Turk J Gastroenterol *2014; 25: 568-70*

An easy method for diagnosing macro-aspartate aminotransferase: A case series

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ABSTRACT

Macro-aspartate transaminase (macro-AST) must be considered when the aspartate transaminase (AST) level is chronically high without any liver, cardiac, or muscle disease. Many specialized laboratory techniques have been recommended for diagnosing macro-AST, including the polyethylene glycol immune precipitate technique, which is simple. This study presents a considerably easier method based on the studies of Davidson and Watson and Castiella et al. Our method is based on the decrease in the plasma AST level after storage of the macroenzyme at 2-8°C for 5 days, and has the advantages of low cost, reliability, and practicality at any health center. In our eight cases of macro-AST, the AST activity at day 6 had decreased by more than 50% from day 1. This method is practical for primary healthcare facilities because of its easy application and accurate results, and obviated the need for unnecessary tests after diagnosis.

Keywords: Aspartate aminotransferase, children, macro-AST, macro-aspartate aminotransferase

Case Report

INTRODUCTION

Macroenzymes are high-molecular-weight compounds that are created by polymerization or formation of complexes with other plasma constituents. Macro-aspartate aminotransferase (macro-AST) is a high-molecular-weight form of aspartate transaminase (AST) (250 kDa) that is produced by formation of a complex with immunoglobulins (IgG, IgA, or IgM) (1). The serum AST activity is one of the basic biochemical parameters used in the diagnosis of liver disease in adults and children. While increased AST activity is generally interpreted as indicative of liver disease, it can also be elevated in the presence of muscle and renal pathologies or hemolytic processes (2). The polyethylene glycol method (PEG) is frequently used to detect macro-AST in plasma. This is based on the principle that macromolecules can be precipitated (3). Alternatively, macro-AST can be diagnosed using electrophoresis or chromatography (4). As macro-AST is a rare condition and diagnostic methods cannot be performed in many centers because of their high cost, the diagnosis is usually delayed, and many unnecessary procedures can be performed on children before the diagnosis is made (5). This has necessitated the development of practical methods for diagnosing macro-AST.

Our method is based on the decrease in the plasma AST level after storage of the macroenzyme, which is less stable, at 2-8°C for 5 days. This method is practical for use in any health center because of its low cost and reliability (1,6). We applied this method in eight patients with isolated high AST levels to evaluate its ability to diagnose macro-AST.

CASE PRESENTATIONS

Patients and methods

The patient group included eight children between 4 and 72 months of age who were admitted to our Department of Pediatric Gastroenterology, Hepatology, and Nutrition between January 2013 and January 2014. All of the patients diagnosed with macro-AST underwent physical examinations and measurement of laboratory parameters, including alanine aminotransferase,

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Received: 27.3.2014 **Accepted:** 12.8.2014
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AST, gamma glutamyl transpeptidase, total and conjugated bilirubin concentration, a complete blood count, immunoglobulins, viral hepatitis markers [anti-cytomegalovirus (CMV) IgM, CMV DNA, Epstein Barr virus (EBV)-specific IgM, Parvovirus B19 IgM, hepatitis B virus surface antigen (HBsAg), anti-HBs, anti-hepatitis C virus IgM, anti-human immunodeficiency virus (HIV)], anti-nuclear antibody, anti-smooth muscle antibody, liver kidney microsomal type 1, serum ceruloplasmin levels, antigliadin antibodies, anti-endomysium antibodies (IgA and IgG), the sweat test, reducing agents in the urine, serum alpha-1 antitrypsin, amino acid, alpha fetoprotein, and acid phosphatase levels, urine organic acid levels, and liver ultrasonography (US) to exclude accompanying liver disease. In all patients, creatine kinase (CK) and CK-MB were also determined to exclude muscle or myocardial disease. There was no history of drug abuse or pharmacotherapy in any patient.

The control group consisted of healthy children from our well-child outpatient clinic and healthcare personal from our hospital. These subjects had no complaints or symptoms, and included children with normal physical examinations, transaminases, and prothrombin times, and no change in liver echo structure on a baseline gray-scale US.

The method recommended by Davidson and Watson (1) and Castiella et al. (6) for the diagnosis of macro-AST was performed in eight cases with known isolated high AST levels followed by a diagnosis of macro-AST. First, two 2-mL blood samples were collected in two separate tubes simultaneously from each case. The AST activity in one of the blood samples was determined immediately, while the other blood sample was stored at 2-8°C for 6 days before being assayed. For each case, a separate control case that matched the AST activity was run first and shown to be normal. Two 2-mL blood samples were also collected from the control and measured similarly. The AST activity of the cases and controls at days 1 and 6 were compared.

RESULTS

The eight cases included four females and four males, ranging in age from 4 to 72 months. Table 1 shows the AST activities of the cases and matched controls on days 1 and 6. On day 6, the AST activities of the eight cases with macro-AST were reduced by more than 50% as compared to the values on day 1, while a decrease of less than 5% was observed in the control cases.

None of the children had symptoms of liver disease, and their physical and psychomotor development was normal. Liver ultrasound did not show any pathology. Infections with viruses (HBV, HCV, CMV, EBV, Parvovirus B19, and HIV) and selected metabolic disorders (galactosemia, tyrosinemia, congenital alpha-1-antitrypsin deficiency, Wilson's disease, and cystic fibrosis) were excluded. None of the patients had biochemical signs of cholestasis (normal conjugated bilirubin concentration and blood serum GGT activity) or muscle pathology (normal serum creatinine kinase activity).

