

Dermatan sulphate for heparin-induced thrombocytopenia and cvc-related deep vein thrombosis in a child with all

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Heparin-induced thrombocytopenia (HIT) type II is an immune-mediated thrombocytopenia, not uncommonly complicated by arterial and venous thromboembolic events.^{1,2} HIT can be classified in two types: HIT type I is a common non-immunologic mild thrombocytopenia of minor clinical significance whereas HIT type II is an immune-mediated thrombocytopenia. HIT type II is caused by platelet aggregation promoted by IgG antibodies against the complex heparin-platelet factor 4. This complex is able to interact with the Fc receptor on the platelet surface leading to platelet aggregation.² The incidence of clinically overt HIT type II in adults is 2.7%, but serum heparin-induced IgG antibodies are found in 7.8% of the patients treated with heparin.³ Information on HIT type II in children are quite limited and essentially based on case reports.^{4,5,6,7,8} In patients with thrombosis and HIT type II, heparin should be discontinued and an alternative anticoagulation strategy is required. A number of pharmacological agents have been evaluated, but there is no consensus about the optimal management strategy. No data are available on the treatment of HIT type II in children. Dermatan sulphate (DS, Mediolanum Farmaceutici, Milan, Italy), a natural glycosaminoglycan acting on the clotting system through heparin cofactor II, has been successfully evaluated in adults with thromboembolic disease who developed HIT type II.⁹⁻¹⁰ We report the first case of HIT type II treated with DS in a child. To a 6 year-old girl affected by common ALL was inserted a percutaneous subclavian central venous catheter (CVC) immediately after diagnosis and prior to chemotherapy. Approximately one month after the insertion of the CVC, the patient presented swollen right upper limb and was admitted to the hospital. Physical examination confirmed a swollen right upper limb and showed a collateral vein circulation. Compressive ultrasonography, immediately performed, did show a venous thrombosis of the omeral, axillary subclavian veins of the right arm. Unfractionated heparin (UH) treatment was immediately started by an intravenous infusion (starting with 10.000 U/24h then adjusting the dose to maintain an aPTT to 1.5 time than normal value). Before UH administration, the platelet count was $151 \times 10^9/L$. After five days of UH therapy, platelet count fell to $33 \times 10^9/L$. UH was stopped and replaced by the LMWH, enoxaparin, 2.000 U t.i.d. and CVC was removed. Two days after enoxaparin administration, platelet count was $22 \times 10^9/L$. An aggregation test confirmed platelet reactivity with UH and showed cross-reactivity with three LMWH, including enoxaparin but not with DS. This agent was started immediately as a continuous intravenous infusion of 15 mg/kg/day and was continued for 17 days at the same dose, targeting an aPTT ratio of 1.5. Anticoagulation with DS was very stable and minor dose adjustments were required. Platelet count began to recover on day 5 and increased up to $181 \times 10^9/L$ in few days. No bleeding or other side effects were observed. Serial testing with compression ultrasonography reveals the recanalization of the subclavian vein after about one month. In conclusion, in this child with HIT type II DS was effective in providing a safe anticoagulation and prompted a recovery of the platelet count. This agent should be considered in patients, including children, with thrombosis and HIT type II, in the presence of a cross-reactivity to LMWH.

Figure 1. Time course of platelet count before and after treatment with dermatan sulphate: UFH: unfractionated heparin, LMWH: low molecular weight heparin (enoxaparin), DS: dermatan sulphate.

Melina Verso*, Ida Mazzarino°, Giancarlo Agnelli*, Maurizio Siefanelli °, Stefania Ceppi °, Francesco Paoletti ^.

*Sezione di Medicina Interna e Cardiovascolare, Dipartimento di Medicina Interna, Università di Perugia, °Divisione di Oncologia Ematologica Pediatrica, Ospedale R. Silvestrini, ^Sezione di Anestesia, Analgesia e Terapia Intensiva, Dipartimento di Medicina Clinica e Sperimentale, Università di Perugia; Perugia.

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Correspondence: Melina Verso & Prof. Giancarlo Agnelli

Sezione di Medicina Interna e Cardiovascolare
Dipartimento di Medicina Interna Università di Perugia,
06123 Perugia, Italy

Phone: + 39. 075.5783395 Fax: +39. 075.5733642 or 5722011

E-mail: agnellig@unipg.it

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