An unusual cause of abdominal pain: spontaneous bilateral adrenal hemorrhage

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Abstract

Bilateral adrenal hemorrhage (BAH) is a rare condition that can lead to acute adrenal insufficiency and death if not recognized and treated promptly. We report the case of a 30-year-old male who presented to the emergency department with acute abdominal pain, nausea, and vomiting. On emergency room admission, the first abdominal CT revealed normal adrenal glands without enlargement, but with the development of hypotension and hypoglycemia, a second CT performed four days later showed enlargement due to hemorrhage in both adrenals. The diagnosis of BAH associated with acute adrenal insufficiency was retained. Prompt treatment with intravenous and oral corticosteroids resulted in successful conservative management. We describe the clinical, biological, radiological and etiological features of this condition based on a review of the literature. (Acta gastroenterol. belg., **2023,** 86, **495-498**).

Keywords: Bilateral adrenal hemorrhage, adrenal hemorrhage, idiopathic adrenal hemorrhage, acute adrenal insufficiency, corticosteroid therapy, bilateral adrenal masses.

Introduction

Bilateral adrenal hemorrhage (BAH) is an uncommon cause of acute adrenal insufficiency, with a mortality rate of 15% (1). BAH is often described as a rare event. According to the Medline search, 1293 publications were reported on this topic. The majority of BAH cases occurred in critically ill patients during septic or hemorrhagic shock (2) and only 139 articles described cases of idiopathic BAH. Its incidence is estimated to be 0.14-1.8% based on postmortem studies. We describe the clinical, biological, imaging and etiological features of this condition in a 30-year-old man admitted to the emergency room for abdominal pain and nausea.

Case history

We report the case of a 30-year-old man admitted to the emergency room with abdominal pain, nausea, and vomiting for a few days. He had no significant medical history and did not use drugs. No recent trauma was described. The physical examination and vital signs in the emergency room was as follows: body mass index 20 kg/m², blood pressure 143/82 mmHg, heart rate 122 beats/min, body temperature 36.5°C and diffuse abdominal pain. The laboratory data showed minor inflammation (Table 1).

The patient was hospitalized for further investigation and follow-up. Abdominal ultrasound and abdominal CT scan revealed nothing unusual, except for a slight layer of fluid at the upper pole of the right kidney, suggesting the onset of pyelonephritis (Fig. 1). During his stay, the patient did not develop fever, acute inflammation, or anemia (Table 1), and gastroscopy did not show ulcers or other abnormal findings. Finally, the patient was discharged after two days, with no clear explanation for these symptoms.

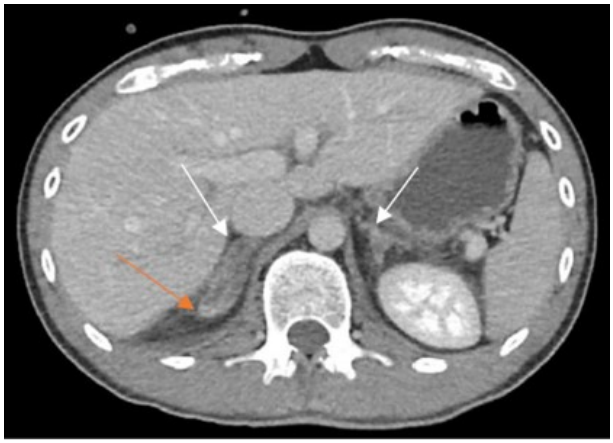

Figure 1. — First abdominal CT scan. Axial sections of the adrenal glands (fine white arrows). Helical mode, thickness 3 mm, injection of 70 cc of iodine contrast at portal time. The radiological contrast agent was slightly visible in the right adrenal gland showing the early onset of hemorrhage (orange arrow).

