CASE REPORT

Adrenal crisis in a patient with acute myeloid leukaemia

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SUMMARY

Adrenal crisis is a group of clinical manifestation predominantly with hypotensive shock, electrolyte imbalance in a patient with adrenal insufficiency or in a patient who was abruptly withdrawn from glucocorticoid treatment acute myeloid leukaemia (AML) is one of the most common acute leukaemia in adults. Though the above diseases are commonly seen in individual patients, the coexistence of both conditions in the same patient is rare. We reported a 64-year-old African-American man with a history of bilateral deep vein thrombosis, who presented initially with fatigue, neutropenia and macrocytic anaemia. The patient developed a small bowel obstruction during his first hospital course, which resolved spontaneously with conservative management after an exploratory laparotomy. While waiting for his bone marrow biopsy, the patient developed hypotension, hyponatraemia and hyperkalaemia for which adrenal crisis was suspected. Later on, laboratory studies confirmed the diagnosis of primary adrenal insufficiency and the bone marrow was conclusive for AML.

BACKGROUND

Adrenal crisis is a group of clinical manifestation predominantly with shock and concomitant with other non-specific symptoms such as anorexia, nausea, vomiting, abdominal pain, weakness, fatigue, lethargy, fever, confusion or coma. It could present in a patient with adrenal insufficiency who has been subjected to serious stress or in patients who are abruptly withdrawn from glucocorticoid treatment.¹ It is more often to observe the distributive shock in the primary adrenal insufficiency patients.² In addition, electrolyte imbalances of hyponatraemia, hyperkalaemia, hyperkalemia are common in laboratory studies. Hyperpigmentation may or may not exist.³ The aetiological factors of malfunction of adrenal gland include infection, haemorrhage, ischaemia, malignancies, etc.

Acute myeloid leukaemia (AML) is the most common acute leukaemia in adults and it accounts for approximately 80% of cases.⁴ AML is a clonal disorder of haemopoietic stem cells. The inhibition of differentiation and accumulation of immature cells in peripheral and bone marrow, as well as reduced production of healthy haemopoietic elements, underscore the pathophysiology of AML. Patients can present with symptoms of anaemia (e.g. fatigue and dyspnoea), neutropenia (infections) and thrombocytopenia (bleeding).⁵ Bone marrow aspiration and biopsy provided a definitive component to the diagnosis of AML. According to the WHO classification, a 20% or more blasts in the peripheral blood or bone marrow is the diagnose of AML.⁶

Though there was a study showing that hyperkalaemia in acute leukaemia could be related to adrenocortical insufficiency,⁷ the coexistence of both conditions is rare in the same individual, as in our case presentation.

CASE PRESENTATION

A 64-year-old African-American man with a history of bilateral deep vein thrombosis presented to our emergency department (ER) initially with headache and fatigue for 4 weeks. The laboratory studies in ER showed neutropenia (white blood cell 2.6 K/ μ L) and macrocytic anaemia (H/H 6.2 g/dL/28.9%, mean corpuscular volume 131.7 fL). The detailed history showed that the patient had unintentional weight loss of 20 pounds in the past 1 month. The physical examination showed a frail African-American man with pale conjunctivae. No other significant abnormality was noticed on examination. After admission, the anaemia workup showed normal serum B₁₂ and folate and low reticulocytes. The stool occult blood was positive and this prompted the scheduling of an esophagogastroduodenoscopy and colonoscopy to identify the source of the gastrointestinal (GI) bleeding. After the bowel preparation for colonoscopy, the patient suddenly developed severe abdominal pain. Abdominal X-ray (figure 1) and CT scan showed small bowel obstruction (SBO). An emergent exploratory laparotomy was performed; however, no abnormality was identified. Repeat CT scan showed total resolution of SBO after supportive care was instituted. Other laboratory studies including serum protein electrophoresis, HIV1/2, hepatitis panel, anti-nuclear antibodies, direct coombs, haptoglobin, prostate-specific antigen and carcinoembryonic antigen were all negative. The patient received a total of 4 units of blood transfusion and was then discharged home to follow-up with a heme-oncologist for an outpatient bone marrow biopsy.

Two weeks later, the patient came back to the ER presenting with shortness of breath and generalised weakness. The physical examination showed that the patient was hypotensive with a blood pressure of 72/48 mm Hg. The laboratory studies showed pancytopenia, hyponatraemia, hyperkalaemia, hypercalcaemia and acute kidney injury. The ER physician suspected adrenal insufficiency and ordered a stat cortisol PM (afternoon), which turned out to be lower than the normal limit. The patient received a stat hydrocortisone 100 mg intravenous and normal saline bolus of 4 L. The patient's blood pressure was stabilised without pressors. The following day, cortisol AM (morning) and cosyntropin stimulation tests were performed and both came back positive for

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Figure 1 Small bowel obstruction was shown in abdominal X-ray (A) and CT (B) (green arrows: air fluid level).

low cortisol AM and no response to cosyntropin. Pertinent positive endocrinology studies included low aldosterone, low testosterone and high-adrenocorticotrophic hormone (ACTH). Pertinent negative endocrinology studies included normal prolactin, thyroid stimulating hormone, luteinizing hormone and insulin like growth factor-1. Further studies performed to determine the aetiology of the presenting adrenal insufficiency including rapid plasma reagin, HIV, fungal panel of *Aspergillus*, *Blastomyces*, *Candida albicans*, *Coccidioides*, *Histoplasma*, purified protein derivative (PPD) test and anti-21-hydroxylase antibody, were negative. The patient was continued with hydrocortisone 20 mg orally twice daily and resolution of the hyponatraemia and hyperkalaemia was noticed within 48 h. So far, the diagnosis of the idiopathic primary adrenal insufficiency had been reached without doubt and the patient was stabilised.

