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CASE REPORT

Concurrent Macro-Aspartate Aminotransferase Diagnosis: Pregnant and Elderly Cases

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SUMMARY

Background: **Macro-aspartate aminotransferase (macro-AST), a high-molecular-weight complex formed by AST binding to immunoglobulins or plasma components, causes persistent enzyme elevation due to delayed renal clearance. Its diagnosis remains challenging due to rarity and nonspecific presentation.**
Methods: **We report two cases of asymptomatic isolated AST elevation: a 25-year-old pregnant woman (AST: 204 - 315 U/L) and an 83-year-old male (AST: 113 - 140 U/L). Both underwent PEG precipitation and refrigeration stability tests to confirm macro-AST.**
Results: **Polyethylene glycol (PEG) precipitation activity (PPA) values for Case 1 and Case 2 were 95.2% and 85.7%, respectively, exceeding the diagnostic cutoff (> 73%). Refrigeration testing revealed a 78.7% AST decline in Case 1 after 7 days, while Case 2 showed stable AST levels, consistent with macro-AST characteristics. Other hepatic and autoimmune markers were normal.**
Conclusions: **Macro-AST should be considered in asymptomatic patients with isolated AST elevation. PEG precipitation is a simple, reliable diagnostic tool. Effective communication between clinicians and laboratories is crucial to avoid unnecessary investigations.**
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KEYWORDS

macro-aspartate aminotransferase, PEG precipitation, isolated AST elevation, pregnant woman, elderly male

INTRODUCTION

Macroenzymes are high-molecular-weight complexes formed under pathological or physiological conditions by enzyme polymerization or binding with plasma components, delaying renal clearance and prolonging enzyme activity elevation. Macro-aspartate aminotransferase (macro-AST), a type 1 macroenzyme with a molecular weight of ~250 kDa, typically arises from the complexation of AST with immunoglobulins or plasma proteins [1]. Macro-AST is rare in pregnant women and individuals over 80 years old [2-4]. Here we report two cases diagnosed on the same day. Both patients presented with isolated AST elevation, no symptoms, and no evidence of liver or systemic disease. The final diagnosis was confirmed via PEG precipitation.

Table 1. PEG precipitation results for patients and controls.

	AST origin (U/L)	AST DIL (U/L)	AST PEG (U/L)	PPA %	AST recovery (%)
Case 1	**211**	**104**	**5**	**95.2**	**4.8**
Case 2	**140**	**70**	**10**	**85.7**	**14.3**
Control A	**40**	**21**	**16**	**23.8**	**76.2**
Control B	**185**	**92**	**85**	**7.6**	**92.4**

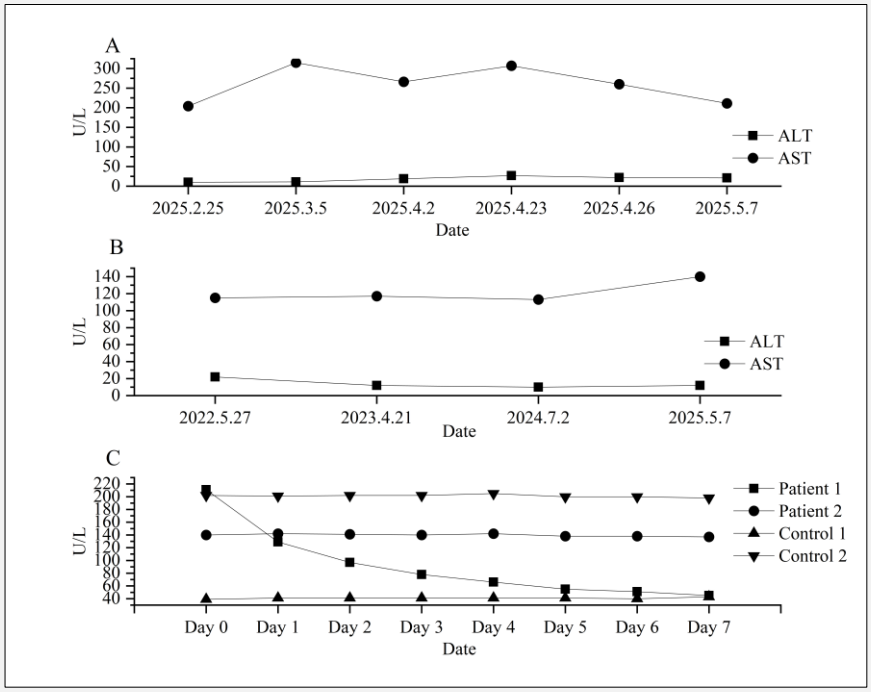

Figure 1. A Tracks AST dynamics in Case 1 during pregnancy, B Shows long-term AST elevation in Case 2, C Illustrates divergent refrigeration stability.