Two days later, he was readmitted in shock to the emergency room leading to admission to the critical care unit. Laboratory data showed hyponatremia at 128 mEq/L (136-145), hypokalemia at 3.2 mEq/L (3.5-5.1) as well as hypoglycemia at 58 mg/dl, and a significant inflammatory syndrome (C-reactive protein at 296.5 mg/L (< 0.5), the biological evolution is summarized in Table 1. Hemocultures were negative. A second follow-up abdominal CT scan showed high density round masses (50 HU) consistent with bilateral adrenal hemorrhage (Fig. 2). The patient was not anticoagulated and did not receive heparin therapy, which can be a cause of internal

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Table 1. — **Evolution of labs parameters**

Labs parameters	*normal values*	*admission* *Day 1*	*Hospital discharge* *Day 2*	*re-admission* *Day 4*	*Day 5*	*Day 6*	*Day 7*	*Day 8*	*Day 9*	*Hospital discharge* *Day 15*	*Follow up* *Day 52*	*Follow up* *Day 96*
WBC (10^9/L)	*(4.0 - 10.0)*	**13.45**	**20.27**	**12**	**12.21**	7.23		6.32	6.71	9.29	6.27	
Hemoglobin (g/dL)	*(14.0 - 18.0)*	16.3	15.4	**18.2**	16.4	14.4		**13.2**	14.5	17.1	16.5	16.7
Hematocrit (%)	*(42 -52)*	47.4	44.9	51.1	45.1	**40.7**		**38.3**	**41.8**	48.4	47.9	
Platelets (109/L)	*(150 - 400)*	204	184	186	176	163		192	220	233	243	
Prothrombin Time (%)	*(70 - 100)*	100	92	88		94			98	97		
PTT-INR	*(0.8 -1.2)*	0.98	1.03	1.06		1.02			0.99	1		
APTT (sec)	*(26 - 40)*	29.5	32.2	35.3		32.2			31.7	33.9		
Sodium (mmol/L)	*(136 - 145)*	142	139	**128**	**131**	139	140	139	141	137	141	137
Potassium (mmol/L)	*(3.5 - 5.1)*	4.1	3.5	**3.2**	**3.4**	4.1	3.8	3.9	4.4	4.4	3.8	4.4
Osmolality (mosm/kg)	*(275 - 295)*	286			262	276					281	
Urea (mg/dL)	*(17 - 43)*	16	14	21	21	14	12	13		22	29	25
Creatinine (mg/dL)	*(0.6 - 1.3)*	0.94	0.84	0.78	0.67	0.85	0.9	0.87		0.92	0.97	0.92
MDRD2 (eGFR/1.73m²) (ml/min)		> 60	> 60	> 60	> 60	> 60	> 60	> 60	> 60	> 60	> 60	> 60
LDH (U/L)	*(< 245)*	**272**	**285**	**290**	245	222						
CRP (mg/L)	*(< 5)*	**5.6**	**7.4**	**296.5**	**239.7**	**112.3**		**28.5**	**19.8**	**19.3**	1.7	
Plasma glucose (mg/dl)	*(75 - 100)*	131	76	**58**	**59**	**67**	105	124	83			
Lactate (mmol/L)	*(0.5 - 2.2)*	**2.85**	**6.39**	0.78								
Cortisol (µg/dL)	*(3.7 - 19.4)*	22.9	32.4	**35,6**					< 1*	5.5*	5.5*	9,8*
ACTH (pg/mL)	*(4.7 - 48.8)*			**178.5**					**220.6**	**392.3**	**123.9**	217
Direct Renin (µU/ml)	*(2.8 - 39.9)*								4	**164**	**72**	
Aldosterone (ng/dl)	*(1.76 - 23.2)*								**1**	2	9	8
Aldosterone/renin ratio (ng/mU)	*(< 23.1)*								2.5	0.1	1.3	1

WBC : White blood cell, PTT : Thromboplastin time, INR : International normalized ratio, APTT : Activated partial thromboplastin time, MDRD : Modification of diet in renal disease, eGFR : estimated Glomerular filtration ra LDH : Lactate dehydrogenase, CRP : C-reactive protein, ACTH : Adrenocorticotropic hormone. *After > 24 hours off hydrocortisone 20 mg/d.

