Extreme hyperferritinaemia: further considerations

In their case report, Sami et al.1 state that very high ferritin concentrations (greater than 10,000 μg/L) have only been described in adult Still’s disease, multiple blood transfusions and severe acute hepatocellular damage. It may be of interest to the authors that such marked hyperferritinaemia has also been documented in patients with the human immunodeficiency virus (HIV) complicated by superinfection with a range of opportunistic organisms, particularly disseminated histoplasmosis.2 We would also like to emphasize that haemophagocytic syndromes, such as haemophagocytic lymphohistiocytosis (HLH), may also produce ferritin concentrations of this magnitude.3,4 A variety of drugs, infections and rheumatological diseases, including but not exclusively adult Still’s disease, may precipitate a haemophagocytic process,5 or it may be a primary disorder. The diagnosis of HLH relies on the patient satisfying sufficient criteria, of which serum ferritin is a part.6

As an aside, it appears that haemophagocytosis is associated with lower glycosylation of circulating ferritin,7 a feature that may extend to other circulation proteins, notably transferrin,8 possibly due to liver involvement by the pathological process. As an illustrative example, a recent case from our laboratory of a five-year-old girl with HLH secondary to Epstein–Barr virus (EBV) infection demonstrated a serum ferritin concentration of 29,600 μg/L at diagnosis and detectable serum asialotransferrin on isoelectric focusing.

A review of all ferritin results greater than 10,000 μg/L from our laboratory network in the past year found 35 results from 30 patients (0.06% of all ferritin requests). Most patients had received multiple transfusions for a variety of reasons (14 cases) or had severe acute hepatocellular damage (9 cases); however, there were four cases of HLH: two adult, both fatal, and two paediatric, both secondary to EBV infection. Three cases of high ferritin were not clearly explained.

DECLARATIONS

Competing interests: None.
Funding: None.
Ethical approval: Not applicable.
Guarantor: GAM.
Contributorship: GAM wrote the first draft, performed the literature review and collected patient data. All authors reviewed and approved the final manuscript.
Acknowledgements: None.

G A Marshall, C J Pretorius and J P J Ungerer
Department of Chemical Pathology, Pathology Queensland, Royal Brisbane Hospital, Herston QLD 4029, Australia
Corresponding author: G A Marshall
Email: George_Marshall@health.qld.gov.au
DOI: 10.1258/acb.2011.011219

REFERENCES


High-sensitivity troponin assays and clinical decisions

The recently published analysis of Aldous et al.1 contributes important information for the interpretation of high-sensitivity troponin (hs-cTn) assays in patients with acute chest pain presenting to the emergency department (ED). A new finding of their analysis is that the introduction of the ‘delta change criterion’ of hs-cTn levels for the diagnosis of acute myocardial infarction (MI) increases specificity at the cost of sensitivity. These results clearly indicate that diagnostic reasoning cannot be reduced on mere mathematical calculations of time-dependent changes of biomarker levels as currently discussed.

Although mathematical calculations and models are important tools in evaluating new biomarkers, diagnostic reasoning in emergency medicine is a complex process including the combination of intuitive and analytical components.2 Therefore, the correct working hypothesis and deduced therapeutic management strategies can only be made using all available information, including clinical signs and symptoms of the patient, results of 12-lead electrocardiogram and levels and dynamics of cTn concentrations to calculate post-test probabilities. Because physician-based subjective calculation of post-test probabilities for an individual patient is prone to errors,3 diagnostic reasoning in patients with acute coronary syndrome should include formal risk assessment using validated risk assessment tools such as GRACE, TIMI or PURSUIT risk scores.4 Moreover, the aim of disposition decisions in the ED is not to identify patients with acute MI or risk of death alone, but to identify patients at increased risk for