CASE PRESENTATION

Case 1

A 25-year-old woman at 21 weeks of gestation was referred to our laboratory for isolated AST elevation (211 U/L) during routine prenatal screening. She had no significant medical history, denied infectious or chronic diseases, and had unremarkable personal and family histories. Physical examination revealed stable vital signs and no abnormalities.

Two months prior, her AST was first noted at 204 U/L (normal range: 13 - 35 U/L) with normal alanine aminotransferase (ALT). Repeated tests showed AST fluctuating between 204 - 315 U/L (Figure 1A). Extensive evaluations - including ALT, alkaline phosphatase, γ-glutamyl transferase (GGT), creatine kinase, lactate dehydrogenase, bilirubin, renal function, thyroid function, viral serology (hepatitis B, syphilis, HIV), and autoimmune liver disease markers (anti-nuclear, anti-mitochondrial, and anti-smooth muscle antibodies) were negative. Liver ultrasound was normal.

Case 2

An 83-year-old man with hypertension and diabetes (managed with losartan, indapamide, and pioglitazone) presented with isolated AST elevation (140 U/L; normal

range: 15 - 40 U/L) during routine checkups. His AST had been elevated for three years (113 - 140 U/L; Figure 1B).

Diagnostic confirmation

PEG Precipitation Test: Equal volumes (200 µL) of 25% PEG 6000 and patient serum were vortexed, incubated for 10 minutes, and centrifuged (10,000 rpm, 10 minutes). Supernatants were assayed for AST (AST PEG). Controls were diluted with saline (AST DIL). The effect of the PEG precipitation test is determined by the percentage of AST recovered after precipitation (AST recovery %), which is measured by 100 x [AST PEG/AST DIL], and the percentage of PEG precipitation activity (PPA) is measured by 100 x [(AST DIL-AST PEG)/AST DIL] [5]. The cutoff point of PPA > 73% was considered positive and PPA < 48% was considered negative, which were the reference standards for diagnosing macro-AST [5]. Both cases met diagnostic criteria (Table 1).

Cold Storage Evaluation: To evaluate enzyme degradation, AST activity was measured at 24-hour intervals over 7 consecutive days of refrigeration (4°C) in serum samples from both patients and two controls. After 1 week at 4°C, AST activity in Case 2 and both control sera remained stable (Figure 1C). In contrast, Case 1 exhibited a marked decline: 38.9% reduction at 24 hours, 54% at 48 hours, and 78.7% after 7 days (Figure 1C).

DISCUSSION

This study reports the first same-day diagnosis of macro-AST in two distinct populations: a pregnant woman and an octogenarian male. The pregnant patient (Case 1) displayed typical macro-AST features, including high PPA (95.2%) and significant cold-induced AST degradation (78.7%). In contrast, the elderly male (Case 2) demonstrated equally high PPA (85.7%) but atypical refrigeration stability - a finding not previously emphasized in the literature [1,4]. This divergence suggests potential heterogeneity in macro-AST complex composition (e.g., IgA vs. IgG binding) or stability mechanisms. The exceptionally high PPA values (> 85%) in both cases reinforce polyethylene glycol precipitation as a robust diagnostic tool, aligning with prior reports of 88.2% sensitivity and 88.9% specificity at a 73.3% cutoff [6]. Mechanistically, genetic variants such as the p.Gln208Glu mutation in GOT1 [7] may predispose individuals to immunoglobulin binding by introducing charged residues on the enzyme surface. The contrasting refrigeration behaviors imply that Case 1 likely involved an IgG-bound complex prone to cold precipitation, whereas Case 2 may represent an IgA or non-immunoglobulin complex with stable conformation.

Clinically, undiagnosed macro-AST risks unnecessary interventions, as exemplified by Case 1's prior hepatoprotective therapy. We propose a pragmatic diagnostic algorithm for isolated AST elevation: after excluding preanalytical errors (hemolysis), muscle injury (CK), and hepatic pathology (ALT/GGT/imaging), PEG precipitation should be prioritized. Laboratories play a critical role in advocating for this test, particularly in pregnancy where physiological enzyme fluctuations may obscure macro-AST [2].

Limitations include the small sample size inherent to case reports and lack of immunofixation or gel filtration chromatography to characterize specific binding partners. The mechanistic basis for divergent refrigeration stability remains speculative and warrants further study. This report highlights two key advances: the first simultaneous diagnosis of macro-AST in a pregnant woman and an elderly male, and documentation of atypical refrigeration stability that expands the phenotypic spectrum of this condition. Proactive utilization of PEG precipitation testing can prevent unnecessary diagnostic procedures and iatrogenic harm. Effective collaboration between clinicians and laboratories remains essential for recognizing this underdiagnosed entity.

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Declaration of Interest:

All authors declare that they have no competing interests.

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