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LETTER TO THE EDITOR

Acute myeloid leukemia presenting as bilateral adrenal hemorrhage

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Dear Editor,

Bilateral adrenal hemorrhage is a rare medical emergency that can result in hypotensive shock and death without prompt treatment [1]. Acute myeloid leukemia (AML) is the most common acute leukemia in adults [2] and is defined by the presence of 20% or more myeloblasts in the marrow or blood [3]. We report here a patient whose initial diagnosis of AML was made following presentation with bilateral adrenal hemorrhage initially without evidence for adrenal insufficiency but later complicated with adrenal crisis.

A 71-year-old female with no significant medical history presented to the emergency department with increasing abdominal pain for 2 days. Her hemoglobin was 9.1 g/dl, platelets were 73×10^9/L, and total leukocyte count was 15.2×10^9/L with 4% blasts in peripheral blood smear. CT imaging (Fig. 1a, b) and MRI (Fig. 1c, d) of the abdomen revealed bilateral adrenal hemorrhage. There were no clinical features of adrenal insufficiency on presentation; cortisol was elevated at 35 μg/dL (ref 3.1–22. μg/dL), and ACTH was elevated at 155 pg/mL (ref 6–50 pg/mL). She underwent marrow evaluation (Fig. 1e–g) 1 day after admission which showed hypercellular marrow for age (80% cellular) and trilineage dysplasia with 20–25% blasts. Karyotype analysis of 15 metaphases revealed complex abnormalities including a stemline abnormal clone with a translocation between chromosomal bands 2q21 and 12p11.2, losses of one copy of chromosomes 3 and 7, and deletions in a 5q and a 12p in twelve cells, as well as subclone with additional aberrations of an extra copy of chromosomes 8 and 22 was noted in two cells. Next-generation sequencing detected pathogenic *TP53* mutation with variant allele frequency of 52.8%. PCR for *FLT3* mutations was negative. She was diagnosed with AML with myelodysplasia-related changes, and she began induction therapy with liposomal daunorubicin and cytarabine (i.e., Vyxeos). Four days after initiation of chemotherapy (13 days after admission), she developed confusion, fever, and hypotension indicating adrenal crisis. She had no electrolyte abnormalities, but her morning cortisol level was found to be low at 0.8 μg/dL. Repeat CT showed unchanged adrenal hemorrhages. She received IV fluids and hydrocortisone (50 mg IV every 8 h) with resolution of symptoms. Hydrocortisone was tapered to 10 mg in am and 5 mg in early pm but had to be increased to 20 mg in am and 10 mg in pm due to orthostatic dizziness, hyperkalemia, and hyponatremia. Bone marrow on induction day 14 showed 15% cellular marrow with 25% blasts. She did not receive re-induction. She experienced count recovery by day 21 after treatment, and bone marrow showed remission. She proceeded with one cycle of liposomal daunorubicin and cytarabine consolidation followed by allogeneic stem cell transplant from matched unrelated donor.

Although AML often presents with bleeding symptoms due to thrombocytopenia and disseminated intravascular coagulation [4], the occurrence of adrenal hemorrhage in this disease is rare, with few published case reports describing adrenal crisis in patients with acute leukemia or myelodysplastic syndrome (MDS) [5–9]. Substantial physiologic stress, including malignancy, can precipitate adrenal hemorrhage, and this process is hypothesized to be mediated by excessive ACTH release, which increases adrenal blood flow [10]. Thrombocytopenia and possible blastic infiltration of the adrenal glands may have predisposed this patient to adrenal hemorrhage, but

