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Case Report

Heparin-induced anaphylactoid reaction associated with heparin-induced thrombocytopenia in the ED

Abstract

Although rare, heparin-induced anaphylactic and anaphylactoid reactions have been previously described in the literature. We present a case of a patient who presented to the emergency department with dyspnea and was subsequently diagnosed with an acute pulmonary venous thromboembolism. Shortly after being started on intravenous unfractionated heparin, she developed sudden cardiovascular collapse leading to a cardiopulmonary arrest. She was successfully resuscitated and, after further diagnostic evaluation, was found to have developed a heparin-induced anaphylactoid reaction.

A 56-year-old woman presented to the emergency department (ED) with 4 days of progressive dyspnea. Fourteen days before her presentation, she underwent a total abdominal hysterectomy and salpingo-oophorectomy at the same institution, during which time she received 2 days of postoperative porcine subcutaneous heparin (Braun) (Figure). She was discharged on postoperative day 2. She had presented to our ED the day prior with the aforementioned symptoms, and spiral computed tomography (CT) was performed to evaluate for pulmonary embolism (PE). This was initially interpreted as normal; however, the patient was called back for reassessment after a subsequent overread identified a lingular segmental PE.

The patient's medical history was significant only for hypertension, uterine fibroids, and her recent surgical procedure as well as prior cesarean section, loop electrosurgical excision procedure (LEEP), and facial surgery. She was a former smoker, used alcohol occasionally, and denied the use of any illicit drugs.

Vital signs on presentation to the ED included the following: blood pressure of 135/76, heart rate of 69, respiratory rate of 18, temperature of 35.7°C, and oxygen saturation of 99% on room air. She was awake and alert and in no distress, with an unremarkable physical examination. Workup in the ED included serial cardiac enzymes, serial electrocardiograms and a chest x-ray, all of which were negative. With the diagnosis of segmental pulmonary embolism, a heparin bolus and drip were started as per hospital protocol.

Approximately 5 minutes after beginning the infusion, the patient became acutely flushed with rapidly worsening dyspnea. Systolic blood pressure dropped to the 90s from 120s, although her heart rate remained within normal limits. The heparin was immediately discontinued; however, she developed agonal respirations and went into cardiorespiratory arrest. Advanced cardiac life support was started, and rapid sequence intubation was performed with subsequent return of spontaneous circulation. The patient's blood pressure was maintained with epinephrine, dopamine, and norepinephrine drips. A repeat chest CT scan demonstrated the previously identified lingular PE, and a head CT was negative for intracranial hemorrhage. Cardiology was consulted for a formal echocardiogram that was

negative for right heart strain or focal wall motion abnormalities. Blood pressure normalized, and the vasopressors were weaned off.

Repeat laboratory results were significant for a drop in platelets from $367 \times 10^9/L$ on ED presentation to $57 \times 10^9/L$ shortly after heparin administration. The patient was started on argatroban and admitted to the intensive care unit (ICU). Enzyme-linked immunosorbent assay and serotonin release assay confirmed the presence of heparin antibody shortly after ICU admission, and she was diagnosed as having had a heparin-induced anaphylactoid reaction associated with thrombocytopenia. She was successfully extubated on day 1 of admission and was discharged after conversion from argatroban to warfarin on hospital day 8. Her platelet count had increased to $358 \times 10^9/L$ on the day of discharge. Review of the patient's platelet levels during her previous hospital stay revealed only 1 measurement of $137 \times 10^9/L$ on postoperative day 1.

Heparin-induced thrombocytopenia (HIT) is an immunoglobulin G-mediated humoral immune response targeted against complexes formed by heparin and platelet factor 4. Upon re-exposure to heparin, heparin/platelet factor 4 complexes are bound by immunoglobulin G with resultant platelet and diffuse inflammatory cell activation [1–3]. This explains the wide spectrum of clinical manifestations seen in heparin re-exposure in the context of HIT. Heparin-induced thrombocytopenia has been documented presenting as arterial and/or venous thrombosis, necrotizing skin lesions at heparin injection sites, and disseminated intravascular coagulation; however thrombocytopenia is the most common clinical manifestation [4]. In addition, soon after the re-exposure to heparin, a small subset of these patients go on to develop anaphylactoid reactions, which can involve multiple systems and display symptoms/signs ranging from fever, flushing, and chills to cardiopulmonary arrest [5–10].

