Bilateral adrenal hemorrhage due to heparin-induced thrombocytopenia following partial nephrectomy – a case report [version 1; peer review: 3 approved]

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Abstract
Heparin-induced thrombocytopenia (HIT) can cause severe life-threatening events such as bilateral adrenal hemorrhage (BAH). A 48-year-old female developed a pulmonary embolus (PE) following partial nephrectomy. The anticoagulation treatment for her PE was complicated by HIT and subsequent BAH. To the author's knowledge, this is the first reported case of HIT-associated BAH following renal surgery.

Keywords
bilateral adrenal hemorrhage, heparin-induced thrombocytopenia, HIT, partial nephrectomy

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Approval Status

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1. Ryan Smith, University of Virginia Medical Center, Charlottesville, VA, USA

2. Boback Berookhim, Memorial Sloan Kettering Cancer Center, New York, NY, USA

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Any reports and responses or comments on the article can be found at the end of the article.
Case presentation
A 48-year-old Caucasian female with a past medical history of hypothyroidism presented to us with an incidentally discovered 3 cm enhancing right renal mass. Her home medications included levothyroxine and oral contraceptives. She underwent an uncomplicated robotic-assisted laparoscopic right partial nephrectomy. The patient received routine perioperative deep venous thrombosis (DVT) prophylaxis with sequential compression devices, (SCD). On postoperative day (POD) 2, she developed new-onset sinus tachycardia and showed depressed pulse-oximetry readings. As subsequent chest computed tomography (CT) scans demonstrated multiple large pulmonary emboli, she was started immediately on a continuous intravenous unfractionated heparin infusion, titrated to target an activated partial thromboplastin time (aPTT) of 64–97 seconds. The patient was transitioned to therapeutic anticoagulation with low-molecular-weight heparin (LMWH) at 1mg/Kg q12hrs on POD 3 and discharged the next day.

On postoperative day 6, she developed syncope and hypotension and was admitted to the hospital. Work up in the emergency room was remarkable for a hematocrit (HCT) of 19%, and a CT scan demonstrated a bleeding pseudoaneurysm in the nephrectomy bed. She responded to red blood cell transfusion (4 units) and emboliza-

The patient presented to the surgeon’s office on postoperative day 13 with progressive lethargy and subjective fevers. She was normo-
tensive but tachycardic, and was admitted with concern for recur-
rent hemorrhage. Laboratory analysis at that time was remarkable for a leukocytosis to (16,000/µL), thrombocytopenia of 49,000/µL (from a pre-operative value of 234,000/µL), hyponatremia to 125mEq/L (baseline of 139mEq/L) and a relatively normal HCT of 31.7%. CT scan of the adrenal glands demonstrated bilateral adrenal gland enlargement and hyperdensity, consistent with BAH (Figure 1). Within 2 hours of initiating 50 mg intravenous hydrocortisone 8 hours, her pulse decreased from 128 beats per minute (bpm) to 107bpm, and her blood pressure increase from 89/54mmHg 115/63mmHg. A percutaneous supra-renal inferior vena-cava filter (IVCF) was placed by interventional radiology and an argatroban infusion started. The patient underwent careful titration to an outpatient regimen of fludrocortisone, hydrocorti-
sone, and fondaparinux. She was discharged with a platelet count of 141,000/µL and serum sodium of 139mEq/L. After 12 months follow-up, the patient remains on non-heparin anticoagulation and steroid supplementation.

Discussion
Heparin-induced thrombocytopenia is an immune-mediated comp-
lication occurring infrequently following exposure to unfrac-
tioned or low-molecular weight heparin. HIT occurs when a complex between IgG antibodies and heparin-platelet-factor-4 forms. The antibodies activate platelets by binding to the FcVIIa receptor, which results in systemic thrombosis and consumptive thrombocytopenia. With their rich arterial supply and single central vein, the adre-
nal glands are particularly susceptible to congestive hemorrhage following venous thrombosis. Adrenal hemorrhage associated with HIT tends to be bilateral, resulting in severe clinical manifestations from abdominal pain, fever and lethargy, to catastrophic hemody-
namic collapse. In the post-surgical patient, these symptoms can be confused with more common complications, such as sepsis or hemorrhage. As undiagnosed cases tend to be fatal, a prompt rec-
ognition is crucial.

Few cases of HIT-associated BAH have been previously described in the literature. Approximately 90% of the patients are post-
surgical, with the most common operations being orthopedic. HIT may be an important cause of BAH, accounting for up to 10% of the cases. To our knowledge, this is the first reported case of HIT-associated BAH following partial nephrectomy in particular, or uro-
logic surgery in general. Our case highlights two critical points; 1) the diagnostic complexity of HIT-associated BAH, and 2) the possibil-
ity of a successful clinical outcome when rapid diagnosis is made.

Consent
Written informed consent for publication of clinical details was obtained from the patient.

Author contributions
Ashley Winter performed the case research and wrote the initial manuscript draft.
Ranjith Ramasamy performed manuscript edits and review.

Competing interests
No competing interests were disclosed.
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References


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The paper highlights a relatively uncommon complication which could easily be overlooked if no thought is given to it.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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Boback Berookhim
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The authors provide a report of an interesting clinical situation following robotic assisted partial nephrectomy. The difficulties of diagnosis and non-specific presentation of potentially life-threatening bilateral adrenal hemorrhage in a patient with previously diagnosed pseudoaneurysm are clearly spelled out. An excellent literature review is provided. This article serves as a reminder to the urologist of the untoward and life threatening potential effects of heparin induced thrombocytopenia, and the importance of prompt diagnosis and treatment of BAH.

Competing Interests: No competing interests were disclosed.
I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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Ryan Smith
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The authors have composed an interesting case report with a good review of the literature. Anticoagulation requirements before and after Urologic surgery have significant importance and can result in a myriad of post-operative complications. Prompt recognition of these is essential to prevent additional patient morbidity. HIT-associated BAH represents a less commonly seen complication following anticoagulation and it is important for surgeons to be aware of this possibility.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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