near normal portal tracts, zone 1 hepatocytes and zone 3 also do not show any significant histological abnormalities (Figure 1A, 1B, 1C).

To confirm the presence of macro-AST, we opted to use the polyethylene glycol (PEG) precipitation method and to assess whether AST activity in the sample decreased following PEG treatment. The precipitation was carried out using the PEG technique and the level of AST showed 171 U/L after the procedure. Our patient underwent a reevaluation of liver function, which indicated that AST levels still remained abnormal (701 U/L). The patient continued to be in good health showing no abnormalities, apart from the isolated AST elevation. She was recommended with Tab. Ursodeoxycholic acid 300 mg (oral, twice daily, 1 month).

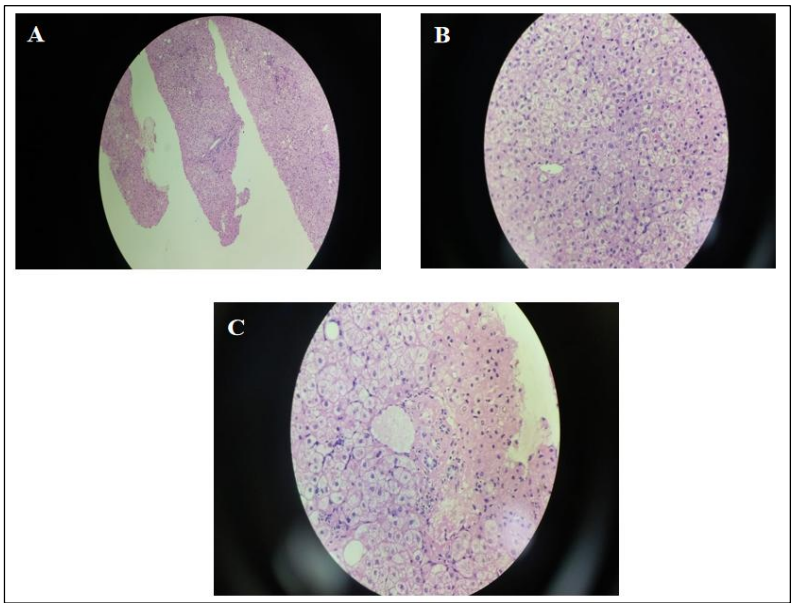

Fig 1: Histopathological examination of liver biopsy
A: liver tissue with preserved hepatic lobular architecture
B: Hepatocytes arranged in cords around the central vein with granular and eosinophilic cytoplasm
C: Focal area showing mild portal inflammation with scattered lymphocytes with partially visible portal tracts

Discussion

As Aspartate aminotransferase (AST) is present in skeletal muscle, conditions like muscle injuries, inflammatory myopathies or rhabdomyolysis may result in body aches along with isolated increases in AST levels. Increased levels of AST may indicate damage to tissues beyond the liver, particularly in muscle, especially when AST levels exceed those of ALT [7]. Iron-deficiency anemia is a frequent contributor to fatigue and dyspnea and it has been noted to sometimes increase of AST levels due to ineffective erythropoiesis or hemolysis [8]. In our case report patient was anemic with Hgb at 5.9 g/dL, presented with the symptoms like body aches and others common symptoms.

If a patient exhibits chronic and isolated AST elevation alongside a negative physical examination, the possibility of macro-AST should be considered. Various reports have suggested that macro-AST was responsible for isolated AST elevation in 60% of healthy individuals [9]. Our patient had abnormal Hgb and Vitamin D3 levels whereas other parameters are within normal ranges.

Abdominal imaging investigations and laboratory testing revealed that our patient was healthy and did not exhibit any indicators of liver or heart disease; nonetheless, during her follow-ups, her AST levels fluctuated. A report indicates that the AST activity of a young woman diagnosed with macro-AST for a duration of 12 years varied between 163

and 500 U/L, still she continued to maintain her health [10], and there have been three documented cases of macro-AST patients in China who remained in good health following 2 to 7 years of monitoring [11].

The detection of macro-AST relies on the capacity of PEG to precipitate Ig-AST complexes by absorbing the available solvent, thereby enhancing their concentration in the solution. AST activity is measured after precipitation, and both AST recovery (%) and PEG precipitation activity (%) are then computed to confirm the presence of macro-AST [12]. In this instance, the PEG precipitation method was used to examine the patient sample. The PEG precipitation technique is a straightforward and cost-effective approach that can be executed in majority of standard laboratories and its effectiveness has been thoroughly validated for the analysis of various macro complexes [13].

Conclusion

In view of isolated elevation of AST levels, without any other disease or signs, a workup on macro-AST should be suggested. PEG precipitation continues to be a straightforward, economical, and dependable diagnostic method that can be regularly utilized in clinical laboratories. Doctors need to recognize benign macro-AST as a potential reason for a persistent and isolated rise of AST levels following liver function tests. Early identification and accurate diagnosis of macro-AST is crucial for both personal and worldwide healthcare.

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Declarations

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Conflict of interest

None declared

Ethical approval

Not required

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