We present a patient who developed an HIT-associated anaphylactoid reaction after heparin administration in the ED. The patient had recently been discharged after being hospitalized for a surgical procedure for which she received 2 days of postoperative heparin prophylaxis and was found to have a pulmonary embolus 14 days later after presenting to the ED with dyspnea. Her presentation is similar to previous case reports of HIT anaphylactoid reactions seen in the inpatient setting. Warkentin and Greinacher [11] describe these patients as lacking classic features of anaphylaxis (eg, urticaria, angioedema, and laryngeal edema) and demonstrating fever, rigors, transient global amnesia, and/or cardiopulmonary arrest. Most of these patients likely would have had a previous exposure to heparin 1 to 4 weeks before the exposure that led to their anaphylactoid event and have later blood samples positive for HIT antibodies, which peak at about 2 weeks after the immunizing heparin exposure [11]. Our patient had most of these characteristics and, interestingly, also developed transient global amnesia after extubation in the ICU. She eventually recovered all memory function early in her hospital stay.

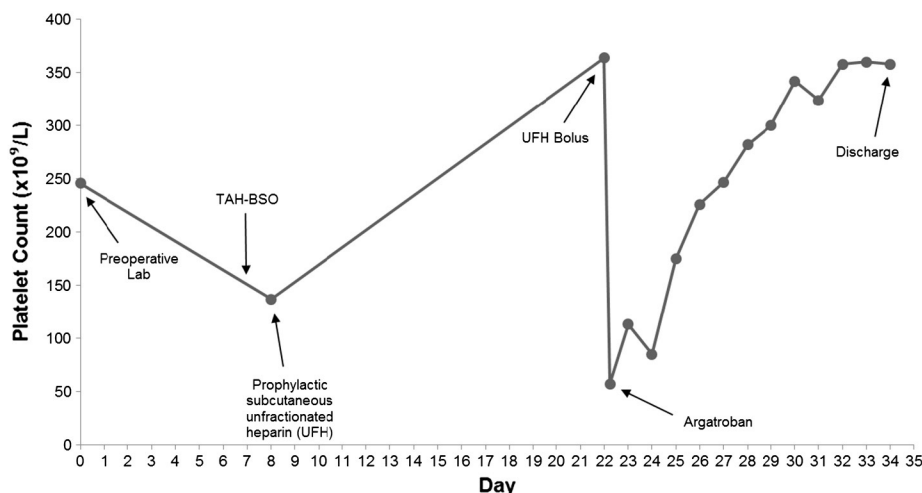


Figure. Platelet counts and events starting from preoperative laboratory results demonstrating normal platelet levels. The patient underwent total abdominal hysterectomy and bilateral oophorectomy (TAH-BSO) on day 7. On day 8, platelet levels were slightly below normal at $137 \times 10^9/L$; however, the patient also was anemic from intraoperative blood loss and was transfused with 1 U of packed red blood cells. No other laboratory results were recorded in the medical record during the rest of her admission. The patient received subcutaneous heparin for deep venous thrombosis prophylaxis on days 8 and 9. On day 22, she was started on an unfractionated heparin bolus and drip after the diagnosis of PE was made in the ED with a platelet drop from $367 \times 10^9/L$ on ED admission to $57 \times 10^9/L$ shortly after the anaphylactoid reaction. Argatroban was initiated before inpatient admission after the discontinuation of heparin. Platelets normalized during the rest of her hospitalization.

Transient global amnesia associated with HIT is rare but well recognized and typically lasts less than 24 hours after cessation of heparin [12]. This case highlights the importance of considering HIT in a patient with recent heparin exposure who presents with complaints related to venous/arterial thrombosis, as it may decrease future morbidity and mortality in similar future patients. Our patient was given a short course of heparin several weeks before her ED presentation for a PE [13–15]; then after re-exposure to heparin, she developed thrombocytopenia and was subsequently found to be heparin antibody positive on laboratory assays, fulfilling the criteria for an HIT diagnosis. In addition, her abrupt cardiopulmonary arrest after heparin administration is consistent with an HIT-associated anaphylactoid reaction [11]. On review of her hospital stay for which she received the heparin several weeks earlier, only 1 platelet level was recorded, which was slightly normal. In retrospect, this would not be enough data to prompt suspicion of HIT during her ED visit upon review of her initial laboratory results. However, HIT should be considered in future patients with similar presentations who present with HIT symptoms such as venous/arterial thrombosis as in our patient or other symptom/signs consistent with HIT coupled with a suspicion of recent heparin exposure. A review of previous platelets levels and confirmation of heparin administration could potentially aid in arousing suspicion enough of HIT to avoid heparin and use alternative anticoagulants. Hopefully, this increased awareness and vigilance would lead to decreased adverse outcomes.

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