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Case Report

Fatal intracranial hemorrhage as the presenting sign of acute promyelocytic leukemia: A case report ☆

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ABSTRACT

Intracranial hemorrhage (ICH) can be a devastating medical event with numerous potential etiologies. In young people under age 40, ruptured vascular malformation is the most common cause of ICH. Without critical review of imaging and laboratory findings and clinical suspicion beyond vascular malformation, alternative etiologies of hemorrhage may be overlooked in the younger age group. Here we present a case of a 22-year-old male presenting with large ICH originally thought secondary to ruptured vascular malformation. After careful review of all imaging and laboratory findings, the patient was found to have hemorrhage secondary to acute promyelocytic leukemia (APL). Though ICH proved fatal in this case, early treatment of acute leukemia with appropriate chemotherapeutic agents and correction of coagulopathy could be life saving for patients with less severe intracranial injury.

Introduction

Intracranial hemorrhage (ICH) can be a devastating medical event caused by a multitude of underlying pathologies. Trauma, uncontrolled hypertension, hemorrhagic conversion of ischemic infarct, ruptured vascular malformation, and amyloid angiopathy are all typical underlying pathologies for patients presenting with acute ICH [1]. In young people (<40 years of age), ruptured vascular malformation is the most common pathology, causing up to 49% of ICHs [2]. Driven by this data, a high suspicion for vascular malformation in young people may cause alternative etiologies to be overlooked. Here we present a case of fatal ICH with high suspicion for underlying vascular abnormality that was instead found to be the presenting sign of acute promyelocytic leukemia (APL, a subtype of acute myelogenous leukemia, AML).

Case report

The patient is a 22-year-old male without significant past medical history who presented to the emergency department (ED) following reported seizure activity at home. En route to the ED emergency medical services noted continued seizure activity, and on arrival to the ED patient was found to have

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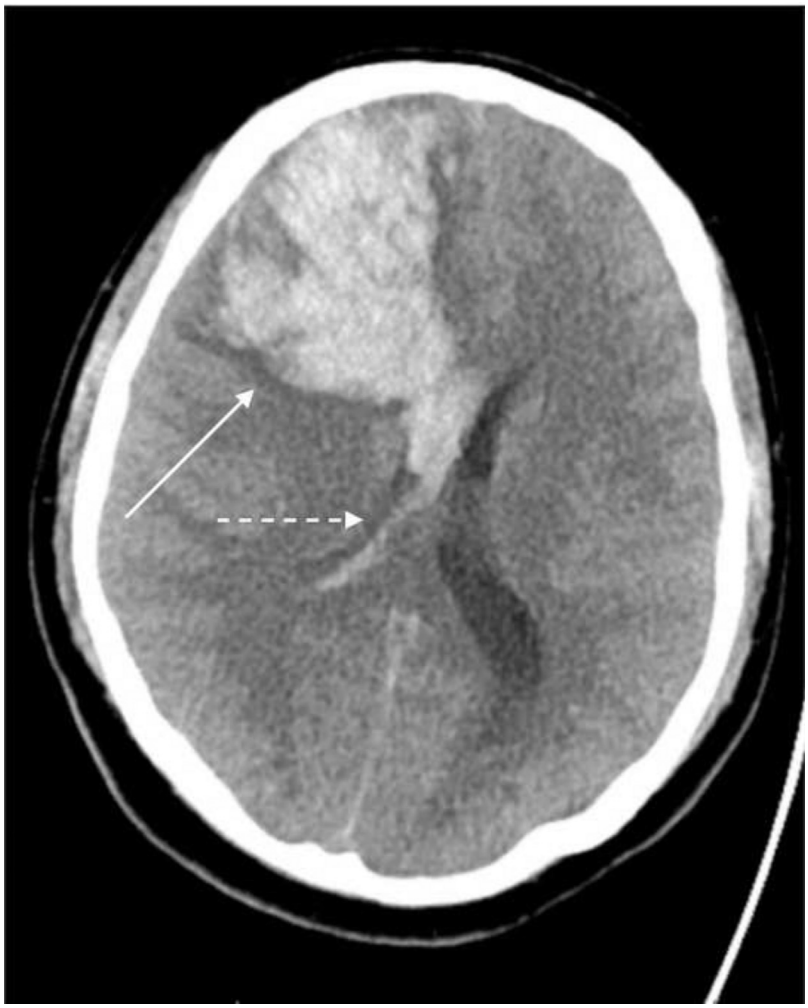

