A CASE OF SPONTANEOUS REGRESSION OF IDIOPATHIC BILATERAL ADRENAL HEMORRHAGE IN A MIDDLE AGED WOMAN: 1 YEAR FOLLOW-UP

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Abstract

Background. Bilateral adrenal hemorrhage is a serious condition that can result in adrenal insufficiency, shock, acute adrenal crisis, and mortality if it is not managed with adequate treatment. We report a rare case of idiopathic bilateral adrenal hemorrhage.

Case presentation. A 50-year-old woman visited our hospital with complaints of right upper abdominal pain. A computed tomography (CT) revealed unilateral left adrenal gland hemorrhage. However, the results of rapid adrenocorticotrophic hormone (ACTH) stimulation test and adrenomedullary hormone function test were normal. Since the patient did not show signs of adrenal insufficiency, corticosteroid therapy was postponed and only supportive management therapy was started. After 1 week, a follow-up CT showed a previously unseen adrenal hemorrhage on the right adrenal gland, but the rapid ACTH stimulation test result was normal. One year later, no hemorrhagic signs were observed on the follow-up CT.

Conclusion. In most cases of idiopathic bilateral adrenal hemorrhage, patients are treated with steroid replacement therapy due to adrenal insufficiency. In some other cases, patients are treated with steroids despite the absence of adrenal insufficiency. Here we reported a very rare case of idiopathic bilateral adrenal hemorrhage sequentially to emphasize that before initiation of adrenal hormone replacement therapy, it is important to determine whether adrenal insufficiency is present. If there is no evidence of adrenal insufficiency, adrenal replacement therapy should be postponed until the presence of adrenal insufficiency is confirmed.

Key words: Idiopathic bilateral adrenal hemorrhage, spontaneous regression.

INTRODUCTION

Bilateral adrenal hemorrhage is a serious condition that can result in adrenal insufficiency, shock, acute adrenal crisis, and mortality if it is not

managed with adequate treatment (1, 2). It frequently occurs in association with extreme physical stress such as during sepsis due to infection, cardiac problems such as myocardial infarction and congestive heart failure, traumas, underlying adrenal tumors, burns, or hypotension related to hemorrhagic diathesis, especially when caused by uncontrolled anticoagulation (3, 4). The symptoms and physical findings of bilateral adrenal hemorrhage are not specific and vary among patients. Idiopathic bilateral adrenal hemorrhage is a very rare entity that may present as an acute condition or an asymptomatic adrenal mass (5-7). In the present study, we report a rare case of a middle-aged woman with idiopathic bilateral adrenal hemorrhage in serial order.

CASE PRESENTATION

A 50-year-old woman visited our hospital with complaint of right upper abdominal. She described the pain as continuous and dull without any associated gastrointestinal symptoms. She was in good health the previous day. On physical examination, her body temperature was 38°C, blood pressure was 176/94 mmHg, pulse rate was 98 beats per minute, and respiratory rate was 20 per minute. Her abdomen was soft with normal bowel sounds, but showed tenderness to deep palpation in the left upper abdomen. She did not have a history of trauma or anticoagulant therapy, medical history, or family history. She never had any acute infection. In addition, no chills, dysuria, hematuria, hematochezia, or melena was observed. Laboratory tests revealed a hemoglobin level of 13.8g/dL, white blood cell count of 10.2 x 10⁹/L, and platelet count of 254 x 10⁹/L. Her C-reactive protein level (1.16 mg/dL) was slightly elevated. Examination of electrolyte levels showed that her potassium level was 3.9 mEq/L and sodium level was 137 mEq/L. Liver

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function tests, renal function tests, coagulation function tests (Prothrombin time/international normalized ratio and activated partial thromboplastin time), and serum amylase and lipase levels were within normal limits.

Serial abdominal flat-plates did not show any obvious air-fluid levels or obstruction. Computed tomography (CT) with contrast of the abdomen and pelvis revealed unilateral diffuse thickening of the left adrenal gland, which was irregular and highly attenuated on pre-contrast scan, consistent with recent bleeding. Heterogeneous enhancement of the left adrenal gland was detected on post-contrast scanning. No definite tumor-like lesion, lymphadenopathy, abnormal fluid collections, and other abnormal anatomical lesions were observed (Fig. 1). To detect adrenal insufficiency, we performed the rapid adrenocorticotrophic hormone

(ACTH) stimulation test, but the patient did not show signs of adrenal insufficiency (Table 1). Moreover, the adrenomedullary hormone function test results were normal. The patient's abdominal pain persisted, but her vitals and other clinical signs were stable over the following 24 hours. Thus, therapy with corticosteroids was postponed and only supportive management therapy was maintained. Supportive management included intravenous fluid (sodium-potassium 10% dextrose solution), gastrointestinal medication (H2-blocker) and pain-control medication (tramadol). Since admission, her blood pressure was 130/80 mmHg without anti-hypertensive medication. The symptoms and signs alleviated during the 1 week of hospitalization, and a follow-up CT scan and rapid ACTH stimulation test were performed. CT, a pre-contrast scan showed an iso-

Figure 1. Computed tomography (CT) with contrast of the abdomen and pelvis. The arrow shows unilateral diffuse thickening of the left adrenal gland, which is irregular and highly attenuated on pre-contrast scan, consistent with recent adrenal hemorrhage (A). Heterogeneous enhancement of the left adrenal gland is detected on a post-contrast scan (B). Whereas significant adrenal gland hemorrhagic lesion is not seen on the right gland (C, D).

