Targeted Temperature Management as a Cause of Liver Injury

TO THE EDITOR:

Targeted temperature management (TTM) is an evidence-based therapeutic modality that is used frequently after cardiac arrest to enhance neurologically intact survival and lower overall mortality by maintaining a lower body temperature.[1] Elevated liver enzymes are a common finding in survivors of cardiac arrest and are often attributed to hypoxic hepatitis, which has been found in up to 13.5% of patients.[2]

In our practice, we saw a 61-year-old man with no known liver disease or alcohol use history who had presented with cardiac arrest. Cardiopulmonary resuscitation was performed followed by percutaneous coronary intervention, and he was subsequently started on TTM protocol at a target body temperature of 32°C to 34°C for 24 hours using an Icy Intravascular Heat Exchange Catheter (ZOLL Circulation, Inc., Chelmsford, MA). He was treated medically with aspirin, ticagrelor, unfractionated heparin, nitroglycerin patch, metoprolol, perindopril, and 2 g of acetaminophen per 24 hours. He had been on no medications prior to presentation.

On presentation, bloodwork revealed an elevated alanine aminotransferase (ALT) (138 IU/L; normal 1-60 IU/L) and lactate dehydrogenase (LDH) (316 IU/L; normal 100-235 IU/L) with normal gamma-glutamyltransferase (GGT). Immediately after resuscitation, ALT and LDH rose to 655 IU/L and 853 IU/L, respectively, while GGT rose to 113 IU/L. Total bilirubin, international normalized ratio, and alkaline phosphatase remained within normal ranges throughout hospitalization. By day 5 following arrest, ALT had reached a nadir at 263 IU/L before rising to 426 IU/L by day 7 following arrest, while GGT rose to 326 IU/L (Fig. 1). Investigations were unsuccessful

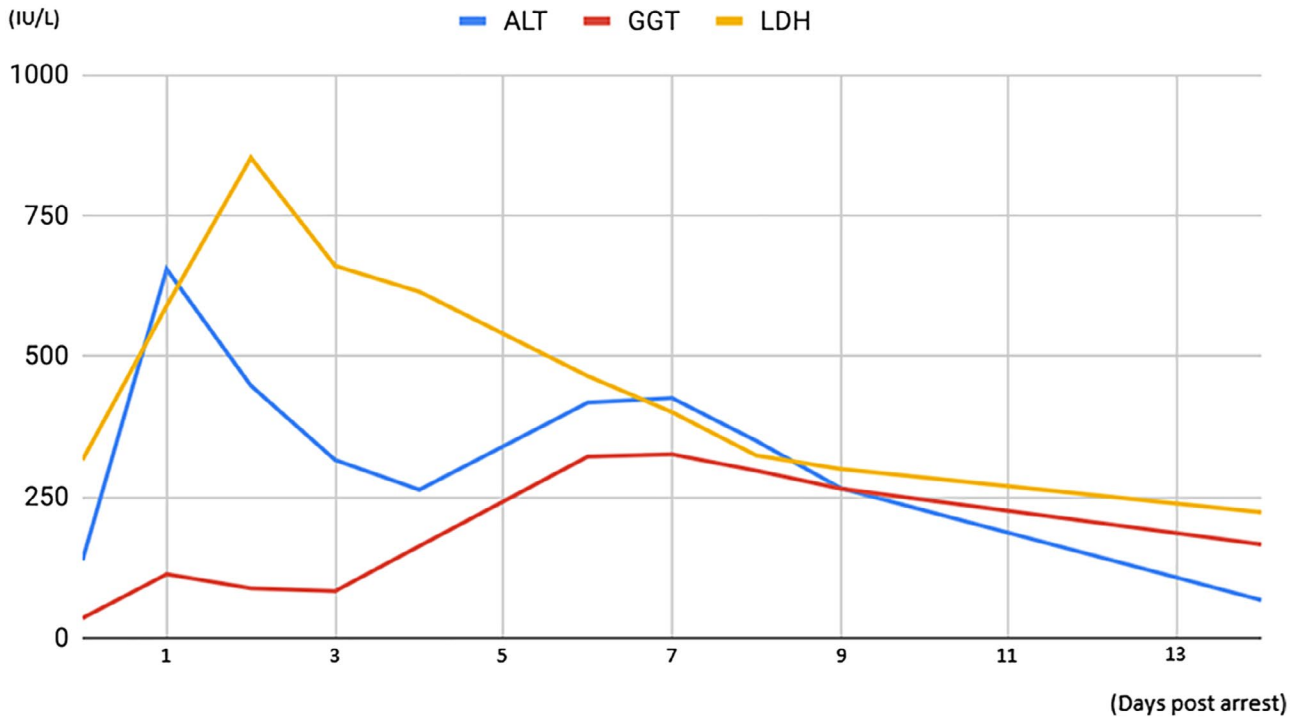

FIG. 1. Trends in liver enzymes following cardiac arrest.

in identifying an etiology for those derangements, and they included a chronic liver disease and viral hepatitis workup along with ultrasound Doppler studies.

The patient described had a delayed rise in liver enzymes, suspicious for being induced by TTM. Whereas hypoxic hepatitis usually manifests as an elevation in liver enzymes along with LDH, this patient's LDH peaked immediately following arrest and proceeded to return to baseline, whereas the ALT and GGT went through another rise. A recent study by Iesu et al. found that acute liver failure (ALF) occurred in 56% of post-cardiac arrest patients admitted to intensive care unit at a median time of 3 days following arrest.[3] Interestingly, TTM was found to have been administered to 94% of patients who eventually developed ALF, versus only to 81% of those who did not develop ALF. Studies are needed to further characterize the incidence and mechanism of elevated liver enzymes after TTM, to direct monitoring and treatment in the future.

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Potential conflict of interest: Dr. Swain advises Gilead and Intercept. He is on the speakers' bureau for Abbott.