Management of Heparin-induced Thrombocytopenia (HIT) cases

Case reports on HIT in extracorporeal circulation have become common recently. Therefore, please refer to the following suggestions to enhance basic knowledge about HIT so that it can lead to safe extracorporeal circulation.

【What is HIT?】

Heparin-induced thrombocytopenia (HIT) is a condition in which the anticoagulant drug heparin induces thromboembolism through an immunological mechanism. Patient who develops HIT rarely show bleeding tendeny and have a high rate of thromboembolism, with a moratility rate from thrombosis of approximately 5%.

【Classification of HIT】

Type I: Thorombocytopenia occurs as a result of mild platelet aggregation due to heparin. Mild thrombocytopenia occurs one to two days after heparin administration, but there are no clinical symptoms or thrombotic complications, and platelet counts recover spontaneously.

Type II: Thrombocytopenia occurs due to transient activation of platelets by heparin-dependent autoantibodies. Serious complications are caused.

【Classification by time of onset】

Typical-Onset: Usually occurs between 5 and 14 days after heparin administration, as it takes at least 4 days from heparin administration for antibodies to be produced in both first-time heparin administered patients and those who have been previously administered heparin.

Delayed-Onset: Symptoms develop within a few days to 3 weeks after heparin administration is stopped.

Rapid-Onset : If heparin is re-administered to a patient who has retained antibodies from the most recent heparin administration (within at least 100 days), the onset of symptoms will be rapid within 1 day.

Spontanesous : Rare cases with patients without a history of heparin administration, who retain HIT antibodies with strong activating potential, develop symptoms after the first heparin administration.

【Diagnosis】

Clinical Diagnosis

It is defined that the platelet count before heparin administration decreases to 50% or less during or after administration of heparin, and that there are no other causes for the decrease in platelet count other than drugs, DIC, MOF and severe infections. Postoperative cases are strongly suspected when there is a decrease of 50% or more from the peak of postoperative platelet recovery by day 14.

Serological Diagnosis

Measurement methods include **immunoassay** and **functional assay**.

① **Immunoassay**

The amount of anti-PF4/heparin antibodies in patient plasma can be measured by enzyme-linked immunoassay (e.g., ELISA), lates agglutination, or chemical-issue immunoassay. It has been reported that a negative result can rule out HIT 99% of the time. However, this method should be used with caution because it has low specificity and false positives are common.

②**Functional Assay**

This method measures the ability of anti-PF4/heparin antibodies to strongly activate platelets, allowing for an accurate diagnosis of HIT.

【Points to note】

1. In Japan, cardiopulmonary management with anticoagulants other than heparin has not been established for cardiovasular surgery.
2. Transducers for blood pressure monitoring and heparinized saline solution for cell salvage devices are also not available.
3. In Japan, only "Argatroban" is approved as a substitute for heparin.
4. Heparin coated material cannot be used. Prepare cannulas, reservoirs, oxygenators, tubing sets, cardioplegia circuits, connectors, etc. that are not coated with heparin.

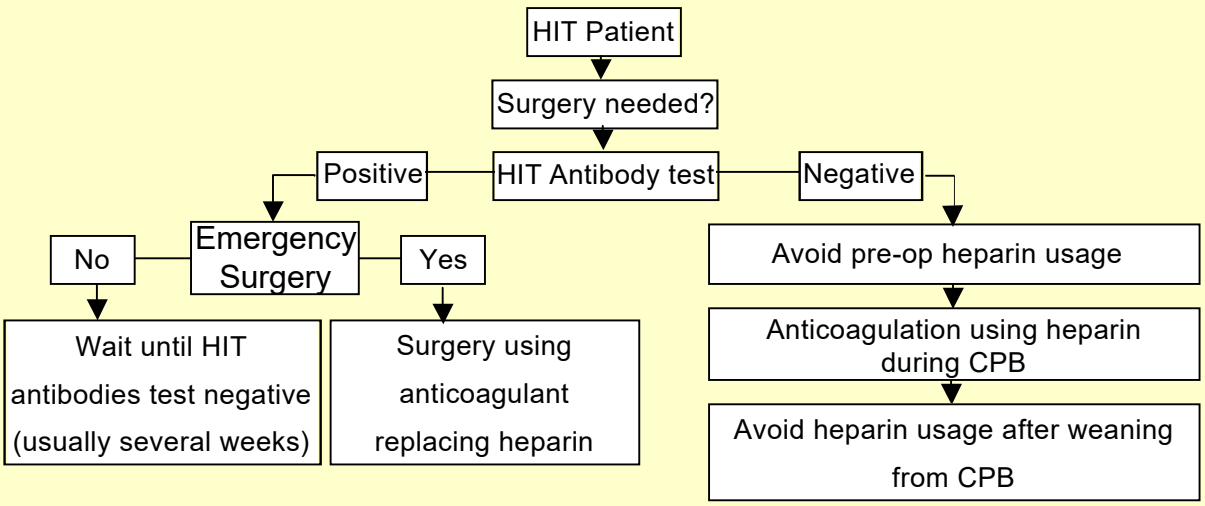
Point 1

In Japan, if a patient with a history of HIT needs surgery requiring cardiopulmonary bypass:

- Wait as long as possible for antibodies to become negative (negative by functional assay and weakly positive by immunoassay)
- If functional assay becomes negative, perform surgery with heparin during cardiopulmonary bypass, discontinue after weaning, and administer selective antithrombins postoperatively if necessary

Before embarking on cardiopulmonary management with argatroban, reconfirm whether the diagnosis of HIT is correct and discuss again with the physician whether or not the patient can wait until HIT antibodies become negative.

In addition, if HIT is suspected during surgery, attempt to wean the patient from cardiopulmonary bypass if possible, and consider using argatroban if it is not possible.



Algorithm for selection of anticoagulation therapy for surgery with cardiopulmonary bypass in patients with HIT

Point 2

Points to note when using argatroban in cardiopulmonary bypass:

- It is recommended to use cardiotomy reservoir.
- Be prepared to change out oxygenators, filter, etc., as they may clot.
- Continuous administration to the circuit is necessary, and the site of administration should be carefully considered.
- Start the suction of cardiopulmonary bypass after the ACT is sufficiently prolonged.
- The dosage of argatroban should be determined in consultation with the physician.
- Considering the half-life of argatroban (40 to 50 minutes), ACT measurements should always be performed every 15 to 30 minutes. If possible, APTT should also be measured.
- Unlike heparin, argatroban does not have an antagonist, so care must also be taken to avoid overdosing.
- Perform frequent ACT measurements after cardiopulmonary bypass.

Supervision:
Dr. Shigeki Miyata
Division of Transfusion Medicine
National Cerebral and Cardiovascular Center