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Case Report

# A heterophile antibody affecting a contemporary but not a high-sensitivity cardiac troponin assay

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A recent case report has indicated that certain high-sensitivity cardiac troponin I (hs-cTnI) assays and not their contemporary versions are susceptible to heterophile antibodies causing falsely elevated results [1]. However, it is imperative to state that not all hs-cTnI assays should be grouped/classified together in this manner as different heterophile antibodies and different hs-cTnI assays may not yield clinically discrepant results when tested together. This is in line to what has been observed when evaluating the effect of macrocomplexes and hs-cTn concentrations, with different assays being more or less affected by these complexes [2,3].

During our transition from Abbott Laboratories' contemporary cTnI assay (ARCHITECT STAT Troponin-I assay) to Abbott Laboratories' hs-cTnI assay (ARCHITECT STAT high sensitive troponin-I assay) [4], a cardiologist questioned the clinical pattern of serial cTnI results on a patient with whom the contemporary cTnI assay yielded persistently elevated results (Table 1). This patient was a middle-aged female who had cTnI measurement performed after a surgical procedure. The elevated cTnI results prompted a cardiac catheterization which showed normal left ventricular systolic function and mild coronary artery disease in the left anterior descending coronary artery (remaining vessels normal) with a subsequent echocardiogram also displaying normal left ventricular systolic function with no regional wall motion abnormalities. She was medically treated from day 10 to day 83 (timeline from first cTnI result) when she was readmitted with noncardiac chest pain with again elevated cTnI concentrations.

Testing with different matrices (lithium heparin and EDTA plasma) **[5]** and with different contemporary cTnI assays indicated that only the Abbott contemporary cTnI assay yielded high concentrations (Table 1). Importantly, for this case report, is the fact that Abbott's hs-cTnI assay yielded undetectable cTnI concentrations when tested with different samples types. As the Abbott hs-cTnI assay was reformulated to prevent interactions with heterophile antibodies (i.e., a chimeric mouse human antibody is used as opposed to only mouse monoclonal antibodies with the contemporary assay), we performed a serial dilution (i.e., 1 in 2, 1 in 4 and 1 in 8 with the zero calibrator as the diluent) as well as testing after incubation with a heterophilic blocking tube (HBT, Scantibodies) for the Abbott contemporary cTnI assay. Deviation from linearity was observed with serial dilutions with percent deviation of 127% (for 1 in 2), 136% (for 1 in 4) and 130% (for 1 in 8) on the patient sample (slope for measured versus calculated = 1.32) as compared to 0% (for 1 in 2), −7% (for 1 in 4), and −8% (for 1 in 8) with a high patient cTnI concentration sample with no interference (slope for measured versus calculated = 0.98). Also, testing after incubation of a sample with a cTnI concentration of 0.36 μg/L with HBT yielded results of 0.09 μg/L (500 μL of sample incubated) and 0.01 μg/L (250 μL of sample incubated), further supporting the presence of a heterophile affecting Abbott's contemporary but not hs-cTnI assay in this patient's sample.

Our report of a heterophile antibody not affecting a hs-cTnI assay should be reassuring to clinicians, especially considering that the majority of companies have or will be transitioning to only manufacturing hs-cTn assays in the future. Our report, on a hs-cTnI assay not evaluated by Baroni and colleagues **[1]**, highlights the need for close collaboration between clinicians and laboratory professionals when investigating clinically discordant results, which can occur with both contemporary and high-sensitivity cTn assays **[1–5]**.

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**Table 1**
Longitudinal testing, different sample types and different cardiac troponin I assays measured on a patient's sample with a confirmed heterophile antibody affecting Abbott's contemporary cTnI assay. Note for the Abbott STAT Troponin-I assay clinically used at our hospital the following comment is listed in the package insert regarding specimen types: heparinized plasma, EDTA plasma and serum specimens may be used for the ARCHITECT STAT Troponin-I assay (package insert REF 2 K41 840,653/R08 Revised March 2010).

| Date | EDTA plasma | Lithium heparin plasma | Lithium heparin plasma | Lithium heparin plasma | Lithium heparin plasma | EDTA plasma | EDTA plasma |
|---|---|---|---|---|---|---|---|
| Day and Time (measurement) | Reported Abbott cTnI [μg/L] | Abbott cTnI [μg/L] | Abbott hs-cTnI [ng/L] | Ortho Clinical Diagnostics cTnI [μg/L] | Siemens EXL cTnI [μg/L] | Abbott hs-cTnI [ng/L] | AccuTnI + 3 cTnI [μg/L] |
| | [#]99th = 0.03 μg/L | 3 mouse monoclonal antibodies | 1 mouse monoclonal & 1 chimeric monoclonal | 3 mouse monoclonal antibodies | 2 mouse monoclonal antibodies | 1 mouse monoclonal & 1 chimeric monoclonal | 2 mouse monoclonal antibodies |
| Day 86 07:25[*] | 0.36 | | | | | 1 | < 0.01 |
| Day 85 23:55 | 0.34 | | | | | | |
| Day 85 15:55 | 0.39 | 0.47 | < 1 | < 0.012 | < 0.02 | | |
| Day 84 07:45 | 0.32 | | | | | | |
| Day 84 06:00 | 0.44 | | | | | | |
| Day 84 01:00 | 0.46 | | | | | | |
| Day 83 21:15 | 0.38 | | | | | | |
| Day 83 15:50 | 0.35 | | | | | | |
| Day 10 13:29 | 0.20 | | | | | | |
| Day 3 06:47 | 0.23 | | | | | | |
| Day 2 08:40 | 0.28 | | | | | | |
| Day 2 00:20 | 0.33 | | | | | | |
| Day 1 16:40 baseline measurement | 0.32 | | | | | | |

[*] HBT (Heterophilic Blocking Tube) and Serial Dilution with zero calibrator performed on this sample.
[#] For up to date 99th percentiles for the different cardiac troponin assays please refer to the IFCC Committee on Clinical Applications of Cardiac Bio-Markers (C-CB) website: http://www.ifcc.org/ifcc-education-division/emd-committees/committee-on-clinical-applications-of-cardiac-bio-markers-c-cb/

## Conflict of interest/disclosures

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