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Case Report

Adrenal Hemorrhage as a Presenting Feature of Essential Thrombocythemia - Report of Two Cases and Review of the Literature

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Abstract

Adrenal hemorrhage, especially when bilateral, is a rare phenomenon and may result in adrenal insufficiency. Causes of this phenomenon are varied and include thrombocytopenic bleeding related to sepsis and hypercoagulable conditions such as myeloproliferative neoplasms (MPN). Here, we report two cases of adrenal hemorrhage as first presentation of *JAK2* V617F positive essential thrombocythemia (ET). The first patient presented with renal vein thrombosis and bilateral adrenal hemorrhage and the second patient presented with unilateral adrenal hemorrhage with no evidence of thrombosis.

Introduction

Adrenal hemorrhage is a rare phenomenon in adults and it can be fatal in cases of bilateral involvement leading to adrenal insufficiency. Both etiology and pathogenesis of adrenal hemorrhage is not fully understood [1,2]. Several systemic diseases have been associated with adrenal hemorrhage such as sepsis, meningococcemia, severe physical stress, trauma and postoperative period [1]. It can also be observed in various thrombotic conditions, such as heparin-induced thrombocytopenia (HIT), antiphospholipid syndrome (APS), COVID 19 infection and myeloproliferative neoplasms (MPNs) [2,3].

Essential thrombocythemia (ET) is a chronic myeloproliferative neoplasm which is associated with an increased risk of thrombohemorrhagic complications [4] and thrombosis or hemorrhage may be the presenting feature in ET in 11-25% to 3.6-37% of cases respectively [5].

We report herein two cases of adrenal hemorrhage as first presentation of *JAK2* V617F positive ET. The first patient presented with renal vein thrombosis and bilateral adrenal hemorrhage and the second patient presented with unilateral adrenal hemorrhage with no evidence of thrombosis.

Case Presentations and Management

Patient No. 1

A 69-year-old man presented to our emergency room (ER) because of 4 days of abdominal pain accompanied by nausea and constipation. His past medical history included only diverticulosis and he was not taking any medications.

Physical examination revealed normal vital signs and left lower quadrant (LLQ) abdominal tenderness, Laboratory tests showed signs of inflammation: leukocytosis of 13K/μL with 81% neutrophils, C-reactive protein (CRP) of 14 mg/dl and platelets of 450K/ μL. The international normalized ratio (INR) was 1.1, fibrinogen 668 mg/dl and factor VIII and von Willebrand factor (vWF)antigen levels were normal. Other laboratory parameters were within the normal range.

A computed tomography (CT) scan of the abdomen was performed and revealed left renal vein thrombosis and bilateral adrenal enlargement with high density without contrast enhancement, consistent with bilateral adrenal hemorrhage (Figure 1).

A short Synacthen test was done and showed increased adrenocorticotropic hormone (ACTH) levels (108 pg/mL) but

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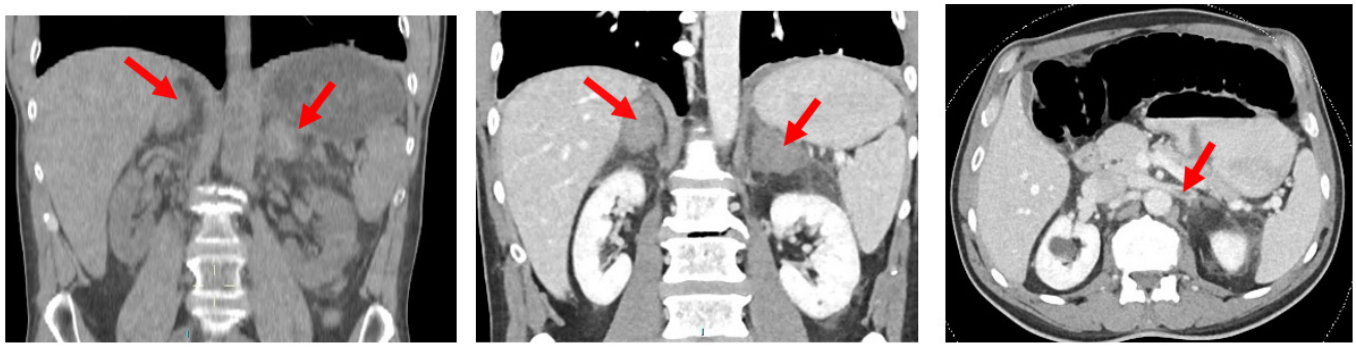

Figure 1: A. Non-contrast coronal CT view of upper abdomen showing bilateral hyperdense adrenal swelling typical of parenchymal hematoma (red arrows). B. Contrast-enhanced coronal CT of the upper abdomen, showing bilateral hypodense non enhanced swollen adrenal glands (red arrows) C. Venous-phase axial CT view of the upper abdomen in demonstrating a filling defect in proximal left renal vein (red arrow).