Well, will this explain all the signs and symptoms in this patient? What about pancytopenia? Due to the delay in the

insurance approval, the patient missed his previously scheduled outpatient bone marrow biopsy appointment. We consulted heme-oncologist for an inpatient bone marrow biopsy during this readmission. Bone marrow biopsy result came back in one week, which showed myeloproliferative disorder. Both peripheral smear and bone marrow aspiration showed abnormal production of leukocyte (figure 2). Flow cytometry showed left-shifted myeloid maturation with increased blasts of 19% and cell karyotype showed abnormalities of 46XY Del (7)(q22q36), and Add (11)(q21). In consideration of the patient's global clinical presentation and the result of the bone marrow biopsy, a diagnosis of AML was made.

DISCUSSION

Though the clinical scenario of both AML and adrenal insufficiency may be individually familiar, the coexistence of both

Figure 2 The peripheral smear and bone marrow smear showed the increased production of abnormal leukocyte in periphery and bone marrow (A, peripheral smear $\times 4$; B, peripheral smear $\times 40$; C, bone marrow $\times 4$; D, bone marrow $\times 40$).

disease processes in the same patient is relatively rare. Some obscure clinical presentations in this patient introduced more difficulties to the diagnoses. For example, while GI symptoms such as nausea, vomiting, diarrhoea and constipation are relatively common in patients with adrenal insufficiency; SBO is an uncommon presentation. So far, there are only few cases of acute mesenteric ischaemia⁸ and acute abdomen^{9 10} reported in adrenal insufficiency patients. GI endoscopic and radiographic studies are usually normal in patients with adrenal insufficiency presenting with GI symptoms,¹¹ and this was observed in our patient who also had both negative esophagoduodenoscopy and colonoscopy studies. The exploratory laparotomy did not identify any ischaemic or mechanic abnormalities of the bowel. Interestingly, an SBO with intussusceptions in an AML patient has been previously reported.¹²

The initial presentation of neutropenia, macrocytic anaemia with low reticulocytes, normal B₁₂ and folic acid and unintentional weight loss in this patient caused a high suspicion for myeloid dysplasia. On review of labs from his first admission, a mild transient hyponatraemia with serum sodium of 131 mEq, came to our attention. Now, we are wondering if this hyponatraemia could be an early hint to his adrenal insufficiency since hyponatraemia and hyperkalaemia are the two major electrolyte abnormalities of primary adrenal insufficiency. Interestingly, a study in 1997 by Demiroğlu *et al*⁷ showed that hyperkalaemia in acute leukaemia was a sign of adrenocortical insufficiency. They compared the adrenal function of 13 acute leukaemia patients with hyperkalaemia (>4.5 mEq) to 20 acute leukaemia patients with normal potassium level. Forty six percent of patients with hyperkalaemia had abnormal ACTH test while only five percent of acute leukaemia patients were with normal potassium levels. They recommended evaluating adrenal function in all acute leukaemia patients to avoid adrenal insufficiency crisis. If a thought of the adrenal insufficiency in this patient came earlier, could we have avoided his adrenal crisis by early steroid treatment? While the complexity in this patient made the early diagnosis quite difficult. First of all, the imbalance of electrolyte is also quite common in acute leukaemia patient,^{13 14} and secondly his history of chronic alcohol abuse may also have contributed to his hyponatremia.

According to the WHO classification, a myeloid neoplasm with 20% or more blasts in the peripheral blood or bone marrow is the standard to diagnose AML. However, the 20% blast threshold is not a mandate, especially in cases associated with specific genetic abnormalities.⁶ For example, our patient had a karyotype abnormality of chromosome 7 long arm q22–36. While the loss of heterozygosity on the long arm of chromosome 7 has been reported in several types of haematological malignancies, seven deletions at q21–36 are associated in AML with aggressive disease and poor prognosis.¹⁵ So, neither the diagnosis nor the treatment of AML should be delayed in this patient regardless of the blast count.

During the second admission, the patient presented with adrenal crisis to our ER. The patient received 100 mg intravenous hydrocortisone stat for the stabilisation of his blood pressure and electrolyte imbalance. Ideally, in a patient without a previous diagnosis of adrenal insufficiency, dexamethasone (4 mg intravenous bolus) is preferred to hydrocortisone because hydrocortisone could potentially interrupt serum cortisol measurement for diagnosis.¹⁶ However, in patients with hyperkalaemia of potassium >6.0 mEq/L (e.g. 6.3 mEq/L in this patient), hydrocortisone should be considered because of its mineralocorticoid activity.

Learning points

- ▶ Though rare, acute myeloid leukaemia (AML) and adrenal insufficiency can coexist in the same patient and a high index of suspicion must be maintained for diagnosis.
- ▶ Electrolyte imbalance in acute leukaemia patients should raise the suspicion for adrenal insufficiency. Patients may benefit from steroid therapy to prevent an acute adrenal crisis.
- ▶ Specific genetic abnormalities may determine the aggression and prognosis of AML in certain patients hence prompting diagnosis; treatment is essential regardless of the blast count in these patients.
- ▶ Dexamethasone is the preferred steroid to use in patients with symptoms suggestive of adrenal crisis (without a prior diagnosis of adrenal insufficiency). Consider hydrocortisone use for patients with severe electrolyte imbalance.

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Competing interests None.

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