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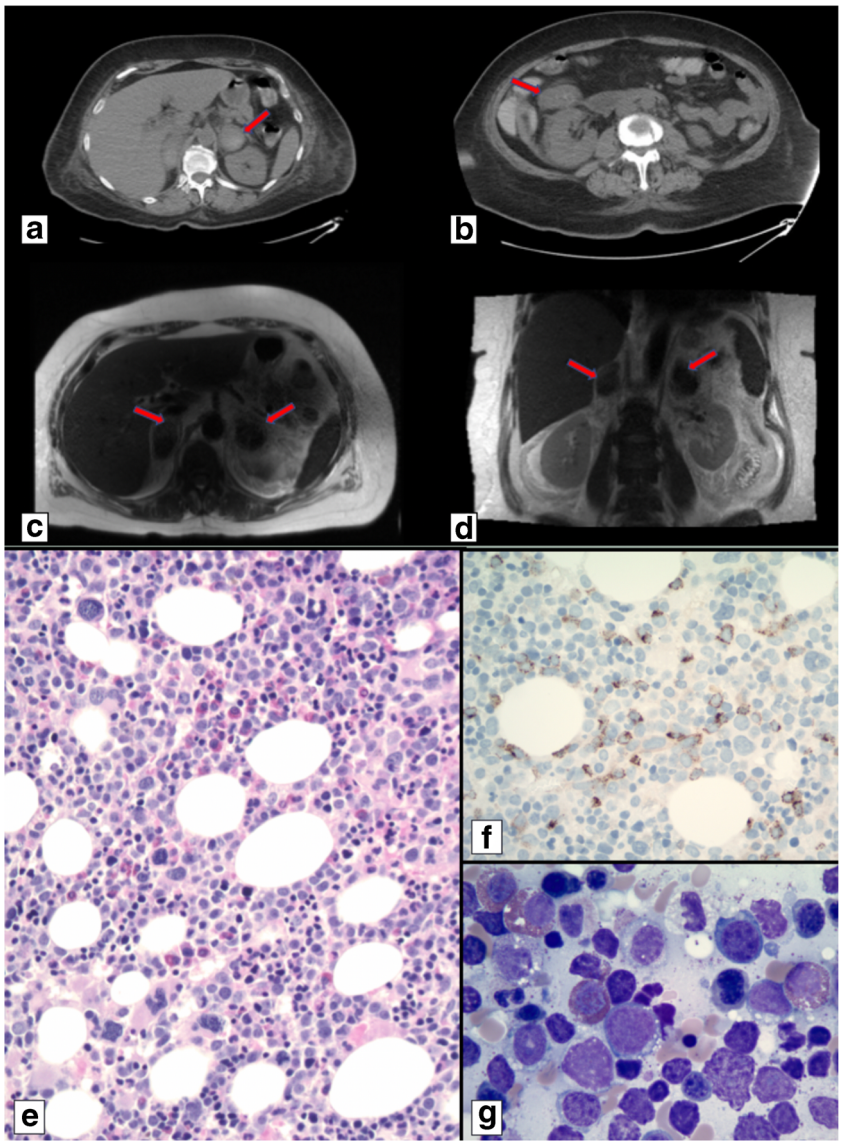

Fig. 1 **a**, **b** Transverse CT of the abdomen with intravenous contrast showing enlargement and diffuse infiltration of periadrenal fat bilaterally, suggestive of adrenal hemorrhage. **c** Transverse and **d** coronal T2-weighted MRI of the abdomen showing bilateral adrenal hematomas with the right adrenal gland measuring up to 4.8 cm and the left adrenal gland measuring up to 3.8 cm. **e** The bone marrow biopsy is hypercellular and shows myeloid left shift with scattered dysplastic megakaryocytes. **f** CD34 stain highlights approximately 20% blasts. **g** Aspirate smear shows scattered blasts as well as erythroid elements with irregular nuclear borders, a sign of dysplasia

notably, she had few blasts in blood, barely reached the 20% cut-off for AML diagnosis in the marrow, and did not possess any other risk factors, as she was not on anticoagulant or antiplatelet therapy, had no history or evidence of coagulopathy or hypercoagulable state, did not have infection, and had no recent surgical history.

Compliance with ethical standards

Conflict of interest NAP consulted for and received honoraria from Alexion, Pfizer, Agios Pharmaceuticals, Blueprint Medicines, Incyte, Novartis; received research funding (all to the institution) from Boehringer Ingelheim, Astellas Pharma, Daiichi Sankyo, Sunesis Pharmaceuticals, Jazz Pharmaceuticals, Pfizer, Astex Pharmaceuticals, CTI BioPharma, Celgene, Genentech, AI Therapeutics, Samus Therapeutics, Arog Pharmaceuticals, Kartos Therapeutics; and received grant funding from Celgene. Other authors (HM, AJS, and KG) report no relevant financial conflicts of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from the individual included in this report.

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