Fig. 1 – CT head obtianed on patient arrival. Solid arrow indicates right frontal lobe hemorrhage. Dashed arrow indicates interventricular extension with midline shift.

anisocoric, non-reactive pupils with extensor posturing in all extremities. Computed Tomography (CT) head without contrast showed a large, flame-shaped ICH in the right frontal lobe causing 1cm of right to left midline shift and uncal herniation, with extension into the frontal horn of the right lateral ventricle (Fig. 1). CT angiography of the head obtained on arrival showed no evidence of vascular abnormality, though suspicion remained high for underlying vascular lesion due to patient age and acute ICH (Fig. 2). Given clinical and radiographic evidence of intracranial hypertension and brainstem herniation, he was taken emergently to the operating room for decompressive hemicraniectomy. Intraoperatively the patient was found to be pancytopenic, with lab results including white blood cell count 4.4, hemoglobin 6.4 with mean corpuscular volume 87.5, and platelet count 7. Peripheral smear subsequently revealed blasts and promyelocytes consistent with APL. The patient was promptly initiated on All-trans retinoic acid (ATRA) and hydroxyurea. Further work up was initiated with PML-RARA and FISH for t(15;17) which were confirmatory for APL. On postoperative day 1 patient had enlargement of ICH with enlarged ventricles on repeat CT head (Fig. 3) and underwent external ventricular drain placement due to concern for developing hydrocephalus. Opening pressure was elevated at 30 mm Hg consistent with elevated intracranial pressure (ICP). On postoperative day 2 the patient had elevated ICP refractory to medical treatment. Further surgical intervention with frontal lobectomy to decrease ICP was discussed, but given continued pancytopenia and multiple ischemic infarcts demonstrated on repeat CT head (Fig. 4), it was determined that the risks outweighed the benefits for further surgical intervention. The patient was then found to be in multisystem organ failure requiring initiation of pressors and dialysis. On postoperative day 3 the decision was made to withdraw care and transition to comfort measures. Patient did not undergo autopsy.

Discussion

There is extensive documentation of ICH in patients suffering from AML. In fact, ICH has been found to be a leading cause of death in patients with AML, second only to infection [3].