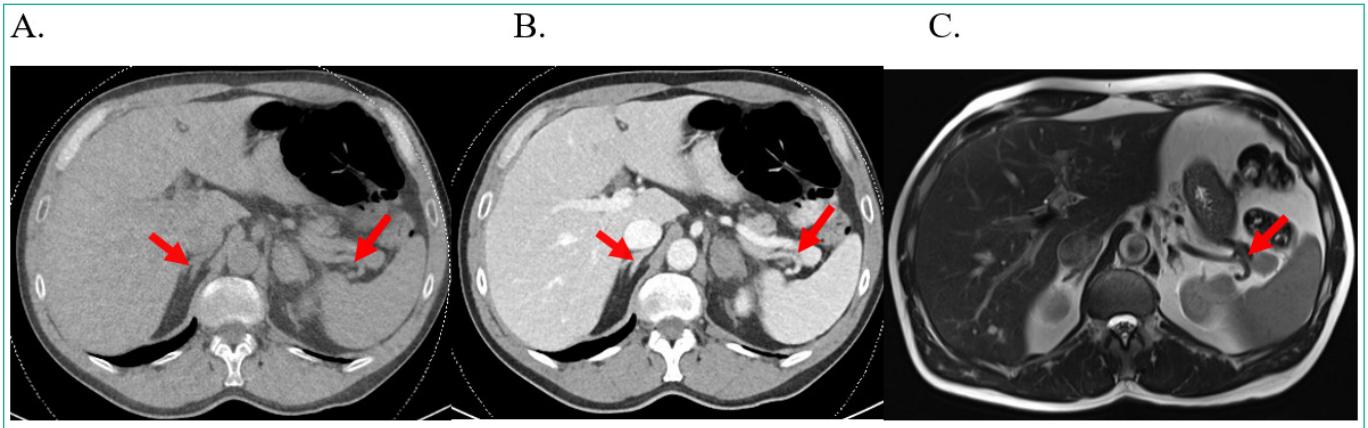

Figure 2: A. Axial CT view in virtual non-enhanced phase of the upper abdomen, demonstrate hyperdense and swollen unilateral left adrenal, with normal adrenal on the right (red arrows). B. Axial view of upper abdomen CT in venous phase with swollen left adrenal with no enhancement and normal adrenal in the right (red arrows). C. 2 months later follow up MRI -T2 sequence shows that the left adrenal glands normal configuration (red arrow).

relatively low cortisol levels (11µg/dL) which confirmed the diagnosis of primary adrenal insufficiency.

Patient No. 2

A 72-year-old-man was admitted to our ER with two days of worsening LLQ abdominal pain. His medical history included only benign prostate hyperplasia and he did not take any regular medications.

Physical examination was normal apart from mild LLQ abdominal tenderness without guarding or rebound and laboratory tests include factor VIII and vWF were within normal range except for thrombocytosis of 733 K/µL.

A CT scan of the abdomen demonstrated left adrenal hematoma (Figure 2) without other abnormalities.

Management

In both cases adrenal hemorrhage was presumed to be related to a myeloproliferative neoplasm given the presence of thrombocytosis, after excluding other causes of thrombosis including infection or malignancies. In addition, hereditary hypercoagulability was excluded.

In both cases the *JAK2*V617F mutation associated the MPNs was found. The second patient underwent bone marrow biopsy which showed proliferation of megakaryocytes and a myeloid: erythroid ratio of 5:1 (normal =3:2) without increased reticulin fibers (Figure 3). These findings were diagnostic of ET by World Health Organization criteria [6].

Both patients began treatment with aspirin and hydroxyurea according to clinical guidelines [14] and the first patient who presented with bilateral hemorrhage and Addison disease also received hydrocortisone and fludrocortisone along with apixaban because of the documented renal vein thrombosis.

