BACKGROUND

Heparin-induced thrombocytopenia (HIT) can develop if immune responses to infections become pathologic in the presence of heparins. Low molecular weight heparin or unfractionated heparin are recommended for prophylaxis and treatment of venous thromboembolic disease in hospitalized patients with Covid-19 infection but may trigger HIT.

CASE REPORT

A 33-year-old previously healthy male was initially evaluated for low grade fever, dyspnea without cough or hypoxia. A Covid-19 PCR swab was negative despite a recent exposure. He was treated with azithromycin. However, his symptoms did not improve, he then developed right leg swelling and hypoxia, so he was re-evaluated. CTA of the chest showed bilateral pulmonary emboli and ground-glass opacities at the lung bases. Venous Duplex Ultrasound showed non-occlusive thrombus in the deep veins of right lower extremity. He was hospitalized and placed on oxygen and heparin. Covid-19 swab was negative again. Laboratory tests before heparin showed a decreased platelet count of 64,000 k/ul, elevated prothrombin time of 16.4 seconds, normal aPTT at 30.8 seconds, decreased serum fibrinogen at 120 mg/dl and markedly elevated D-dimer at 59,966 ng/ml. Lupus anticoagulant and anti- phospholipid antibody tests were negative. On heparin at the desired therapeutic aPTT target range, the right leg became significantly swollen and painful by day five. Platelet count had decreased further to 39,000 k/ul. Repeat doppler examination of the right leg now showed more severe and extensive deep venous thrombosis. D-dimer had increased to 125,133 ng/ml. The HIT 4T score was 4, suggesting intermediate probability. Rapid HIT immunoassays on 2 separate samples were positive. Heparin was discontinued and he was placed on argatroban. Serotonin release assay came back positive. Suspicion for Covid-19 infection remained high and so a Covid-19 serology sample was obtained which was positive for IgG. He did not receive any COVID specific treatments. As viability of his leg appeared threatened, he underwent right iliofemoral vein thrombectomy with arteriovenous fistula creation. He improved on argatroban and was transitioned to apixaban with aPTTtarget range, the right leg became significantly swollen and painful by day five.

OBJECTIVE

Our aim is to alert clinicians that HIT occurs in association with Covid-19 infections even in the absence of prior exposure and may not be easily recognized without a high index of suspicion.

To learn more about the connection between infection and HIT

To learn if HIT is truly a heparin and infection induced phenomenon or response to any negatively charged polysaccharide

To review the report of unusual thrombotic events along with thrombocytopenia that developed after vaccination with recombinant adenoviral vector encoding the spike protein antigen of COVID 19 Virus

PATHOGENESIS

Yves Gruel, Hervé Watier, Bacteria and HIT: a close connection?, Blood, 2011

DISCUSSION

Current consensus guidelines for thromboprophylaxis and treatment of thromboembolism in hospitalized patients with Covid-19 infection recommend heparins as primary therapy to reduce morbidity and mortality. Heparin has also been recently demonstrated to tightly bind Covid-19 virus and could act as decoy molecule to neutralize the virus providing additional rationale for heparins to be the preferred anti-thrombotic agents in this clinical setting. However, our report in addition to the two previous reports of HIT in Covid-19 patients illustrate that HIT can be a complication in the setting of Covid-19 infection. Further, our report also highlights that HIT with thrombosis can occur in a spontaneous manner in the absence of prior heparin exposure, which has been so far studied only in bacterial infection with the hypothesis that Platelet factor 4 (PF4) can bind to negatively charged polysaccharides on the surface of bacteria, triggering an immune response. There has been a report of case series of 11 patients of vaccination induced immune thrombotic thrombocytopenia mediated by PF4 antibodies clinically mimicking autoimmune HIT.

REFERENCES