



EUROPEAN
HEMATOLOGY
ASSOCIATION

EHA-TSH Hematology Tutorial on Immune Hematological Disorders

Self-assessment Case – Heparin Induced Thrombocytopenia

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Introduction

- A 52-year-old male patient with acute myocardial infarction due to multivessel disease has underwent coronary artery bypass surgery.
- Graft occlusion after 6 days
- Hematology consultation was required.



Whole Blood Count

On the 6th day of post operation:

- WBC $8.7 \times 10^9/l$
- RBC $5.3 \times 10^{12}/l$
- Hb 13,6 g/l
- Hct 0.44 l/l
- MCV 88.2 fl
- Platelet count $51 \times 10^9/l$ (Before operation: $245 \times 10^9/l$)
- MPV 11 fl

- History: acute myocardial infarction 2 years ago, right coronary artery total occlusion, recanalized and rapamycin eluting stent was placed.
- Current treatment: clopidogrel (stopped 2 days), standard heparin (therapeutic dose)

Q1) Which of the following may be a risk for HIT?

1. Male gender
2. Surgery
3. Age <60 years
4. Increased MPV
5. Clopidogrel use



Probability Score

- **T**hrombocytopenia: 2 points
- **T**iming: 2 points
- **T**hrombosis: progressive or recurrent: 1 points
- **O**ther: None apparent: 2 points

Q2) What is the most likely diagnosis?

1. Type I HIT
2. Delayed-onset HIT
3. Disseminated intravascular coagulation
4. Immune thrombocytopenia
5. Type II HIT

Type I and II HIT

	Type I	Type II
Timing of onset after start of heparin	1-4 days	5-10 days
Platelet count (nadir)	100 x10 ⁹ /l	Usually >20 x10 ⁹ /l median nadir 60 x10 ⁹ /l
Antibody mediated?	No	Yes
Thromboembolic event/sequeale	No	30-80%
Management	Observe	Stop heparin and anticoagulate with a nonheparin drug



Initial Management

- Heparin was stopped
- A non-heparin anticoagulant was considered
- PF4-heparin ELISA test was requested



Further Evaluation

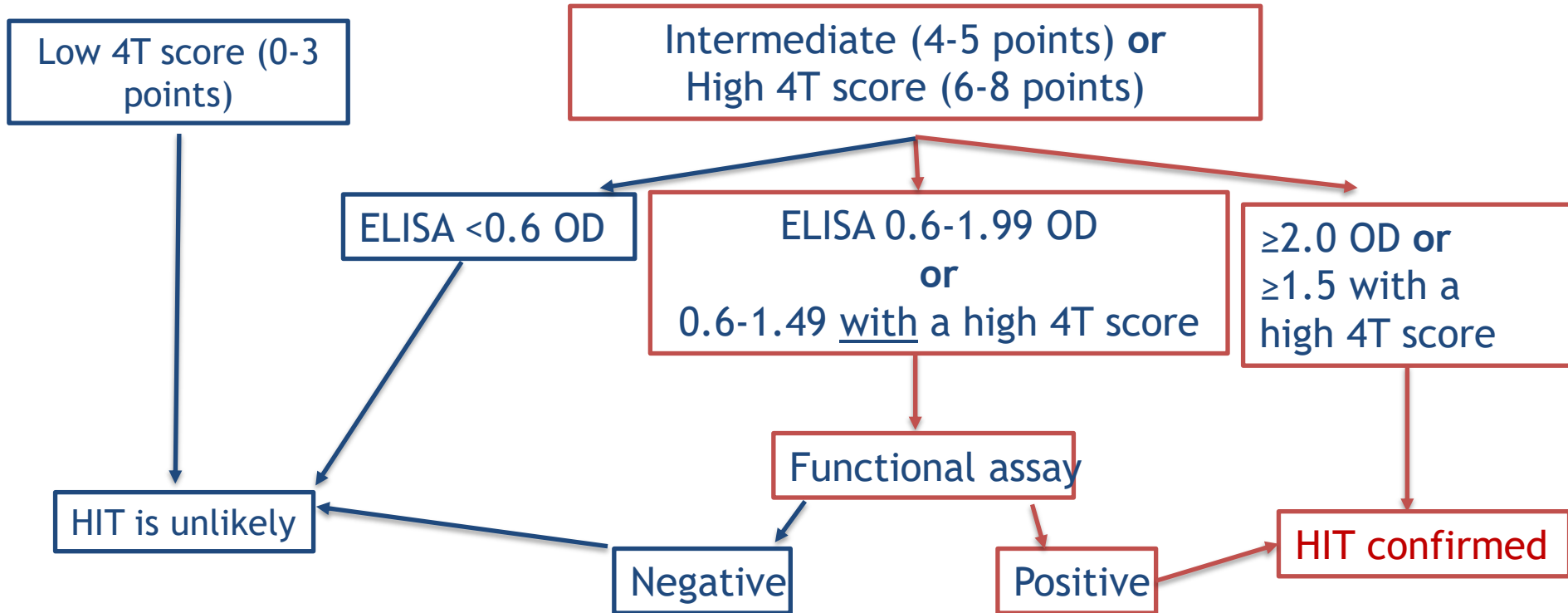
- PF4-Heparin ELISA (Immunoassay): 1,0 OD

*OD: Optical Density

Q3) What is the most probable diagnosis?

