

2023

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### Recommended Citation

Acharya, Indira; Pokharel, Ashik; and Weisman, David S. (2023) "Spontaneous retroperitoneal hematoma in vitamin C deficiency," *Journal of Community Hospital Internal Medicine Perspectives*: Vol. 13: Iss. 2, Article 8.

DOI: 10.55729/2000-9666.1161

Available at: <https://scholarlycommons.gbmc.org/jchimp/vol13/iss2/8>

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# Spontaneous Retroperitoneal Hematoma in Vitamin C Deficiency

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## Abstract

Retroperitoneal hematoma is rare but potentially life-threatening. It is commonly caused by traumatic or iatrogenic vascular injury, retroperitoneal neoplasm, coagulopathy, chronic anticoagulation, or fibrinolytic therapy. However, retroperitoneal hematoma due to vitamin C deficiency is rare. Here, we report a case of 40 years old man who developed retroperitoneal hematoma in context of very low vitamin C. To our knowledge, this is the second described case of retroperitoneal hematoma from vitamin C deficiency.

**Keywords:** Retroperitoneal hematoma, Vitamin C deficiency, Iatrogenic vascular injury, Fibrinolytic therapy

## 1. Introduction

Retroperitoneal hematoma occurs when blood accumulates into space immediately behind the posterior reflection of abdominal peritoneum.<sup>19</sup> It is often occult and underappreciated by clinicians.<sup>22</sup> Most of the time, patients don't present with clinically plausible signs and symptoms until ample amount of blood loss has occurred.<sup>4</sup>

Retroperitoneal hematoma is classified as traumatic and nontraumatic.<sup>1</sup> Traumatic retroperitoneal hematoma comprises blunt and penetrating trauma (gun-shot wound, stabbing). Nontraumatic retroperitoneal hematoma can be either spontaneous or iatrogenic in etiology.<sup>2</sup> Spontaneous retroperitoneal hematomas are more varied, relatively rare with a high degree of morbidity and mortality.<sup>23</sup> Etiologies include anticoagulant and fibrinolytic therapy, renal or adrenal malignancies, gynecologic or obstetric conditions (hemorrhagic cysts, ovarian torsion, ectopic pregnancy), coagulopathy and aneurysmal dilations of aorta.<sup>3</sup> Iatrogenic causes include injury during aortic and femoral artery cannulation during percutaneous interventions (PCI) or endovascular procedures or direct injury during abdominal or pelvic exploration.<sup>4</sup>

Diagnosis of retroperitoneal hematoma requires a high index of suspicion. The single most useful

laboratory measurement to narrow the differential diagnosis towards ongoing retroperitoneal bleeding is falling hemoglobin.<sup>22</sup> But it may take some time with or without crystalloid volume resuscitation to recognize an acute hemorrhage.<sup>5</sup> Other useful studies include prothrombin time, international normalized ratio, partial thromboplastin time, and thromboelastography to identify a patient's anti-coagulation status.<sup>5</sup> The computed tomographic (CT) cross-sectional imaging of the abdomen with intravenous contrast has been identified as the unrivaled study for confirming diagnosis.<sup>6–9</sup> It can conveniently and expeditiously identify the specific hematomal location, concomitant injuries, and determine if bleeding is ongoing.<sup>10</sup>

Vitamin C deficiency disrupts collagen synthesis in a blood vessel wall resulting in a loss of capillary integrity and blood seepage into the tissue.<sup>16</sup> Retroperitoneal hematoma due to vitamin C deficiency is a rare and potentially life-threatening condition. Timely supplementation of vitamin C mitigates the bleeding risk by strengthening the collagen molecules of the blood vessel wall. Here, we present a patient with retroperitoneal hematoma who developed subsequent complications with significant morbidity and mortality. To our knowledge, this is the second systematically described case of

Received 4 November 2022; revised 24 December 2022; accepted 5 January 2023.  
Available online 10 March 2023

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<https://doi.org/10.55729/2000-9666.1161>

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retroperitoneal hematoma due to vitamin C deficiency.

## 2. Case presentation

A 40-year-old man with hypertension, Graves' disease on methimazole and ESRD on HD from hereditary focal segmental glomerulosclerosis, presented with abdominal discomfort for 4 days. Vitals were significant for hypotension with BP of 70/40 mmHg and sinus tachycardia with heart rate of 104 beats/min. Physical examination showed bilateral scleral icterus and right iliac fossa tenderness without guarding, rebound tenderness, or visible flank ecchymosis.

