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Olgu Sunumu / *Case Report*

Pre-Analytical Interference Causing Misleading hs-cTnT Elevation in a Pediatric Patient

Pediatrik Bir Vakada hs-cTnT Yüksekliğine Neden Olan Preanalitik İnterferans

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ABSTRACT

High-sensitivity cardiac troponin T (hs-cTnT) assays are crucial in evaluating chest pain, but their increased sensitivity makes them susceptible to pre-analytical interferences. False-positive results may lead to unnecessary clinical interventions, especially in pediatric populations—a 14-year-old male patient presented with chest pain. Two simultaneously collected blood samples showed significantly different hscTnT levels: <5.4 ng/L in the first sample (processed from an aliquot) and 31.7 ng/L in the second (analyzed from the primary tube). Reanalysis of the second sample after centrifugation yielded 45.2 ng/L. However, hs-cTnT measured in the EDTA plasma sample and in a freshly collected sample were both <5.4 ng/L. ECG and echocardiographic findings were normal. The inconsistent hs-cTnT values were attributed to pre-analytical factors such as fibrin clots or gel droplets in the primary tube. These artifacts can interfere with immunoassays and produce falsely elevated results, despite being visually undetectable. The consistent normal results in EDTA plasma and the freshly collected sample confirmed the presence of a preanalytical error. Pre-analytical variability can significantly impact hs-cTnT testing, leading to misleading clinical interpretations. Laboratory professionals and clinicians must collaborate when test results do not align with clinical findings to prevent misdiagnosis and unnecessary intervention

Keywords: Preanalytic interference, Hs Cardiac Troponin T, Misleading elevation

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ÖZET

Yüksek duyarlıklı kardiyak troponin T (hs-cTnT) testleri, göğüs ağrısının değerlendirilmesinde kritik öneme sahiptir; ancak artan duyarlılıkları, bu testleri preanalitik girişimlere karşı hassas hale getirir. Yanlış pozitif sonuçlar özellikle pediatrik hastalarda gereksiz klinik müdahalelere yol açabilir. 14 yaşında erkek bir hasta göğüs ağrısı şikâyetiyle başvurdu. Aynı anda alınan iki kan örneğinde hs-cTnT seviyeleri arasında belirgin fark görüldü: İlk örnekte (ayrılmış bir alikottan işlenen) <5.4 ng/L, ikinci örnekte ise (birincil tüpten analiz edilen) 31.7 ng/L olarak ölçüldü. İkinci örneğin santrifüj sonrası yeniden analizinde değer 45.2 ng/L'ye yükseldi. Ancak, EDTA plazma örneğiyle ve taze alınan yeni bir örnekle yapılan hs-cTnT ölçümleri her ikisinde de <5.4 ng/L olarak bulundu. EKG ve ekokardiyografi bulguları normaldi. Tutarsız hs-cTnT değerleri, birincil tüpte bulunan fibrin pıhtıları veya jel damlacıkları gibi ön-analitik faktörlere bağlandı. Bu tür yapılar, immünassaylerle yapılan testleri bozarak yanlış şekilde yüksek sonuçlara neden olabilir, hatta çoğu zaman görsel olarak fark edilemezler. EDTA plazma örneği ve taze alınan örnekte elde edilen tutarlı ve normal sonuçlar, preanalitik bir hatanın varlığını doğruladı. Preanalitik değişkenlik, hs-cTnT testlerini önemli ölçüde etkileyerek yanıltıcı klinik yorumlara yol açabilir. Test sonuçları klinik bulgularla uyumlu değilse, laboratuvar uzmanları ve klinisyenlerin iş birliği içinde olması, yanlış tanı ve gereksiz müdahalelerin önlenmesi açısından büyük önem taşır.

Anahtar Sözcükler: Preanalitik interferans, Hs Kardiyak Troponin T,yalancı yükseklik

MAIN TEXT

Troponin testing is one of the primary diagnostic tools used in the evaluation of patients presenting with chest pain. High-sensitivity troponins (hs-Tn) have the ability to detect slight elevations above the 99th percentile of the healthy population distribution (1,2). Due to the high analytical sensitivity of high-sensitivity cardiac troponin (hs-cTn) assays, unexpected increases in test results without a clear clinical explanation are becoming increasingly common in daily practice (3).

The false-positive elevations in hs-Tn levels due to preanalytical sample quality issues have become a genuine concern for clinical laboratories. This issue is further exacerbated by the progressively lowering thresholds for ruling in and ruling out myocardial infarction.

In our laboratory, VACUSERA 5 ml Serum Gel and Clot Activator tubes(Ref no: 435305) were used for hs Troponin T analysis. Vacusera Serum Separator Tubes contain inert gel; during centrifugation, gel forms a stable barrier between serum and blood cells. High-sensitivity Troponin T was analysed by electrochemiluminescence immunoassay (ECLIA) on the Roche Cobas e801 immunoassay analyser.

Patient Information: In this case report, we present a 14-year-old male patient with inconsistent Troponin T levels in simultaneous blood samples. The patient, who applied to the pediatric outpatient clinic with complaints of chest pain, was referred to the pediatric cardiology department after routine blood tests were requested. The pediatric cardiologist, who was unaware of the previous tests, independently requested the same cardiac markers (hs-cardiac Troponin T, NT-proBNP, Creatine Kinase (CK), CK-MB). Two gel separator biochemistry tubes were collected and sent to the laboratory separately.