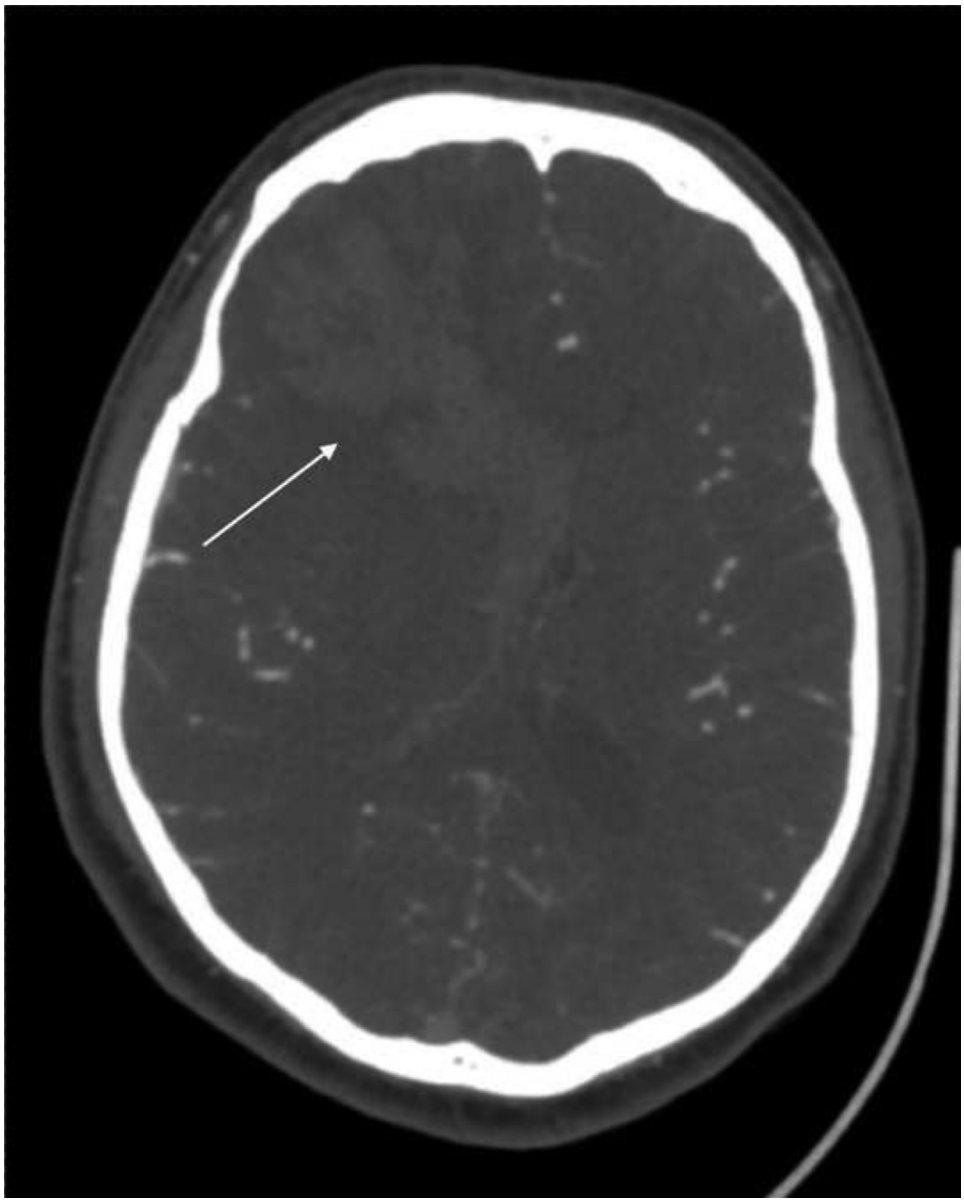

Fig. 2 – CT angiography (CTA) head obtained on arrival. Solid arrow indicates where potential vascular malformation would expect to be seen.

Clinical factors such as hyperleukocytosis (White blood cell count >100,000), prolonged prothrombin time, sepsis, and disseminated intravascular coagulation (DIC) have been found to increase the risk of ICH in patients with hematological malignancy [3].

A case report by Balmages et al. discusses a 55-year-old woman who was diagnosed with AML after presenting to urgent care with easy bruising over the course of several weeks. Patient's laboratory investigations on initial evaluation were concerning for AML, and she was scheduled for oncological evaluation. Patient then presented to the emergency department prior to scheduled oncology follow up with continued bruising and lower extremity pain, and at this time patient's laboratory findings were consistent with the APL subtype of AML. She was initiated on ATRA and transferred to a higher level of care, but unfortunately had progressive altered mental status before transfer was completed. Her Glascow Coma Scale declined to 1-1-1 with fixed, dilated pupils by the time of presentation to tertiary care center, and CT head showed large ICH. It was determined that surgical intervention was not within her wishes, and she expired within 24 hours [4].

While a majority of reports of intracranial hemorrhage associated with acute leukemia are in patients with a known diagnosis, such as the patient noted above, we have identified few case reports of patients with acute intracranial hemorrhage as the first presenting sign of acute leukemia. A report by Patil et al. discusses a case of a 17-year-old male presenting with acute intracranial hemorrhage as the presenting sign of Acute Lymphocytic Leukemia (ALL). Similar to our case, on presentation the patient was found to have anisocoric pupils