Table 1. On admission, the results of rapid ACTH test

	ACTH (pg/mL)	Cortisol (ug/dL)	Aldosterone (ng/dL)
(Base)	9.04	15.28	5.9
(30min)		27.93	16.9
(60min)		32.21	15.8

attenuated infiltrative lesion on the right adrenal gland, which was considered to be delayed adrenal hemorrhage in serial order. Furthermore, a non-enhancing hypodense lesion was also seen in the medial rim on delayed phase imaging. In addition, on comparing these results with the previous CT report, the peri- and para-renal infiltration lesion associated with the left adrenal gland hemorrhage was slightly alleviated in the recent CT. The highly attenuated hematoma of the left adrenal gland was slightly lowered on the pre-contrast scan, and an

Table 2. After 1 week of hospitalization, the results of rapid ACTH test

	ACTH (pg/mL)	Cortisol (ug/dL)	Aldosterone (ng/dL)
(Base)	25.85	19.15	1.5
(30min)		31.25	7.6
(60min)		33.60	7.4

approximately 1 cm-sized hematoma-like lesion with low attenuation was seen on delayed phase imaging (Fig. 2). Importantly, because the results of the rapid ACTH test were within normal limits, supportive management therapy without steroids was maintained (Table 2).

After 3 weeks, abdominal magnetic resonance imaging (MRI) was performed to evaluate the adrenal gland. It revealed bilaterally reduced adrenal hematomas, which, compared to the previous abdominal pelvic CT, seemed to be improving. There were no

Figure 2. One week from the baseline. Follow-up CT of the abdomen and pelvis. The peri- and para-renal infiltration lesion associated with the left adrenal gland hemorrhage is slightly alleviated. And the highly attenuated hematoma of the left adrenal gland is slightly lowered on the pre-contrast scan (A). On delayed phase imaging, an approximately 1 cm-sized hematoma-like lesion with low attenuation is seen on the left adrenal gland (B). A pre-contrast scan shows an iso-attenuated infiltrative lesion on the right adrenal gland, which is considered to be delayed adrenal hemorrhage in serial order (C). A non-enhancing hypodense lesion of size 1.6 cm x 0.3 cm is seen in the medial rim on the right adrenal gland (D).

Figure 3. One month from the baseline. Magnetic resonance imaging (MRI) of the abdomen and pelvis. Both adrenal hematomas are reduced in size as compared to the previous abdominal pelvic CT, and a 2-cm x 1-cm heterogeneous signal intensity of hematoma is seen (A, white arrow). There are no contrast extravasations to both peri-renal spaces and peri-adrenal glands on enhanced T1W1 images of the gland (B).

Figure 4. CT scan of the abdomen and pelvis at 1 year from baseline. No significant abnormal findings or adrenal gland hemorrhagic lesions are seen. Both adrenal glands are of normal shapes.

Table 3. The result of insulin tolerance test

	0 min	30 min	60 min	90 min	120 min
ACTH (pg/mL)	17.25	105.20	144.90	114.50	50.91
Cortisol (ug/dL)	10.11	16.07	27.43	27.32	27.75

contrast extravasations to both peri-renal spaces or peri-adrenal glands on enhanced T1W1 images of the gland (Fig. 3). In addition, an insulin-tolerance test (0,15 UI/kg, i.v.) at this point showed normal values (Table 3). After discharge, the patient visited our clinic regularly for 1 year, during which period she had no specific symptoms. Follow-up abdominal pelvic CT showed no hemorrhagic lesions of both adrenal glands, and both glands were of normal shape. In addition, there were no abnormal findings on CT (Fig. 4). Follow-up laboratory tests showed a basal cortisol level of 16.88 µg/dL and an aldosterone level of 4.0 ng/dL.

DISCUSSION

Adrenal hemorrhage is an uncommon condition of serious concern, as it may result in adrenal insufficiency and death (8). The exact incidence of adrenal hemorrhage in the general population is unknown (8-10). Bilateral adrenal hemorrhage is especially very rare. Adrenal hemorrhage may be caused by several factors including infection, cardiac problems such as myocardial infarction and congestive heart failure, trauma, antiphospholipid syndrome, burns, pregnancy, heparin-associated thrombocytopenia, thrombophilic syndromes, anticoagulant therapy and abdominal surgery (3, 4, 11, 12). The differential diagnosis for adrenal hemorrhage includes granulomatous infection, amyloidosis, septic shock, myocardial infarction, deposits from metastatic tumor, infiltrative diseases (e.g., lymphoma and