The pre-analytical system automatically aliquoted patient's first sample, and the second sample was processed directly from the primary tube. The results are shown in Table 1. The hemolysis indices of both samples were similar, suggesting that hemolysis was not responsible for the discrepancy in hs-cTnT results. Due to the high hs-cTnT result, the measurement was repeated in the plasma of the EDTA-containing complete blood count sample of the patient and measured as <5.4 pg/mL. For further investigation, the second sample was re-analyzed after re-centrifugation and aliquotation, and the hs-cTnT result was 45.2 pg/mL.

Table 1. The results of the different samples
Tablo 1. Farklı örneklerin sonuçları

	HIL indices Hemolysis, Icterus, Lipemia indices)	hs Troponin T (ng/L) (<14 ng/L)*	Creatinin kinase(U/L) (41-171)*	CK-MB (µg/L) (<4,87)*	NT proBNP (ng/L) (<125)*
First sample(aliquoted sample)	H:9 (<10)* L:9 (<10)* I:1 (<2)*	< 5,4	131	1,78	<50
Second sample (primary sample tube)	H:5 (<10)* L:6 (<10)* I:1(<2)*	31,7	132	1,77	<50
EDTA plasma		<5,4			
After centrifugation and aliquoting of second sample		45,2			

*Reference ranges

After consulting with the patient's physician and confirming that both the ECG and echocardiography findings were normal, it was decided to re-collect a new sample from the patient. This blood sample was to be collected vertically (without delays), ensuring that it would be immediately delivered to the laboratory for analysis. The hs-cTnT level of the new sample was <5.4 pg/mL.

Informed consent was obtained to participate in the study and a new sample was drawn for re-evaluation.

DISCUSSION

Numerous publications have reported false-positive results for troponin testing, and many pre-analytical or analytical issues may be the cause of such interferences (4,5,6). Several mechanisms may cause false positivity, including various immune complexes (macro-troponin), heterophilic antibodies, contrast agents, and anti-troponin antibodies (7,8). Precipitation techniques with polyethylene glycol (PEG) may be employed to investigate the presence of macrotroponin and immune complexes. Heterophilic blocking tubes may also help mitigate the interference caused by heterophilic antibodies.

The significant discrepancies observed between our patient's initial and re-analyzed hs-cTnT results were primarily attributed to pre-analytical factors. The possibility of pre-analytical interference, such as incomplete clotting, fibrin remnants, gel droplets, or sample heterogeneity, may have contributed to this inconsistency. The first sample had been processed from an aliquot, while the second was directly analyzed from the primary tube. Interestingly, re-centrifugation and re-aliquotation of the second sample led to a further increase in the hs-cTnT value. In contrast, results from the EDTA plasma and the newly drawn serum sample both showed <5.4 ng/L, which aligned with the first aliquoted result. This supports the hypothesis that the observed elevation was due to a spurious preanalytical event, likely related to the handling of the primary sample tube, such as undetectable microfibrin clots or gel interface issues. Some studies have shown that fibrin clots can lead to falsely elevated troponin values due to assay interference (9,10).

In our laboratory, preanalytical sample quality is routinely monitored using **HIL indices** (Hemolysis, Icterus, Lipemia), which were within acceptable ranges for both samples in this case. Thus, hemolysis or other common interferents were excluded. However, invisible microclots or gel migration can still interfere with

immunoassay detection even when standard indices are normal.

Additionally, the patient's cardiac biomarkers, including **CK, CK-MB, and NT-proBNP,** were also measured and found to be within normal reference ranges. These biomarkers provide valuable supportive evidence against myocardial injury. Particularly in pediatric patients, elevated hs-cTnT values must be interpreted cautiously, and the concordance of normal CK, CK-MB, and NT-proBNP levels with normal ECG and echocardiography further reinforces the conclusion that the troponin elevation was not clinically significant.

The literature emphasizes the importance of preanalytical variables in hs-cTnT testing. In a study, a **9.5% false-positive rate** was reported in an unselected emergency department population, where samples showed elevated hs-cTnT but normal hs-cTnI levels (11). It has also been shown that **residual white blood cells and platelets in plasma samples** can cause false-positive hs-TnT results (12). Therefore, the choice of collection tube and sample matrix is critical. Some authors suggest that "**Rapid Serum Tubes**" may reduce false-positive troponin T results when compared with "**Plasma Separator Tubes**" (12). Moreover, **recentrifuging serum/plasma** before troponin testing or using specific collection tubes may help mitigate such interferences in routine laboratory practice.

In response to this case, we investigated whether this was an isolated incident or potentially **related to a specific lot** of collection tubes. A retrospective review of other patients' hs-cTnT results analyzed using the same Vacusera serum gel tube lot (Ref no: 435305) revealed no similar discrepancies or abnormal elevations. This indicates that the interference observed in our case was a **patient-specific, preanalytical issue** rather than a systematic or lot-dependent problem.

CONCLUSION

False-positive troponin T results can lead to unnecessary hospital admissions, prolonged monitoring, additional diagnostic investigations, and even invasive procedures. Therefore, when results appear clinically inconsistent or contradictory, clinicians need to consult with a laboratory specialist to ensure accurate interpretation and appropriate patient management. This case clearly demonstrated that preanalytical variables can significantly impact troponin T results, emphasizing the need for strict adherence to standardized procedures.

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