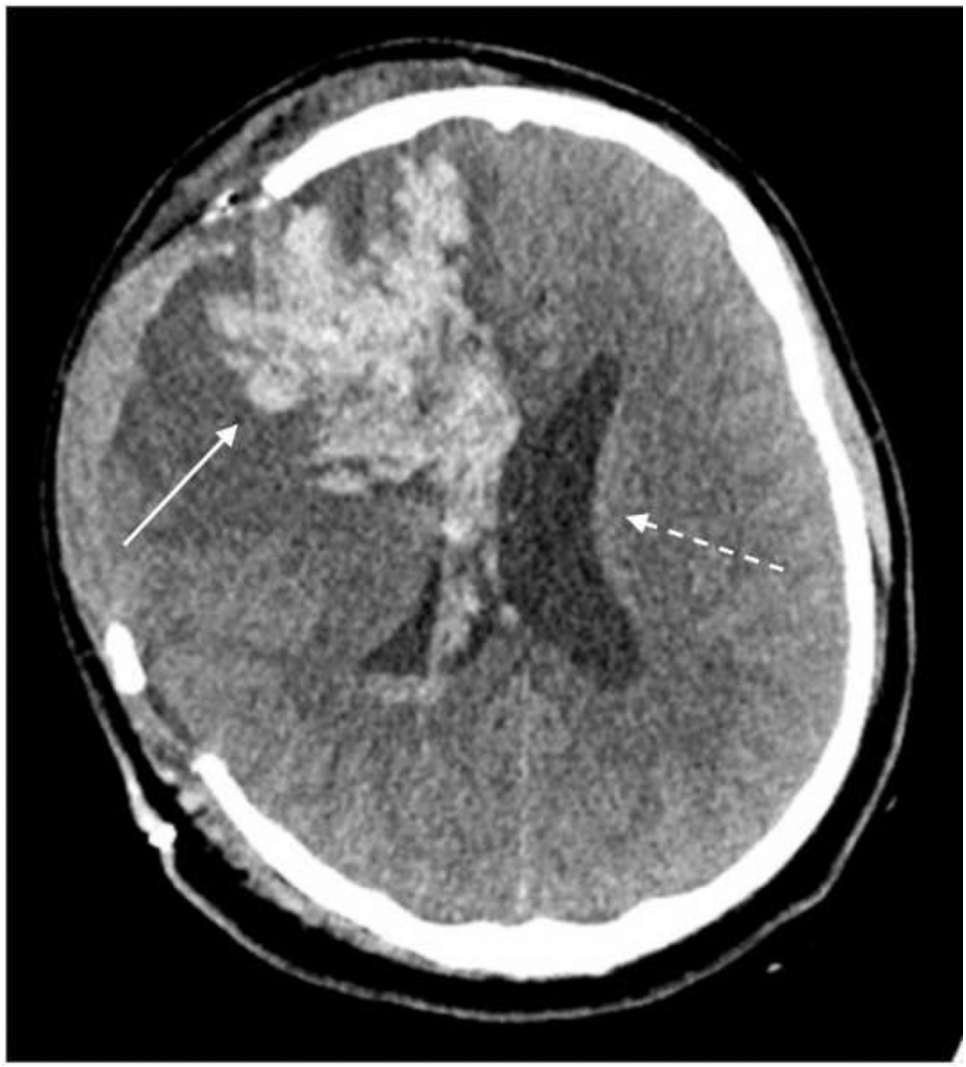

Fig. 3 – CT head obtained post-operative day one status post craniectomy. Solid arrow indicates expanded right frontal lobe hemorrhage. Dashed arrow indicates ventricular expansion consistent with developing hydrocephalus.

with flexor posturing, with presenting laboratory evaluation showing thrombocytopenia and peripheral smear consistent with ALL. Intracranial imaging showed large, right sided intracranial hemorrhage, he was taken for decompressive hemicraniectomy, but quickly progressed to brain death despite maximal surgical and medical therapies [5]. Sakai et al. describe the case of a 15-year-old male who was found by family in cardiopulmonary arrest. The patient was not transported to a medical facility for evaluation as he was found to have expired on EMS arrival. Autopsy was performed showing multiple subcutaneous and intramuscular hemorrhages, as well as large right hemispheric ICH with intraventricular involvement. Histopathologic evaluation of bone marrow and peripheral blood smear were consistent with APL [6].

In each patient described above, the ultimate cause of death was ICH due to DIC, a known severe complication of acute leukemia. Additionally, ICH due to DIC in the setting of previously undiagnosed acute leukemia has been described in few other case reports, including those of a 53-year-old patient with APL [7], a 31 year old patient with AML [8], and a 55 year old patient with ALL [9]. In the first case we present, the patient promptly began treatment for acute leukemia based on laboratory values that raised suspicion for the diagnosis, though ultimately treatment was initiated too late. Patients in the second and third case, similar to our patient, had unknown etiology of ICH, no previous signs or symptoms of acute leukemia, and did not begin chemotherapy prior to progressing to death.

Early initiation of pro-hemostatic agents like ATRA is paramount in the initial management of AML. When major hemorrhagic complications can be avoided, most patients with AML can be cured of this otherwise deadly disease [10]. In the case reported here, no medical treatment would have altered the outcome given the devastating brain injury from his hemorrhage. However, in patients with smaller intracranial hemorrhage or less severe brain injury, early diagnosis and treatment of acute leukemia and coagulopathy could be lifesaving.