leukemia), adrenal crisis, pheochromocytoma, adrenal adenoma, and adrenal carcinoma (13). The pathogenesis of bilateral adrenal hemorrhage is still unknown (11). The adrenal gland receives a rich blood supply from the aorta and the inferior phrenic and adrenal arteries, which form a subcapsular plexus. Necrosis and hemorrhage may occur during hypotension and stress as a result of ischemia or during adrenal stimulation from vascular engorgement and stasis (11, 14, 15). Further, platelet aggregation followed by venous thrombosis, vasoconstriction, disruption of the vascular endothelium and regional hypotension can also lead to hemorrhage (16, 11). These factors are major contributors to the pathogenesis of adrenal hemorrhage, all of which lead to intramedullary ischemia and bleeding ensues with reperfusion of these damaged vessels. Besides the pathogenesis of bilateral adrenal hemorrhage is still under research (17). Clinical manifestations of adrenal hemorrhage can vary depending on the degree of hemorrhage. Many patients do not show specific signs of adrenal insufficiency, which usually occurs in those with damage of >90% in the adrenal cortex. Clinical symptoms associated with adrenal insufficiency caused by adrenal hemorrhage include pain, fever, nausea, vomiting, fatigue, weakness, obtundation, anorexia, dizziness, tachycardia, back pain, epigastric pain and hypotension (18, 14). However, symptoms could be limited and include abdominal or flank pain, abdominal tenderness or distension, palpable abdominal mass, nausea, vomiting, weakness, and weight loss. The laboratory findings also vary between patients and may include anemia, eosinophilia, leukocytosis, hypoglycemia, and electrolytes abnormalities (19, 20). Abdominal CT (with or without intravenous contrast) is the most reliable and widely used method for detecting adrenal hemorrhage (21). A hyperdense mass seen on non-intravenous contrast- enhanced CT with no enhancement after intravenous contrast or with enhancement only in a pattern of a thin peripheral rim is valuable (22, 23). Several studies have supported the use of MRI for diagnosing adrenal hemorrhage, as it has high sensitivity and specific results (3, 7, 24). Adrenal hemorrhage can show high signal intensity on T1-weighted images. MRI may also be useful for distinguishing subacute hemorrhage from chronic hemorrhage. Due to its rarity, there is no consensus on the optimal approach and management of adrenal hemorrhage thus far (23). Generally, the treatment of adrenal hemorrhage can be selected depending on whether adrenal insufficiency is present. If adrenal insufficiency due to adrenal hemorrhage is suspected,

adrenal hormone replacement therapy (either with glucocorticoids alone or glucocorticoids combined with mineralocorticoids) should be started promptly (25). However, before deciding whether to administer steroid therapy, it is important to examine the results for laboratory tests such as electrolyte levels, blood glucose levels, ACTH levels, and serum cortisol levels. If the patient does not have an urgent condition, a rapid ACTH test must be conducted. Only a few cases of idiopathic bilateral adrenal hemorrhage have been reported in the literature worldwide, most patients are treated with steroid replacement therapy because of adrenal insufficiency (11, 10). In some cases, steroid therapy is administered to prevent progression to adrenal insufficiency in advance, although the patient has not yet developed adrenal insufficiency (17). In our case, since the patient had no critical symptoms and abnormal laboratory findings that are associated with adrenal insufficiency, we initiated and maintained supportive management with close monitoring. Our patient presented with continuous dull abdominal pain. Surprisingly, she had no history of trauma or anticoagulant therapy, no medical history, and no family history. On admission, owing to her complaints of abdominal pain with mild febrile symptoms, we suspected acute enteritis. However, we were able to rule out infectious diseases because of no growth on blood culture, near-normal C-reactive protein level, and low body temperature. As adrenal hemorrhage can be associated with rheumatic disease such as antiphospholipid syndrome, we performed an autoantibody blood test including tests for antinuclear antibody, anti-ribonuclear protein antibody, lupus anticoagulant, anti-cardiolipin antibody, anti β_2 glycoprotein antibody, and antiphospholipid antibody. The antinuclear antibody and anti-RNP antibody test results were positive, whereas all the others were negative. To interpret these results, we consulted rheumatologists, who analyzed the patient's symptoms and laboratory results of rheumatology and concluded that the patient did not have any specific rheumatoid diseases. Therefore we ruled out the possibility of antiphospholipid syndrome.

As a result, any of other known causative factors were not found. Importantly, the patient case shows that abdominal pain can be related to idiopathic adrenal hemorrhage without symptoms of adrenal insufficiency. Close observation and along with symptom control and without steroid therapy may be sufficient to manage non-symptomatic idiopathic bilateral adrenal hemorrhage.

In conclusion, we presented the case of a 50-year-old woman with bilateral adrenal hemorrhage caused by an idiopathic condition. Through this case, we emphasize that before initiation of adrenal hormone replacement therapy, it is important to determine whether adrenal insufficiency is present. If there is no evidence of adrenal insufficiency, adrenal replacement therapy should be postponed until the presence of the adrenal insufficiency is confirmed.

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Conflict of interest

No conflict of interest relevant to this article was reported.

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