Heparin-induced thrombocytopenia without thrombocytopenia in an intensive care unit
Thrombopénie induite par l’héparine sans thrombopénie vraie dans une réanimation

Heparin-induced thrombocytopenia (HIT) is a side effect of heparin therapy, mediated by PF4 antibodies to heparin. It is associated with the risk of multiple arterial and venous thromboses, and a high morbidity and mortality. Indeed, the lack of recognition of HIT and the lack or the delay in treatment interruption can lead to serious consequences [1]. A 56-year-old man was admitted to our intensive care unit on January 4, 2011, for complete left hemiplegia and impaired consciousness. A CT scan of his brain showed a right capsulolenticular hemorrhagic stroke, with some blood in the right lateral ventricle, causing a midline shift. He was receiving aspirin for peripheral arterial disease and was treated for severe hypertension. Excessive consumption of alcohol was noted, as well as active smoking. The patient had to be intubated, ventilated, sedated and a monitoring of his intracranial pressure was initiated on January 5, 2011. The platelet count was 310,000/mm³ before any heparin therapy (table 1). A left subclavian venous access was implemented. On January 7, 2011, a severe pneumococcal pneumonia was diagnosed, requiring intravenous antibiotics.

On the same day, a central catheter thrombosis was diagnosed. Treatment with intravenous heparin was started, and the catheter was withdrawn. A right internal jugular vein (IJV) catheter was then introduced on January 9th. The platelet count was 195,000/mm³ the day of left subclavian catheter removal. Again, a right IJV catheter thrombosis occurred on January 22nd, under effective heparin therapy, prompting the withdrawal of the material. On February 11th, a CT scan was performed. It highlighted a massive thrombosis of the left femoral and iliac veins. A bilateral pulmonary embolism was also diagnosed. A permanent filter was then placed into the inferior vena cava on February 16, 2011, to avoid further pulmonary embolisms (table 1).

In the presence of these multiple venous thrombosis, occurring under well-conducted anticoagulant therapy with intravenous heparin then LMWH, anti-heparin-induced thrombocytopenia (HIT) antibodies were sought, despite the absence of thrombocytopenia.

Références

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### Table I

**Sequence of events**

<table>
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<tr>
<th>Date</th>
<th>January 5th</th>
<th>January 7th</th>
<th>January 9th</th>
<th>January 18th</th>
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<th>January 31th</th>
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<td>0</td>
<td>Intravenous heparin, day 1</td>
<td>Heparin, day 3</td>
<td>Heparin, day 12</td>
<td>Heparin, day 17</td>
<td>Intravenous heparin, day 25</td>
<td>Heparin: stop LMWH Day 1</td>
<td>LMWH: Stop Danaparoid, day 1</td>
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<td>Platelet count per mm$^3$</td>
<td>310,000</td>
<td>195,000</td>
<td>224,000</td>
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<td>Mutation of the prothrombin gene: absence</td>
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<td>PF4 antibodies</td>
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Pending the outcome of the assays, which came back positive for anti-PF4 (DiaMed Kit®), anticoagulation with Danaparoid was initiated. Subsequently, a relay with VKA was conducted. The patient was discharged to a rehabilitation center on March 17th, with a left arm monoplegia only. 

In patients who did not receive heparin within 100 days, the onset of symptoms associated with HIT usually occurs between 5–10 days after starting the treatment (seroconversion and early fall of platelets count) and 7 to 14 days (thrombocytopenia peak). The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy recommends to exclude HIT in patients receiving heparin, or who have received heparin within the previous 2 weeks when the platelet count falls by 50% or more, and/or when a thrombotic event occurs, between days 4 to 14 following initiation of heparin, even if the patient is no longer receiving heparin therapy when thrombosis or thrombocytopenia have occurred (Grade 1C) [1].

In our case, many thrombotic events were observed between the 25th day and 34th day of treatment with UFH and LMWH. There was a 38% fall in platelet count between the day 12 and the day 17 of UFH, without thrombocytopenia. However, the diagnosis of HIT has been raised a few days later, because of additional thrombotic complications. Of note, the patient was treated for a severe infectious event, causing an inflammatory state and probably a thrombocytosis which likely masked the thrombocytopenia. Here we could have been objected the absence of a confirmatory test. However, the combination of multiple and extensive thrombosis under well-conducted anticoagulant therapy, with a high pre-test probability (the 4T’s scoring) and the positivity of antibodies to macromolecular platelet factor 4-heparin complexes on the immunodiffusion test (DiaMed Kit®), made the diagnosis of HIT very likely.

Our patient’s 4T’s score [2] was indeed high and declined as follows: 1 (30–50% platelet fall) + 1 (Platelet fall occurring after the day 10 of treatment) + 2 (New thrombosis) + 2 (No other evident cause) = 6.

In addition, it seems that performing a confirmatory test increases the costs of care but does not always improve diagnostic specificity [3].

In conclusion, in patients receiving UFH or LMWH in intensive care units as in the postoperative setting [4], a pro-inflammatory state is frequent and may mask thrombocytopenia. Furthermore, relative thrombocytopenia may occur after 10 days of treatment. Hence, HIT should be sought on clinical criteria in association with PF4 antibodies determination, even in the absence of thrombocytopenia, to avoid severe HIT complications. The 4T’s scoring system is a helpful tool.

Disclosure of interest: The authors declare that they have no conflicts of interest concerning this article.

References


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Isolated camptocormia revealing sporadic late onset nemaline myopathy

Camptocormie isolée révélant une myopathie à bâtonnets tardive

Camptocormia is an abnormal posture with marked flexion of thoracolumbar spine that abates in the recumbent position. Causes of camptocormia include neurological disorders, psychogenic origin and idiopathic camptocormia [1–3]. Sporadic...