Isolated Increase in Serum Aspartate Aminotransferase in an Asymptomatic Young Nepalese Female

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A 36-year-old female came to our clinical laboratory for a general health check up. She was not feeling ill and she did not have any history of significant illnesses in the past. Routine tests included complete blood count, kidney function, liver function, lipid panel, uric acid, fasting blood glucose, thyroid function tests, and urine routine and microscopy.

All her parameters were normal except serum aspartate aminotransferase (AST) level, which was significantly raised with a value of 195U/L (Reference range: 7 to 42 U/L). Other liver indices such as serum alanine transaminase, alkaline phosphatase, and bilirubin were in normal range. The patient was enquired about the factors that might have raised her AST level. There was no history of drug intake, and the patient denied use of alcohol, illicit drugs, and herbal medications. Her hepatic imaging revealed normal liver morphology with no evidence of steatosis. She was then counseled for repeat testing of serum AST after one month, when her repeated serum AST was 220 U/L. She was advised to consult a gastroenterologist and was asked to have a laboratory work-up for all etiologies of hyperaminotransferasemia. Her coagulation profile was normal, as were the peripheral blood smear and creatinine phosphokinase level. Viral and autoimmune liver disorder testing was also normal. A test for celiac disease was negative. To rule out the possibility of any interference in our assay system, her serum sample was sent to another laboratory, which also showed a raised value of AST. Analysis of AST was performed both with and without pyridoxal phosphate in the reagent.

All these results raised the possibility of macroAST. We verified the possibility of macroAST in our patient's serum using polyethylene glycol (PEG) precipitation method. Patient serum was subjected to precipitation with PEG 6000 immediately after collection. Two hundred microliters of 25% PEG was added to equal quantity of serum sample and fully mixed. It was then centrifuged at 1500 g for 30 min. The supernatant was isolated for AST analysis which yielded the value of 23 U/L, which is within normal range. PEG precipitable activity of more than 89% was noticed when compared to AST value measured on same day before PEG precipitation. This decrease in serum AST in our case after PEG treatment can be due to the

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Table 1. Polyethylene glycol-precipitable activity (PPA) of case and control.

	AST-activity (IU/L)		
	Without PEG	**With PEG**	**%PPA**
Case	220	23	89
Control 1	121	67	45
Control 2	98	49	50

effect of PEG and not due to presence of macro enzyme. Therefore, control studies on other samples with raised AST were conducted to investigate this observation (Table 1). No effect of PEG was seen in the control sample. Finally the diagnosis of macro-enzyme (macroAST) was made, and patient counseled.

MacroAST forms when circulating immunoglobulin G (IgG) or immunoglobulin A (IgA) complexes with AST that results in a higher molecular weight molecule, which remains in circulation *(1)*. Laboratory diagnosis of macroAST can be done by gel filtration chromatography, ultracentrifugation, use of protein A or protein G beads and use of polyethylene glycol (PEG) to precipitate the macroAST *(2)*. PEG precipitation method can easily be performed in most of the clinical laboratories. PEG precipitation is very cost effective when employed early in the workup, compared to other diagnostic workup of increased aminotransferase. AST recovery of 50% (median) with reference interval of 26% to 88% after PEG treatment was found in a study of reference range for AST after PEG precipitation *(3)*. Several studies *(4)* have suggested the percentage PEG precipitable activity cutoff point of 73% for macroAST, and 18%–53% reference range for normal AST.

MacroAST has been rarely found to be associated with diseases like ulcerative colitis and monoclonal gammopathy of undermined significance. Usually, it is a benign condition with no clinical significance *(5)*.

Incorporation of early testing for macroAST by clinical laboratories in any sample with raised AST is cost effective compared to testing for all etiologies of raised AST.

CONCLUSION

Patients having persistently raised AST level without other abnormal liver indices should be tested for macroAST. Early diagnosis of macroAST avoids unnecessary investigations or invasive procedures and decreases patient anxiety.

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REFERENCES

1. Nagamine M, Okochi K. Complexes of immunoglobulins A and G with aspartate aminotransferase isoenzymes in serum. Clin Chem 1983;29:379–81.
2. Krishnamurthy S, Korenblat KM, Scott MG. Persistent increase in aspartate aminotransferase in an asymptomatic patient. Clin Chem 2009;55:1573–5.

3. Wyness SP, Hunsaker JJ, La'ulu SL, Roberts WL. Reference intervals for six enzymes after polyethylene glycol precipitation and ultrafiltration. Clin Chim Acta 2011;412: 1161–2.
4. Davidson DF, Watson DJ. Macroenzyme detection by polyethylene glycol precipitation. Ann Clin Biochem 2003; 40:514–20.
5. Werner T, Vargas HE, Chalasani N. Macro-aspartate aminotransferase and monoclonal gammopathy: a review of two cases. Digest Dis Sci 2007;52:1197–8.