DISCUSSION

Since macroenzymes are seen more frequently in adults with autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis, and ulcerative colitis, it is thought that impaired immune tolerance and an increased tendency for autoimmune diseases play a role in their pathogenesis (7). However, the pathogenesis of macroenzymes remains unclear, and no genetic tendency has been described (8). The situation is different in children, in whom AST is not generally accompanied by other diseases. While macro-AST is more frequent in adults, isolated macro-AST is more frequent in children (1).

Although macro-AST is rare, it has an important place in determining the clinical approach to patients with isolated high levels of AST. Detection of this biochemical abnormality obviated the need for expensive tests and unnecessary interventional procedures, including liver biopsies (9).

Macroenzymes in serum can be detected using electrophoresis, PEG methods, heat stability measurements, and gel chromatography (10). While the PEG method described by Davidson and Watson (1) is used most commonly, many laboratories and health centers cannot perform this test. Consequently, the limited access to diagnostic tests has resulted in the development of more practical techniques for diagnosing macro-AST. Davidson and Watson (1) and Castiella et al. (6) observed that the AST activity of blood samples containing macro-AST that were stored at 2-8°C for 5 days decreased by 65% starting at 48 h, while the decrease in controls over the same period of time

Table 1. AST levels in the patient and control groups

	AST day 1	AST day 6	Decrease (%)
1. Patient	120	48	60
Control	39	37	5
2. Patient	89	43	51.7
Control	32	32	0
3. Patient	78	33	57.7
Control	34	33	2.9
4. Patient	189	91	51.9
Control	29	29	0
5. Patient	133	50	62.4
Control	38	36	5
6. Patient	91	30	67
Control	27	26	3.7
7. Patient	93	38	59.1
Control	36	36	0
8. Patient	155	51	67.1
Control	38	37	2.6

AST: aspartate aminotransferase; normal range, 0 to 40 U/L.

was less than 2%. We also used this method to detect macro-AST in the eight cases with isolated high levels of AST included in this study after eliminating possible liver, cardiac, and renal diseases as causes. In all eight cases, the AST decreased by more than 50%, while the decrease in the controls was less than 5%. The low stability of macro-AST was the greatest factor in this decrease. Although eight cases might seem to comprise a small study population, it is actually a large sample because isolated macro-AST is rare in pediatric patients.

Although macro-AST is seen infrequently in children, it is important to determine the cause of isolated high AST levels. Given the limited availability of diagnostic methods in primary and secondary healthcare facilities, these children can undergo many invasive tests without making a diagnosis of macro-AST. The easy application and accuracy of this method, which has been described previously, shows it to be practical for primary healthcare facilities. Nevertheless, the accuracy of this method must be verified in a larger case series.

Ethics Committee Approval: Ethics committee approval was received for this study.

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - Ö.F.B.; Design - T.E.; Supervision - T.E., F.Ç.Ç., T.K.; Resource - S.L., D.G.; Materials - Ö.F.B., S.L., D.G.; Data Collection&/or Processing - Ö.F.B., S.L., D.G.; Analysis&/or Interpretation - Ö.F.B.; Literature Search - Ö.F.B.; Writing - Ö.F.B., T.E.; Critical Reviews - Ö.F.B., T.E., T.K., F.Ç.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has not received any financial support.

REFERENCES

1. Davidson DF, Watson DJ. Macroenzyme detection by polyethylene glycol precipitation. Ann Clin Biochem 2003; 40: 514-20. [CrossRef]
2. Lebensztejn DM, Kaczmarski M, Semeniuk J. Elevated aminotransferases activity in blood serum as a biochemical sign of muscular dystrophy in children with suspected damage of liver cell. Med Sci Monit 1997; 3: 929-31.
3. Levitt MD, Ellis C. A rapid and simple assay to determine if macroamylase is the cause of hyperamylasemia. Gastroenterology 1982; 83: 378-82.
4. Chung YW, Sohn JH, Baek CH, et al. Macro-aspartate aminotransferase in a patient with chronic hepatitis C. Korean J Gastroenterol 2006; 47: 229-32.
5. Litin SC, O'Brien JF, Pruett S, et al. Macroenzyme as a cause of unexplained elevation of aspartate aminotransferase. Mayo Clin Proc 1987; 62: 681-7. [CrossRef]
6. Castiella A, Aguayo FJ, Rueda M, Fernandez J, Zapata E. Macro-aspartate aminotransferase (Macro-AST) a rare cause of hypertransaminasemia: Another way to diagnosis? J Clin Gastroenterol 2006; 40: 655. [CrossRef]
7. Galasso PJ, Litin SC, O'Brien JF. The macroenzymes: A clinical review. Mayo Clin Proc 1993; 68: 349-54. [CrossRef]
8. Klonoff DC. Macroamylasemia and other immunoglobulin-complexed enzyme disorders. West J Med 1980; 85: 88-90.
9. Briani C, Zaninotto M, Forni M, Burra P. Macroenzymes: Too often overlooked. J Hepatol 2003; 38: 119. [CrossRef]
10. Stasia MJ, Surla A, Renversez JC, Pene F, Morel-Femelez A, Morel F. Aspartate aminotransferase macroenzyme complex in serum identified and characterized. Clin Chem 1994; 40: 1340-3.