

Persistent Elevation of Aspartate Amino Transferase: Macroenzymes: Case Report

Aspartat Aminotransferazda Israrcı Yükseklik: Makroenzimler

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ABSTRACT Macroenzymes are usually due to the formation of an autoantibody–enzyme complex that leads to an increase in the amount of circulating enzyme. Macro-aspartate transaminase (macro-AST) is rarely considered in an asymptomatic patient with isolated elevation of AST. We describe a case of chronic elevation of serum aspartate aminotransferase (AST) activity due to the presence of a macro-enzyme form of AST (macro-AST) in a 33 years old woman followed up for 2 years. The persistent elevation of AST with normal other liver enzyme levels make us to search for the presence of Macro-AST. Patient serum was screened for the presence of macro-AST using a polyethylene glycol (PEG) precipitation technique. The serum treated with PEG after venipuncture revealed low free AST activity. We think that the importance of this condition is to avoid unnecessary, time consuming and expensive clinical and laboratory procedures after diagnosis.

Key Words: Aspartate aminotransferases; polyethylene glycols; follow-up studies

ÖZET Makroenzimler otoantikör-enzim kompleksi oluşumu sonucu ortaya çıkar ve dolaşımdaki enzim miktarında artışa neden olurlar. Makro-aspartat aminotransferaz (makro-AST) varlığı, izole AST yüksekliği olan asemptomatik bir hastada nadiren düşünülmektedir. Biz bu çalışmada, AST değerindeki yükseklik nedeni ile 2 yıl süresince takip edilen 33 yaşında bir kadın hastayı sunduk. Diğer karaciğer enzimlerinin normal olmasına rağmen sürekli AST yüksekliğinin saptanması nedeniyle hastanın serumunda polietilen glikol (PEG) presipitasyon yöntemi ile makro AST varlığı araştırıldı ve hastada düşük serbest AST aktivitesi ortaya çıktı. Biz makro-AST'nin, tam için gereksiz, zaman alıcı ve pahalı tetkikleri engellemesi nedeni ile önemli olduğunu düşünüyoruz.

Anahtar Kelimeler: Aspartat aminotransferazlar; polietilen glikoller; takip çalışmaları

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Macroenzymes are complexes consisting of normal enzymes or isoenzymes that are created by polymerization or formation of complexes with other plasma constituents.¹ These enzyme forms are as a rule detected in patients with continuously elevated serum enzyme activity that cannot be explained and is inconsistent with the general clinical picture.

The aspartate aminotransferase macroenzyme (macroAST) was first described in 1978.² Later on, this macroenzyme has been reported in a few patients with various diagnoses including liver disease, however, it was also found in healthy subjects.³ The prevalence of macro AST among the pa-

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tients evaluated for isolated elevation of AST is 13.1-60% for adults and 38.6% for children but overall, the macro-enzymes among the general population has the prevalence of 0.5-2.5%.⁴ Macro enzymes can be found in healthy population but can also be seen in some disease conditions with higher incidence, such as rheumatoid arthritis, monoclonal gammopathy, chronic HVC, resolved acute hepatitis C, and in allergen injection immunotherapy.⁵⁻⁹

We describe a case of chronic elevation of serum aspartate aminotransferase (AST) activity due to the presence of a macro-AST.

CASE REPORT

A 33 years old woman was admitted to our hospital with the complaints of mild fatigue without fever, arthralgia, myalgia and weight loss. Her physical examination was normal with normal vital signs. In her laboratory test, isolated elevation of AST level was detected. Increased AST levels were first detected about 2 years ago, and up to this time, she had several times of AST measurements, all of which were fluctuating between 199-436 U/L. She denied alcohol intake or use of any hepatotoxic drugs. She had no history of viral hepatitis or contact with individuals affected by A, B or C hepatitis. She had not undergone any transfusions of blood or blood products. Genetic and autoimmune liver diseases were excluded with normal results of antinuclear antibody (ANA), antimitochondrial antibody (AMA), smooth muscle antibody (SMA), anti-liver-kidney microsomal antibody (LKMA), ceruloplasmine and alpha-1-antitrypsin. Her biochemical analysis was; ALT 8 U/L (0-55), AST 278 U/L (5-34), ALP 50 U/L (40-150), GGT 12 U/L (9-36), albumin 4.4 g/dL (3.4-5), glucose 88 mg/dL (70-100), total bilirubin 0.5 mg/dL (0.2-1.2), creatine phosphokinase 42 U/L (29-168), TSH 3.10 (0.35-4.94). Abdominal ultrasonography showed normal liver echogenicity, morphology and structure with normal biliary system.

At this point, the presence of macro-AST was suggested and ultimately confirmed by

means of a polyethylene glycol precipitation (PEG) assay.¹⁰

AST activity was determined in serum of our patient and two control subjects before and after treatment with polyethylene glycol. To this end, 100 µL serum was added to either 100 µL of PEG 6000 solution (250 g/L in 9 g/L saline) or 100 µL saline (9 g/L) and held at room temperature for 1 minute prior to centrifugation at 15000g for 10 minutes. AST activity was determined by using Abbott methods on the Architect c8000 analyzer on both the supernatant and the saline dilution. Next, the polyethylene glycol-precipitable activity (PPA%) for AST was calculated as: $PPA\% = 100 \times [(AST_{activity} - AST_{activity-PEG}) / (AST_{activity})]$. The results of the polyethylene glycol precipitation procedure are shown in Table 1. Our patient demonstrated that 96% AST activity was precipitated with polyethylene glycol, confirming the presence of macro-AST.

DISCUSSION

Because of its wide tissue distribution, elevated AST levels have low specificity for any single disease. Historically, AST has been used clinically to diagnose hepatitis, myocardial infarction, and skeletal muscle disease. AST increase in the absence of ALT increase indicates cardiac or skeletal muscle disease. A rare cause of increased AST is the complexing of AST with an immunoglobulin, producing a macroenzyme that is not cleared from the circulation. Macro AST does not appear to be pathological in itself but their presence has been associated in some case reports with several pathological conditions such as autoimmune hepatitis, unspecified autoimmune diseases.¹¹⁻¹³ Our patient was asymptomatic and the different inves-

TABLE 1: Effect of polyethylene glycol (PEG) precipitation.

	PEG	AST _{activity} (IU/L)+PEG	PPA%
Patient	278	10	96
Control 1	200	145	28
Control 2	220	155	30

PPA: Polyethylene glycol-precipitable activity.

tigations didn't show any of these pathological conditions.

There are various techniques of detecting macro-AST.¹⁴ PEG precipitation technique separates proteins by virtue of their solubility and is a useful method for identifying macroenzymes.¹⁵ Early recognition of macro-AST, proven by simple PEG precipitation, can avoid time-consuming and invasive investigations.

Macro-AST is rare, but it has an important place in determining the clinical approach to patients with isolated high levels of AST.⁴ The possibility of a macroenzyme should be considered in the presence of an unexplained and isolated increased enzyme activity. This biochemical abnormality which does not have any specific treatment should be noted in medical records of the patient. It prevents costly and unnecessary investigations.

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