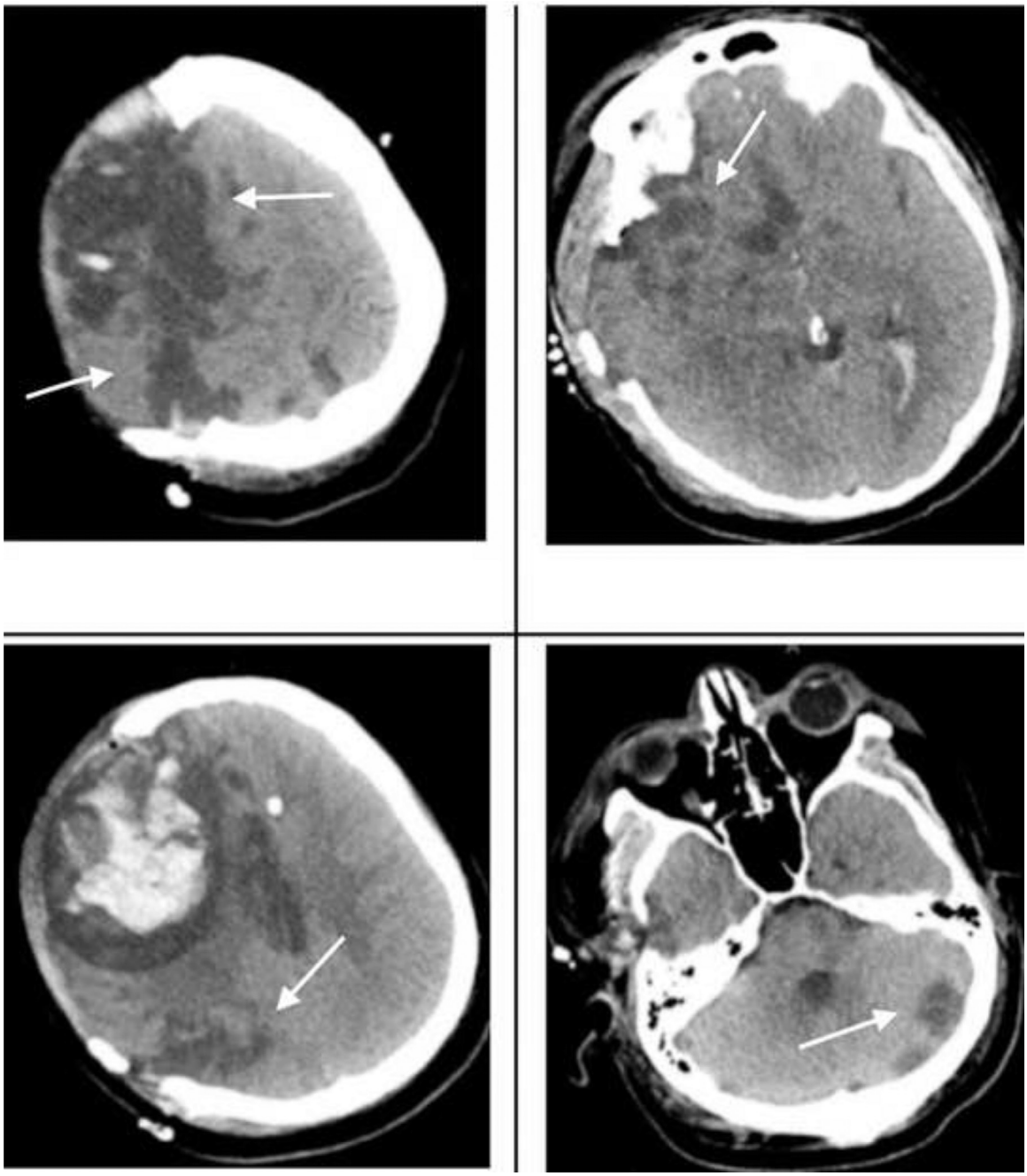

Fig. 4 – Multiple slices of CT head obtained on post-operative day 2. Solid arrows indicate hypodensity consistent with multifocal ischemic infarcts.

Conclusion

Intracranial hemorrhage is a common cause of sudden death in patients diagnosed with APL, and this case adds to a paucity of reports of intracranial hemorrhage as the presenting sign of APL. The early consideration of APL and urgent initiation of ATRA is necessary for treatment and prevention of early death secondary to hemorrhagic complications in patients with APL [11]. We hope that this report highlights that APL should be considered in previously healthy patients presenting with acute ICH and DIC. This is particularly true in the younger population, where suspicion of alternative etiology such as vascular malformation may lead to delayed diagnosis and treatment.

Patient consent

Informed consent was obtained from patient's next of kin for submission and publication of this manuscript

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