Laboratory diagnostics (Table 1) were remarkable for normocytic anemia, transaminitis, elevated alkaline phosphatase and total and direct bilirubin. Generally, the AST: ALT ratio is used as the hemolytic marker. In our case, anemia and elevated liver enzymes suggested further hemolysis workup; however, normal lactate dehydrogenase, haptoglobin, and absolute reticulocyte count ruled out hemolytic anemia. His mean arterial pressure remained low despite fluid resuscitation and 1 PRBC transfusion. CT of the abdomen and pelvis with iv contrast showed a 4.5 × 3.3cm, retroperitoneal hematoma, anterior to the right psoas muscle (Fig. 1) with blood extending into the extraperitoneal pelvis (Fig. 2). It also showed a punctate radiodensity in the right inferior hepatic lobe with no biliary dilatation. Interventional radiology was consulted for possible embolization for retroperitoneal hematoma.

Table 1. Laboratory diagnostics.

Parameters	Normal range	Result
Hemoglobin (gm/dl)	11–14.5	7.7 (Baseline Hb: 10)
WBC (k/uL)	4–10.8	10.2
Platelet (k/uL)	145–400	248
AST (units/l)	0–33	132
ALT (units/l)	10–49	50
Alkaline phosphatase (units/l)	46–116	679
Total bilirubin (mg/dl)	0.3–1.2	14.3
Direct bilirubin (mg/dl)	0–0.3	11.43
Absolute reticulocyte count (million/uL)	0.02–0.1	0.076
Immature reticulocyte %	2.2–15.7%	16%
Haptoglobin (mg/dl)	40–280	44
Lactate dehydrogenase (units/L)	87–241	189
Serum Sodium (mmol/L)	136–145	135
Creatinine (mg/dL)	0.60–1.10	1.16
Blood urea nitrogen (mg/dL)	9–23	21
PT (seconds)	11.8–14.6	23
INR	0.8–1.2	1.6

The patient's hospital course was complicated by multiorgan system failure, continuous gingival bleeding, ongoing abdominal pain, hypotension requiring vasopressors and intubation. Further workup for bleeding diathesis revealed severe vitamin C deficiency (<5 umol/L, normal range 23–140 umol/L). Factor assays showed normal Factor VII and Von Willebrand factor activity. Initial PT and PTT were slightly prolonged (23 S and 51 S respectively), however the mixing study showed absence of factor inhibitor. The patient received PRBC, cryoprecipitate, FFP and platelet transfusion multiple times. His vitamin C deficiency was treated with 500 mg of intravenous vitamin C daily and 2000 mg of oral vitamin C twice daily with the achievement of normal level of blood vitamin C within 10 days.

The AST: ALT ratio, more than or equal to one, has reasonable specificity and sensitivity for a diagnosis of cirrhosis of the liver.<sup>25</sup> The patient's deranged liver function was thought to be due to liver injury from methimazole he used to take for his hyperthyroidism and hyperbilirubinemia was thought to be related to vitamin C deficiency-related hemolytic anemia. Elevated alkaline phosphatase signified the possibility of obstructive pathology at the bile duct but an ultrasonogram of the abdomen showed cirrhotic liver with no intra or extrahepatic biliary ductal dilatation, which was further confirmed by unremarkable magnetic resonance cholangiopancreatography. A liver biopsy was recommended once stable. The colonoscopy was unremarkable. Esophagogastroduodenoscopy showed a nonbleeding esophageal ulcer, clotted blood in the gastric fundus and a few angiectasias in the stomach that were cauterized.

Repeat computerized tomography of the abdomen and pelvis showed 5.1 × 3.8 × 6.4 cm right retroperitoneal hematoma containing foci of hyperacute hemorrhage, suggesting ongoing bleeding. Due to ongoing vasopressor support, he was unstable for any IR intervention. After a prolonged ICU course, the patient was transitioned to palliative care with compassionate extubation after discussions with his family.

The primary etiology of his coagulopathy and bleeding disorder was multifactorial from hepatic and renal dysfunction causing coagulopathy of liver disease and uremic platelet dysfunction but seemed primarily due to scurvy as his vitamin C level was undetectable.