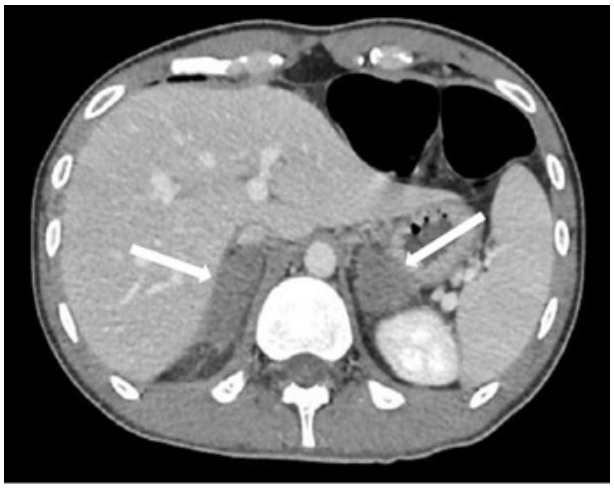

Figure 2. — 4 days later, CT scan showed high-density round masses (50 HU) corresponding to bilateral adrenal haemorrhage (white arrow).

bleeding. Retrospective analysis of the first abdominal CT scan showed very early but inconspicuous adrenal hemorrhage (orange arrow) without adrenal gland enlargement (Fig. 1).

By adding plasma cortisol to the initial laboratory tests, we found that plasma cortisol was elevated for the first two days and then decreased markedly, with a significant increase in adrenocorticotropic hormone (ACTH) levels, consistent with acute adrenal insufficiency (Table 1).

An intravenous infusion of sodium fluid and corticosteroids was initiated, followed rapidly by a normalization of the blood pressure and glucose. On the 8th day of admission, the patient was discharged in excellent physical condition, treated with hydrocortisone 20 mg daily.

One month later, a magnetic resonance imaging (MRI) of the abdomen was performed to exclude any malignant adrenal process that might have been involved in the hemorrhage. The hematomas were still present but had decreased in size (*not shown*). In addition, CT and MRI scans did not reveal any vascular abnormalities of the adrenal glands.

Six weeks after diagnosis, the patient's condition improved. Blood tests revealed no anemia, and cortisol levels remained low with high ACTH after withdrawal of hydrocortisone 24 hours earlier (Table 1). Hydrocortisone 20 mg daily was continued. In the absence of low blood pressure, the patient did not receive mineralocorticoids.

After 4 months, a clinical, biological, and abdominal CT evaluation was performed. After 5 days of discontinuation of hydrocortisone treatment, the patient was asymptomatic and did not have a tanned skin. Cortisol plasma at 8:00 am was 9.8 µg/dL (3.7-19.4), ACTH was 217 pg/mL (4.7-48.8) and aldosterone was 8.0 ng/dL (2.52-39.2 ng/dL). Primary adrenal insufficiency persists, it is defined as relative because baseline cortisol level is less than 10 µg/dL (3). Therefore, the option chosen was to discontinue corticosteroid therapy and prescribe hydrocortisone to be used only for acute events. On the other hand, abdominal CT scan revealed near-normalization of the dimensions of both adrenals.

Discussion

BAH is an uncommon condition that is usually described in sepsis and/or shock (e.g., Waterhouse-Friedrichsen syndrome associated with meningococcal sepsis), trauma, surgery or anticoagulant therapy.

Other associated etiologies have also been reported such as antiphospholipid syndrome, underlying adrenal tumors (e.g., adenoma, carcinoma, metastasis, or lymphoma). Lastly, adrenal amyloidosis with coexisting monoclonal gammopathy has been reported to be associated with BAH (4).

However, in some cases the exact cause of acute adrenal hemorrhage is unknown and is referred to as "idiopathic" hemorrhage. In our case, the etiologic investigation eliminated the most common causes of BAH (4), hemoglobin and platelet levels were normal (5). No autoimmune diseases such as systemic lupus erythematosus and antiphospholipid syndrome was found (antinuclear antibodies and anti-cardiolipin β2 antibodies are within normal values) (6).

In addition, some infections with CMV, EBV, toxoplasmosis, varicella virus or SARS-CoV-2 have been associated with BAH (7) (8). In our case, these investigations were all negative.

Finally, CT angiography or MRI did not reveal any specific vascular anatomical abnormality or tumor process (4). In addition, adrenal masses are rarely accompanied by bleeding (9).

BAH can occur late, up to 3 weeks after a sepsis, shock or postoperative period (1). In our case, the adrenal hemorrhage was not visible until the second CT scan, 4 days after the onset of symptoms. The majority of patients admitted to the emergency room have normal laboratory parameters, which do not reflect adrenal bleeding (5). Nevertheless, in case of acute hemorrhage, some biological parameters such as D-dimer or Lactate dehydrogenase (LDH) might guide the diagnosis because they are very high as shown in our case.