Review of the Literature

MPNs are associated with a variable risk of thrombohemorrhagic complications, involving either major vessels or the microcirculation. The annual incidence of these events in ET is estimated to be approximately 2 per 100 patients [7] with most thrombotic events occurring at diagnosis [8].

The *JAK2* gene mutation is an independent thrombogenic factor and may be present in more than half of patients with ET, it is associated with both venous and arterial thrombotic conditions [2]. Several pathophysiological mechanisms may explain a possible contribution of the *JAK2* V617F mutation in the risk of thrombosis (including increased aggregation and thrombus formation [9].

Adrenal hemorrhage as a presentation of ET is rare and must

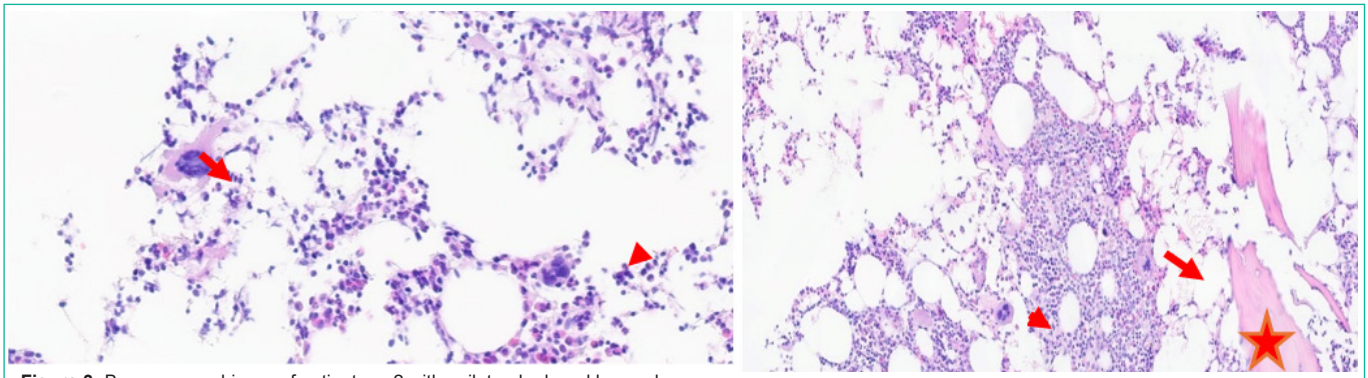

Figure 3: Bone marrow biopsy of patient no. 2 with unilateral adrenal hemorrhage.
Megakaryocytes (red arrows) forming loose clusters with hyperlobated and staghorn like nuclei (arrowheads) and reticulin fibers (red star).

be promptly diagnosed because it may be fatal especially with bilateral involvement leading to adrenal insufficiency [10]. The pathophysiology of adrenal infarction is not fully understood but one theory relates to the gland's complex microvascular system, having a rich arterial network with only one vein for drainage: into the vena cava on the right, and into the left renal vein on the left [11]. Adrenal vein thrombosis associated with ET may cause venous hypertension inducing an ischemic necrosis followed by hemorrhagic infarction [12]. The association between renal vein thrombosis and adrenal hemorrhage is well established in newborns but rarely reported in adults occurring more frequently on the left side while bilateral infarction is described only with inferior vena cava (IVC) thrombosis [10].

Adrenal hemorrhage has been associated with systemic diseases such as sepsis, heparin-induced thrombocytopenia (HIT), antiphospholipid syndrome (APS), COVID 19 infection, polycythemia vera (PV) and ET [2,3].

In this report we describe two patients with different entities one with a left renal vein thrombosis and bilateral adrenal hemorrhage without IVC thrombosis and the other with left sided adrenal hemorrhage with no evidence of thrombosis. It is still unclear whether left renal vein thrombosis was the first presentation of ET or may explained bilateral adrenal hemorrhage.

Spontaneous hemorrhage in ET usually occur in the context of extreme thrombocytosis with platelets > $1500x10^9$ /L [13] and may be associated with an acquired vWF deficiency [1,13]. In both of our cases there was neither extreme thrombocytosis nor vWF deficiency. Other established risk factors for thrombosis in ET are age above 60 years, history of previous thrombotic event and presence of the *JAK2* V617F mutation [11]. Notably both of our patients both were older than 60 and both had the *JAK2* V617F mutated but neither had a history of thrombosis.