## 3. Discussion

Retroperitoneal hematoma must remain on the differential diagnosis for unexplained drop in

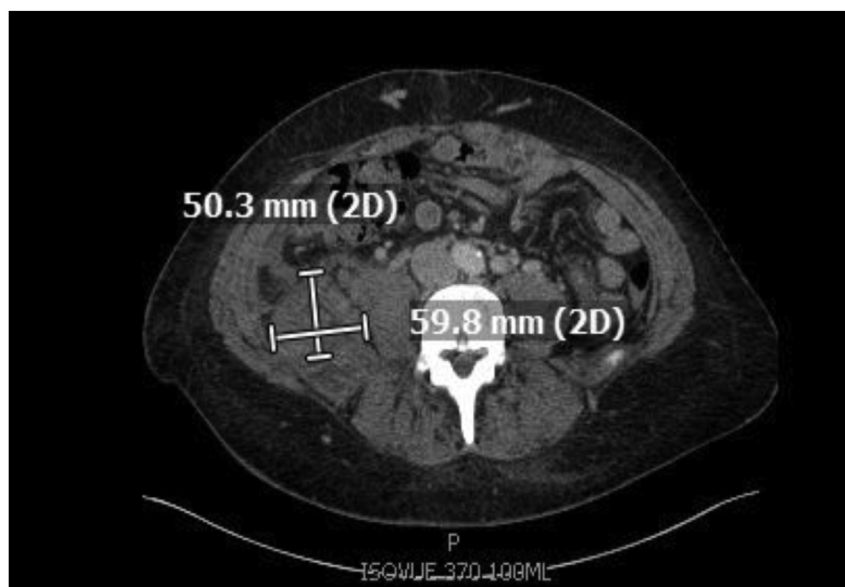


Fig. 1. Ct abdomen and pelvis w Iv contrast-right retroperitoneal hematoma lateral to psoas muscle measuring 6 x 5cm (transverse by AP).

hemoglobin. Initial diagnosis may be overlooked leading to unnecessary complications.<sup>24</sup> Scurvy is a rare nutritional deficiency in the developed world, typically associated with individuals who are at risk of malnourishment, such as those with alcohol use disorder, malabsorption, and those who experience homelessness.<sup>11-13,17</sup> However, it should also be considered in patients receiving renal replacement therapy.<sup>14,15</sup> Vitamin C is obtained in the diet by potassium-rich food, but these foods are restricted

for HD patients. Vitamin C is an antioxidant and is significantly consumed in dialysis patients due to ongoing oxidative stress in the context of metabolic acidosis and volume overload.<sup>27</sup> The deficiency may also arise from dialytic vitamin C clearance as it is completely water-soluble, not bound to proteins, and has a relatively low molecular weight of 176Da.<sup>8,15</sup> While in non-dialyzed patients, the main reason for lower plasma level of vitamin C is due to increased urinary losses.<sup>8</sup>

