

## Reference

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## How to improve the management of a patient with heparin-induced thrombocytopenia?

To the Editor,

Heparin-induced thrombocytopenia (HIT) is an adverse drug reaction caused by immunoglobulin G platelet-activating antibodies against platelet factor 4 (PF4)/heparin complexes, leading to venous and arterial thromboembolism (1). I read with keen interest the case report describing a fatal case of probable HIT in a young man who experienced pulmonary embolism (PE) and concomitant deep vein thrombosis (2). The case of this patient with intracardiac thrombus formation and severe ischemic stroke highlights the high risk of thromboembolic events in patients with HIT despite anticoagulant treatment with fondaparinux (5 mg/d), which was ineffective in case of the patient even when the platelet count increased to 150.000/uL. However, without any description of the patient's weight, it remains unclear whether the dosage of fondaparinux was appropriate. The use of vitamin K antagonist (VKA) after normalization of the platelet count, along with the administration of low-molecular-weight heparins or non-VKA oral anticoagulants immediately after the diagnosis of PE in a hemodynamically stable patient could lower the risk of HIT development and significantly improve the prognosis (1, 3). The rationale for choosing unfractionated heparin (UFH), the most common cause of HIT, in the patient was not presented.

In 2018, we had reported our experience with the diagnosis and management of patients suspected of having HIT (4). We have also observed a male patient with PE who was heterozygous for factor V Leiden, as in the present case; was receiving UFH; and was found to have intracardiac thrombi at diagnosis; however, fondaparinux (7.5 mg/d) was effective in that patient (Undas unpublished data). A major limitation of this report is the lack of laboratory confirmation of HIT. On the basis of our experience, we consider that the most commonly used anti-PF4/heparin antibody enzyme immunoassays can frequently detect clinically irrelevant antibodies, with a risk of

overdiagnosis. However, a high OD value above 2 well correlates with the positive results of specific assays, e.g., a platelet serotonin-release assay, and such assays can be used in low-income countries such as Poland and Turkey (1, 4). Considering other strong prothrombotic factors, authors did not present conclusive evidence for the absence of occult cancer, which might contribute to the resistance to the anticoagulant used (5). Autopsy could clarify such uncertainties. This interesting report supports not using UFH as a first-line therapy in most PE patients and treating PE vigorously to prevent life-threatening thrombotic events, including HIT, especially in young patients without serious comorbidities.

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## Author's Reply

To the Editor,

We would like to thank the authors for their interest in our article titled "Mitral valve and right ventricular thrombi possibly caused by heparin-induced thrombocytopenia" and for taking

time to express their opinions (1). In the authors' letter to the editor, they mention potential concerns with the diagnosis and management of HIT.

Anticoagulation is the cornerstone of treatment for acute pulmonary embolism (PE). Unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), and fondaparinux are the main options as anticoagulants in the treatment of acute PE. We totally agree with the authors. Both 2014 and 2019 ESC Guidelines on the diagnosis and management of acute PE recommend that if anticoagulation is parenterally initiated, LMWH or fondaparinux should be used in most patients (Class I-A) (2, 3). However, it is important to note that the use of UFH in the treatment of low-to-moderate PE patients is not contraindicated.

Fondaparinux is an anticoagulant pentasaccharide that specifically inhibits activated factor X. Major cardiovascular guidelines regarding acute PE recommend fondaparinux as one of the first-line treatment options in low- to moderate-risk patients (3). Moreover, a recent study has indicated that fondaparinux has efficacy and safety equivalent to those of argatroban and danaparoid in patients with suspected heparin-induced thrombocytopenia (HIT) (4). On the basis of these recommendations, fondaparinux is subcutaneously administered at a dose of 5 mg per day in patients weighing <50 kg (our patient weighed 48 kg).

In the case report, we have mentioned that a detailed evaluation of the patient for the presence of cancer was performed by an oncologist. Malignancy markers were negative, and positron emission tomography/computed tomography (CT) and whole-body CT were evaluated in detail. Moreover, in this case report, we specifically mentioned the necessity of platelet function test or serological tests for confirming the diagnosis of HIT. This is the major limitation of our case report.

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