Combined strategies help patients with adverse heparin reaction before heart surgery

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New evidence suggests that therapeutic plasma exchange and appropriate blood testing could help patients who are in urgent need of heart surgery, but have a history of an adverse reaction to the blood thinner heparin, according to a study, published online today in *Blood*, the Journal of the American Society of Hematology (ASH).

Many patients who take blood thinners will eventually require some form of heart surgery, which requires the administration of large quantities of heparin to prevent clots. Some patients who have taken heparin develop what is known as heparin-induced thrombocytopenia (HIT), in which they develop antibodies against the heparin, activating platelets and paradoxically forming clots.

When patients with a history of HIT require urgent heart surgery, physicians must test for the presence of HIT antibodies to determine whether the patient can be re-exposed to heparin during the procedure. While HIT antibodies generally dissipate naturally, they can sometimes remain at high levels, requiring physicians to take measures to lower them for patients who urgently require heart surgery. To lower HIT antibodies in these patients, a procedure has been advocated called therapeutic plasma exchange (TPE), in which blood is taken from the patient, plasma is removed, and blood and replacement fluids are reinfused into the patient.

Hematologists use two types of tests to measure HIT antibodies and to determine patient readiness for heparin re-exposure during surgery. These include a functional platelet serotonin-release assay and a highly sensitive enzyme-immunoassay. While the functional assay measures release of serotonin, a direct marker of platelet activation, the immunoassay casts a wider net, detecting both clinically significant and insignificant levels of HIT antibodies. If the more widely used immunoassay indicates presence of HIT antibodies in a patient, surgery is usually delayed or plasma exchange must be performed.

While practitioners have historically understood the two assays to provide similar conclusions, new evidence suggests that the functional assay may characterize HIT antibody levels as relatively low while an immunoassay result could indicate the opposite. This evidence is summarized in a new case report in which a 76-year-old female with kidney cancer and previous HIT required urgent cardiac surgery to remove a tumor that had spread to her heart. After both her initial functional and immunoassays indicated the presence of HIT antibodies, her doctors deemed her ineligible for surgery. But after repeated TPE, the research team performed both the functional and immunoassays on the patient again and this time observed strikingly different results.

"We were surprised to see that levels of HIT antibodies in this patient fell very quickly according to the functional assay, yet the antibodies detected by the immunoassay remained high," said lead study author Theodore Warkentin, MD, of McMaster University in Canada. "This suggested to us that while physicians in many situations may be waiting for the immunoassay to indicate lower antibody levels, patients in urgent need of heart surgery may be ready much earlier than the results suggest."

To better understand the dissociation observed between results of the two tests, Dr. Warkentin's team developed a model comparing functional and immunoassay results among 15 HIT blood samples, which were sequentially diluted and tested with both assays to mimic the effects of

repeated TPE. The researchers observed that HIT antibody levels as measured by the functional assay decreased rather quickly, while the immunoassay continued to indicate high levels.

This evaluation suggests that the sensitivity of the immunoassay may provide an overly conservative estimate of HIT antibody levels in patients and their clinical relevance. The analysis illustrates how quickly platelet-activating properties can decline in a patient, either naturally or by using TPE. The observations also support the use of repeated TPE as a therapeutic strategy prior to planned heparin re-exposure among patients with a recent HIT episode who require urgent cardiac surgery.

"Based on these findings, physicians should consider utilizing both of these tests when preparing a patient with a history of HIT for urgent heart surgery, considering the functional assay result as the stronger indicator of a patient's readiness," said Dr. Warkentin. "For these patients, TPE can be a useful option to help rapidly reduce their remaining HIT antibody levels, minimize their risk of developing clots, and get them into the operating room sooner."

More information: *Blood*, www.bloodjournal.org/content/e … blood-2014-07-590844

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