In the sparse reports of adrenal hemorrhage associated with ET [2,8], clinical features were non-specific and included abdominal pain, fever, fatigue, nausea, vomiting, hypotension and coma [2,14]. Laboratory investigations may reveal hyponatremia, hyperkalemia, leukocytosis, eosinophilia, anemia, low levels of cortisol and high levels of ACTH [14]. Heightened awareness and clinical suspicion are required to diagnose this life-threatening condition, CT scanning is sufficient to confirm the radiological diagnosis in most cases of adrenal hemorrhage [2,14].

However, not all patients with bilateral adrenal hemorrhage presented with features of adrenal crisis. One of our patient presented with abdominal pain with normal blood pressure, his had leukocytosis and mild hyponatremia with no other findings suggesting Addisonian crises. CT scanning revealed bilateral adrenal hemorrhage and a synacthen test confirmed the diagnosis of adrenal insufficiency. Our other patient presented with no evidence of adrenal insufficiency and the diagnosis of left adrenal hemorrhage was made on CT scanning with no clinical or laboratory signs of adrenal infarction.

To our knowledge adrenal hemorrhage as complication of ET has only been described in patients previously diagnosed with ET. In this report both patients ET was diagnosed only after the thrombo-hemorrhagic event Furthermore, we describe here a unique case of bilateral adrenal hemorrhage with isolated left renal thrombosis.

In conclusion, ET is associated with an increased risk of thrombo-hemorrhagic complications**.** Adrenal hemorrhage especially when it is bilateral is a rare thrombotic complication and may be the first presentation of ET. This condition may be fatal, and a high level of suspicion is a prerequisite for timely diagnosis. Adrenal insufficiency should be suspected in patients with abdominal pain, hypotension and relevant laboratory findings such as hyponatremia and hyperkalemia. Moreover, when the diagnosis of bilateral adrenal hemorrhage is confirmed, underlying etiologies such as ET should be considered.

References

1. JM, ZB, WS, GK. Bilateral adrenal swelling as a cause of chest, back, and upper abdominal pain in essential thrombocythemia and polycythemia vera is due to microvascular ischemic thrombosis rather than to hemorrhage. *Annals of Hematology*. 2002; 81: 691.
2. Hada Y, Yamada A, Kobayashi T, et al. Bilateral adrenal infarction that developed in latent essential thrombocythemia. *Intern Med*. 2023; 63: 419.
3. Pachipala K, Gutknecht D. Bilateral adrenal hemorrhage associated with essential thrombocytosis. Am J Hematol. 2006; 81: 150-151.
4. Kojima K, Fujii N, Takata S, et al. Bilateral adrenal hemorrhage in essential thrombocythemia. Ann Hematol. 2002; 81: 350-351.
5. Elliott MA, Tefferi A. Thrombosis and haemorrhage in polycythaemia vera and essential thrombocythaemia. *Br J Haematol*. 2005; 128: 275.
6. Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016; 127: 2391-2405.
7. Barbui T, De Stefano V. Management of venous thromboembolism in myeloproliferative neoplasms. Curr Opin Hematol. 2017; 24: 108–114.

8. Gensous N, Jourde W, Salles K, James C, Guy A, Duffau P. Adrenal insufficiency revealing bilateral adrenal hemorrhage related to JAK2 V617F-positive essential thrombocythemia: About two cases. *Blood Coagulation & Fibrinolysis*. 2023; 34: 228.

9. Fleischman AG, Tyner JW. Causal role for JAK2 V617F in thrombosis. *Blood*. 2013; 122: 3705-3707.

10. Loke TKL. Adult adrenal haemorrhage: An unrecognised complication of renal vein thrombosis: A case report. EJR. 2000.

11. Bashari WA, Myint YMM, Win ML, Oyibo SO. Adrenal insufficiency secondary to bilateral adrenal hemorrhage: A case report. *Cureus*. 2020.

12. Burnet G, Lambert M, Annet L, Lefebvre C. Unilateral adrenal hemorrhagic infarction in essential thrombocythemia. *Acta Clinica Belgica*. 2015; 70: 461.

13. Elliott MA, Tefferi A. Pathogenesis and management of bleeding in essential thrombocythemia and polycythemia vera. *Curr Hematol Rep*. 2004; 3: 344-351.

14. Dineen R, Thompson C. Sherlock: Adrenal crisis: prevention and management in adult patients. Ther Adv Endocrinol Metab. 2019; 10: 1-12.