Marked but Transitory Elevation of Hepatic Transaminases after Subcutaneous Calcium Heparin Administration

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Heparin is a widely used drug in the management of venous thrombosis. Its adverse effects are not only related to its anticoagulant properties: they also include thrombo-cytopenia [1], cutaneous thrombotic complications [2], disorders of electrolytes [3], and mild elevations of hepatic transaminases [4]. Mild increases in transaminase levels are quite frequent [5] and are usually not accompanied by increases in bilirubin or alkaline phosphatase. We describe a patient who showed severe augmentation of hepatic enzymes after the administration of a single dose of calcium heparin.

A 70-year-old Caucasian woman was admitted to our department for chest pain lasting for 8 h. The clinical history revealed chronic ischemic cardiomyopathy and a recent (1991) diagnosis of chronic lymphatic leukemia. The features of the pain were consistent with myocardial ischemia although the electrocardiogram, as well as the assay of specific myocardial enzymes did not show any change. Physical examination did not detect any signs of heart failure.

The patient was treated with intravenous nitrates and subcutaneous calcium heparin (7,500 IU every 8 h). On the second day, after a total dose of 15,000 IU heparin, we recorded a marked increment of aspartate (962 U/l) and alanine (ALT) transferase (839 U/l, γ -glutamyl transferases (197 U/l), lactate de-hydrogenase (1,339 U/l) and conjugated bilirubin (35 μ mol/l). No other biochemical parameter was modified, and in particular platelets remained normal. In order to clarify the meaning of these results, liver echogra-

phy, serology for hepatitis A, B and C viruses, carcinoembryonic antigen and α -fetoprotein assays were performed without bringing any insight into the cause of the hepatic disorder.

Furthermore, we could reasonably exclude a liver infiltration by the lymphoproliferative disorder because the disease was at stage 0 (according to the Rai classification) and because of the rapid normalization of laboratory parameters without any specific therapy. In fact, the laboratory findings returned to normal values within 15 days, and a few hours after the first determinations, the figures were already reduced to half, although anticoagulant therapy was not discontinued.

At the time of admission, the patient was taking oral coronary dilators (nitrates). A possible role of these compounds in the increase in the transaminases seems unlikely for two reasons: firstly, nitrates have never been claimed to increase transaminase levels; secondly, the patient had been

taking these compounds for the last 2 years prior to admission, before heparin was started, and basal transaminase levels were normal. However, we do not know whether the combination of nitrates and heparin may have contributed to the degree of elevation.

We thus suggest that laboratory findings in our patient might be attributed to heparin, although, to our knowledge, there is no report of such a marked elevation. The underlying mechanism is not known, but it is likely to be induced by an idiosyncratic hepatic damage [6].

References

King DJ, Kelton JG: Heparin-associated thrombocytopenia. *Ann Intern Med* 1984;100: 535-540.

White PW, Saad JR, Nensel RE: Thrombotic complications of heparin therapy. *Ann Surg* 1979;190:595-608.

Edes TE, Sunderrajan EV: Heparin-induced hyperkalemia. *Arch Intern Med* 1985;145: 1070-1072.

Dukes GE, Sanders SW, Russo J, Swenson E, Bumakis TG, Saffle JR, Warden GD: Transaminase elevations in patients receiving bovine or porcine heparin. *Ann Intern Med* 1984;100: 646-650.

Monreal M, Lafoz E, Salvador R, Roncales J, Navarro A: Adverse effects of three different forms of heparin therapy: Thrombocytopenia, increased transaminases, and hyperkalemia. *Eur J Clin Pharmacol* 1989;37:415-418. Lance RP: Drug-induced allergic hepatitis. *Semin Liver Dis* 1990;10:305-315.