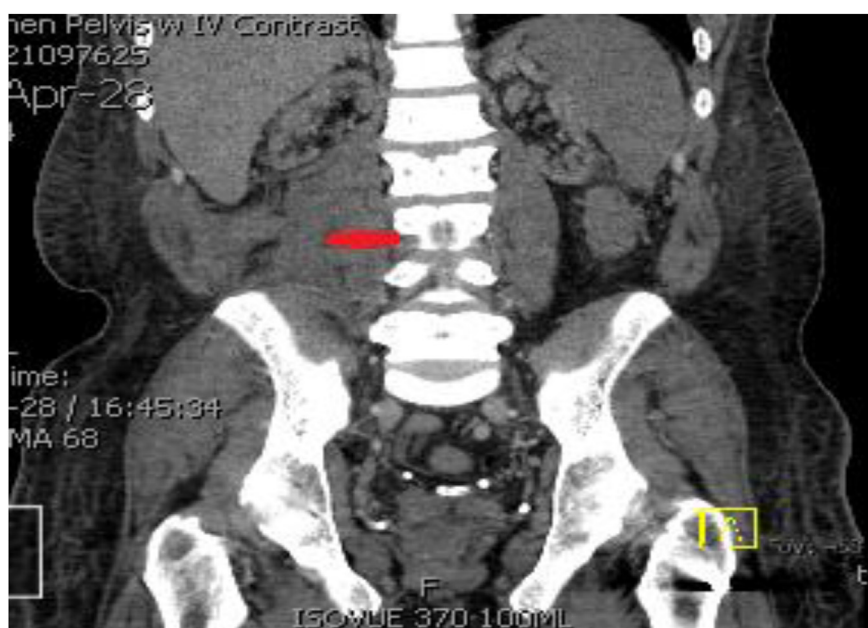


Fig. 2. CT abdomen and Pelvis w Iv contrast -Right retroperitoneal hematoma extending into retroperitoneal pelvis.

Vitamin C has a role in synthesis of collagen type IV which is the main constituent of blood vessel walls. It allows hydroxylation and crosslinking of pro-collagen catalyzed by lysyl hydroxylase. Lack of vitamin C leads to epigenetic DNA hypermethylation and inhibits the transcription of collagen found in blood vessels.<sup>16</sup> The vascular fragility from the impaired collagen formation results in hemorrhage that can occur in almost any organ.<sup>13</sup> In addition, the role of vitamin C in iron absorption causes those with scurvy to be more prone to have iron deficiency anemia.

Leucocyte ascorbic acid level reflects total body store of vitamin C and is more accurate as it is less affected by acute dietary changes.<sup>18</sup> A leukocyte vitamin C level of 0 mg/dL is indicative of latent scurvy, zero to 7 mg/dL is consistent with deficiency and greater than 15 mg/dL is adequate. Serum testing for low plasma vitamin C less than 0.2 mg/dL is usually consistent with scurvy. Determination of leukocyte ascorbic acid level, compared to plasma ascorbic acid level, is quite complex as its interpretation is complicated by different concentrations of vitamin C in various leukocyte cell fractions.<sup>26</sup> Leucocyte ascorbic acid level was not obtained in our patient as it wasn't routinely done at our center.

Vitamin C deficiency manifests symptomatically after 8–12 weeks of inadequate intake.<sup>15</sup> The recommended dietary dosage of vitamin C in the non-deficient adult is 110 mg/day.<sup>16</sup> The standard treatment for scurvy comprises supplementation with 300–1000 mg of vitamin C (orally, intramuscularly, or intravenously) for at least 1 month until the resolution of clinical sequelae.<sup>22</sup> Alternative treatment regimens include one to 2 g for up to 3 days followed by 500 mg daily for a week followed by 100 mg daily for up to 3 months.<sup>16</sup> Studies have shown that intravenous administration of Vitamin C results in concentrations as much as 70-fold higher than those achieved by maximum oral consumption.<sup>20</sup> Our patient was treated with both oral and intravenous vitamin C with the achievement of a blood vitamin C level of 137  $\mu\text{mol/L}$  (normal blood vitamin C level: 23–114  $\mu\text{mol/L}$ ) in ten days. In addition to Vitamin C supplementation, education to the patient on lifestyle modifications to ensure adequate intake and cessation of alcohol and tobacco use is imperative.<sup>21</sup>

#### 4. Conclusion

Retroperitoneal hematomas can have a nonspecific presentation like abdominal discomfort, hypotension, and anemia. Diagnosis relies on a high index of suspicion which can be further confirmed

by CT imaging of the abdomen and pelvis. Spontaneous retroperitoneal hematoma is multifactorial and relatively rare condition that carries a high mortality. Deficiency of vitamin C causes impaired collagen formation and vascular fragility that results in hemorrhage in almost any organ including the retroperitoneum. Causes of vitamin C deficiency can be a nutritional deficiency, alcohol use disorder, malabsorption, homelessness, or renal replacement therapy. Chronic kidney disease patients are at high risk of developing subclinical vitamin C deficiency because of dietary restriction, loss through the dialyzer, and increased consumption of vitamin C to counteract the ongoing oxidative stress due to metabolic disturbance. Mitigation of risk factors and timely diagnosis and supplementation with an oral or iv form of Vitamin C is empirical for the prevention of dreadful consequences. Vitamin C supplementation minimizes the bleeding risk by maintaining the integrity of collagen molecules, thereby reducing their susceptibility to damage.

#### Conflict of interest

None.

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