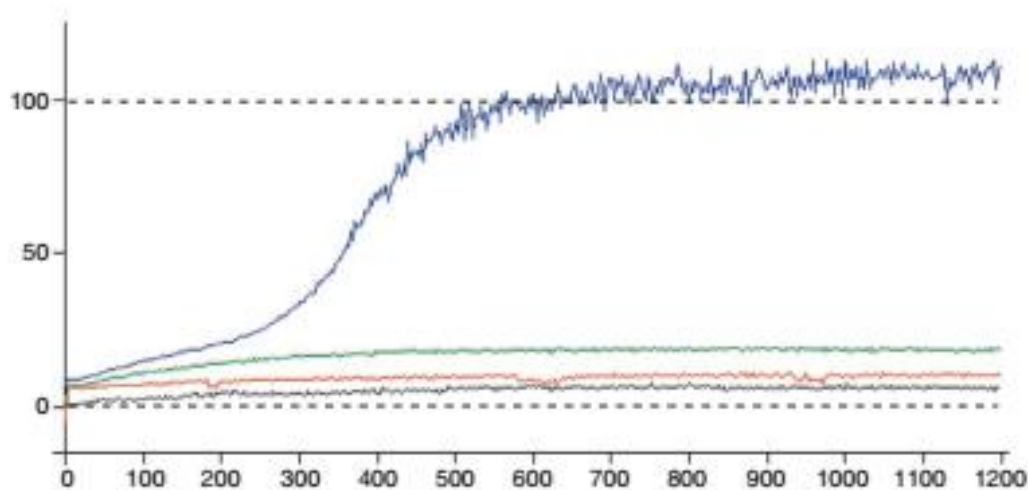
1. Low 4T score, low ELISA OD: HIT diagnosis is ruled out
2. High 4T score, high ELISA OD: HIT diagnosis is confirmed
3. Intermediate 4T score, intermediate ELISA OD: go to functional assay
4. Intermediate 4T score, high ELISA OD: HIT diagnosis is confirmed
5. High 4T Score, intermediate ELISA OD: Go to functional assay

Interpretation of HIT antibodies with 4Ts score



Functional Assay

- Heparin-induced platelet activation (HIPA) was positive



Q4) What may be the choice for initial anticoagulation?

1. Low molecular weight heparin
2. Acetylsalicylic acid
3. Clopidogrel
4. Warfarin
5. Argatroban



Course of disease

- The patient was scanned for lower extremity deep vein thrombosis and a left popliteal vein thrombosis was detected.

Q5) What should be the duration of anticoagulation?

1. 3 weeks
2. 6 weeks
3. Until platelet normalization
4. 1 month
5. 3 months



Follow-up

- On the seventh day of heparin withdrawal, platelet count: $55 \times 10^9/l$

Q6) What is the wisest course of action?

1. Re test for PF4 heparin antibodies
2. Re test for HIPA
3. Request serotonin release assay
4. Request PF4 dependent P-selectin expression assay
5. Confirm with blood smear and confirm heparin withdrawal. Look for additional reasons



Discussion

Q1: Risk factors for HIT include surgery, use of unfractionated heparin, heparin dose, female sex and aging.

Q2: Type I HIT is a mild and transient condition occurring in the first 2 days of exposure

Q3: For high probability 4T score and PF4 heparin ELISA between 0.6 and 1.49 OD, functional assays are recommended.

Q4: Warfarin should be avoided for initial anticoagulation. Direct thrombin inhibitors or a DOAC may be commenced.

Q5: For patients with documented venous thromboembolism, 3 months of anticoagulation is recommended.

Q6: Platelet recovery is generally observed within 7 days, but delayed responses may be observed due to persistent HIT antibodies or even heparin exposure.



References

1. Dacie and Lewis Practical Haematology 12th Edition, 2017 Elsevier
2. Cuker A, Arepally GM, Chong BH, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia. *Blood Adv.* 2018 Nov 27;2(22):3360-3392.
3. Linkins LA, Dans AL, Moores LK, et al. Treatment and prevention of heparin-induced thrombocytopenia: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012 Feb;141(2 Suppl):e495S-e530S.
4. Lo GK, Juhl D, Warkentin TE, et al. Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. *J Thromb Haemost* 2006; 4:759



Probability Score

Category	2 points	1 point	0 point
Thrombocytopenia	>50% fall or Nadir $\geq 20 \times 10^9/l$	30-50% fall or Nadir $10-19 \times 10^9/l$	<30% fall or Nadir $< 10 \times 10^9/l$
Timing of thrombocytopenia or other events	Clear onset between days 5-10 and <1 day if previous heparin exposure in last 30 days	Onset after day 10 or day <1 if previous heparin exposure in last 30-100 days	Onset <4 days from the start of heparin with no recent exposure
Thrombosis or other events (eg skin)	New thrombosis	Progressive or recurrent thrombosis OR suspected but not yet proven thrombosis	None
Other cause for thrombocytopenia	Not other cause	Possible other cause	Definite other cause