Follow-up CT scans are useful to monitor adrenal masses, decreasing size and density of adrenal masses will confirm the diagnosis, as we have shown well. The MRI can be helpful in confirming the adrenal hematoma with T1 hypersignal and in ruling out other causes such as adrenal tumors or vascular anomalies.

Adrenal insufficiency progressed early for our patient and did not need confirmation by an adrenocorticotropic hormone stimulation (ATCH) test. If adrenal insufficiency is associated with BAH, glucocorticoid and mineralocorticoid replacement therapy should be initiated without delay. Treatment modalities depend on the extent of the hemorrhage and the degree of adrenal hormone insufficiency. Often, the management of the hemorrhage will be conservative, consisting of close monitoring with

repeated biological and CT imaging, as we did in our patient's case (10).

Conclusion

We present a rare case of a 30-year-old man with idiopathic bilateral adrenal hemorrhage associated with cortisol insufficiency. This affection can be diagnosed with delay. It is important to replace corticosteroids promptly if associated acute adrenal insufficiency is suspected. Keep in mind that this condition can occur without an underlying etiology with almost quasi normal improvement after 4 months (11).

Conflicts of interest

No conflicts of interest present.

Funding

None.

Informed consent

The patient provided consent for the publication of the images. The patient's identity has been kept confidential.

References

1. KHAKWANI A.S., WAQAR F., KHAN U.A., ANWAR M.N. A Case of Bilateral Adrenal Hemorrhage: The Exceptional Cause of Adrenal Insufficiency. *Cureus*., 2022, **14**: e23413.
2. MAY C.J., ASIA M., KARAVITAKI N., ARLT W., GUEST P., O'REILLY M.W. Bilateral adrenal haemorrhage. *QJM An International Journal of Medicine*., 2017, **110** :169-171.
3. REZNIK Y., BARAT P., BERTHERAT J., BOUVATTIER C., CASTINETTI F., CHABRE O., *et al*. SFE/SFEDP adrenal insufficiency French consensus: Introduction and handbook. *Ann Endocrinol* (Paris)., 2018, **79**:1-22.
4. MEHMOOD K.T., SHARMAN T. Adrenal Hemorrhage. In: StatPearls. StatPearls Publishing, Treasure Island (FL), 2022.
5. BHANDARI S., AGITO K., KRUG E.I. Bilateral adrenal hemorrhage in polycythemia vera. *J Community Hosp Intern Med Perspect*., 2016, **6**:32416.
6. CARON P., CHABANNIER M.H., CAMBUS J.P., FORTENFANT F., OTAL P., SUC J.M. Definitive adrenal insufficiency due to bilateral adrenal hemorrhage and primary antiphospholipid syndrome. *J Clin Endocrinol Metab*., 1998, **83**:1437-9.
7. NIEMEYER C.S., MESCHER T., GRIGGS R., ORLICKY D.J., WILKERSON G.K., BUBAK A.N., *et al*. Histopathological Analysis of Adrenal Glands after Simian Varicella Virus Infection. *Viruses*., 2021, **13**: 1245.
8. SHARRACK N., BAXTER C.T., PADDOCK M., UCHEGBU E. Adrenal haemorrhage as a complication of COVID-19 infection. *BMJ Case Rep*., 2020, 13:e239643.
9 BHATTACHARYA P., ZAKARIA R., STONELAKE S., BUTLER B., SARMA D., MAHESWARI M., *et al*. Haemorrhagic shock from solid tumours of the adrenal gland: a case of bleeding primary adrenal lymphoma. *Ann R Coll Surg Engl*., 2021, **103**:101-105.
10. SIMON D.R., PALESE M.A. Clinical update on the management of adrenal hemorrhage. *Curr Urol Rep.*, 2009, **10**:78-83.
11. BASHARI W.A., MYINT Y.M.M, WIN M.L., OYIBO S.O. Adrenal Insufficiency Secondary to Bilateral Adrenal Hemorrhage: A Case Report. *Cureus*., 2020, **12**:e8596.