Case Report

Blast crisis of chronic myeloid leukemia initially presenting as severe acute intracerebral hemorrhage

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Abstract

Intracerebral hemorrhage (ICH) is frequent pathology in emergency department. Coagulopathy leading to ICH are rare. Intracerebral hemorrhage is a leading cause of mortality among patients diagnosed with chronic myelogenous leukemia (CML). In this report we discussed the case of a previously healthy male patient, who presented with fatal ICH, newly diagnosed with blast crisis in CML.

Keywords: Blast crisis, intracerebral hemorrhage, leukemia

Introduction

Chronic myelogenous leukemia (CML) is a clonally myelopoliferative disorder of the hematopoietic stem cell. Intracerebral hemorrhage (ICH) is a leading cause of mortality among patients diagnosed with CML. It accounts for 5–10% of stroke events. Coagulapathies leading to ICH are rare, and are divided to acquired and congenital disorders of homeostasis including bleeding due to neoplasm.[1] CML is one of these acquired coagulopathies that can be rarely accompanied of ICH in acute blastic phase. Primary care physicians should maintain a high index of suspicion for hemorrhagic complications in patients presenting with new onset CML. This report highlights the importance of primary care physicians in gaining familiarity with medications uncommonly used in emergency. The author's hope is that this will improve primary care physician medical practice by highlighting the emergent nature of the complications of CML. In this report we discuss the case of a previously healthy male patient who was presented to emergency department ambulating, alert and oriented and while en route to a higher level of care quickly deteriorated before further interventions could be implemented diagnosed as CML in blast crisis from ICH as first presentation.

Case Report

A previously healthy 65-year-old male with no medical or surgical history presented to the emergency department for a minor head trauma caused by a drop height. His symptom begun that evening. He progressively began to have severe intensity headache which were not relieved with pain killer. He did not complain of fever, chills, abdominal pain but was nauseous after dinner. His wife decided to bring him to emergency department to consult. While en route to hospital he became acutely altered and lost consciousness with vomiting.

Upon initial evaluation, the patient had a temperature of 98°F, pulse of 87/min, respiratory rate of 18/min, blood pressure of 180/80 ml of Hg, pulse oximetry showed 100% saturation on room air. Glasgow scale was 12. A hemeplegia of left hand side

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was objectified. The patient pupils were equal and reactive to light. Abdominal palpation noted a diffuse abdominal distention with a splenomegaly beyond the umbilicus and a painless hepatomegaly. Skin examination showed no purpuric spot.

One hour after his arrival to community ED, right pupil was fixed and dilated. The patient presented a seizure at the second hour of his arrival in hospital and two episodes of vomiting. He was given 50 g manitol and after half an hour another 50 g manitol was administered. An anti-convulsion treatment was then indicated; the patient received 15 mg/kg of phenobarbital in 20 min. The patient continued to have headache despite the analgesic treatment.

Initial laboratory data was significant for WBC count of 51.7 × 10^9/L, platelets of 16 × 10^9/L, and hemoglobin of 9.2 g/dL. Prothrombin time (PT) was 45% and international normalized ratio (INR) was 1.7. Examination of blood smears allowed presuming the diagnosis of CML (19% metamyelocytes, 26% myelocytes, and 3% promyelocytes) [Table 1 and Figure 1].

A contrast enhanced computerized tomography (CT) of the head was performed at the second hour after the trauma, which showed a large parenchymal hematoma in right subcritical parietal lobe (72 mm × 47 mm × 42 mm) without enhancement after injection of contrast and surrounded by edema. The mass effect exerted from this hematoma resulted in right to left 10 mm midline shift. There were no vascular abnormalities to explain this ICH, nor bone fracture [Figure 2].

Even after osmotherapy by a 20% mannitol (50 gm) his right pupil became fixed and dilated shortly thereafter, and another 50 gm mannitol was administered. The patient condition deteriorated further and patient became comatose with Glasgow coma score which was 1-1-1. His pulse was 43/min, blood pressure was 236/98 mm of Hg, respiratory rate was 13/min, and oxygen saturation ratio was 98% on 15 L by nonbreathable mask. He was incubated for airway protection. Patient was emergently evaluated by Neurosurgery department and discussed with patient's family member about the chance of mortality associated with ICH of this size of 72% and that full recovery even he survived at all, would be unlikely. Patient parties refused for any surgical intervention in view of his chances of significant recovery were unrealistic.

An abdominal ultrasound was performed, showing an enlarge spleen of 30 cm height with regular contours and an increase kidney size. He developed sudden circulatory arrest in a matter of hour. Cardiopulmonary resuscitation was carried without recovery of spontaneous circulation. The patient died within 16 h of his arrival to the Emergency. The patient's autopsy showed a hemorrhagic brain mass in right parietal lobe. Abdominal autopsy done revealed splenomegaly with homogenous hepatomegaly.

Discussion

Spontaneous ICH accounts for 5–10% of stroke events and has a high mortality.[2] Multiple pathological etiologies can cause ICH including trauma, cerebrovascular disease, and coagulation disorders.[3] The medical history with unusual headache, focal

Table 1: Results of laboratory investigations on admission

Variable	Value	Reference range
White blood cell (×10^9/L)	51.7	4.0-11
Hemoglobin (g/dL)	9.2	13.5-17.5
Platelet count (×10^9/L)	16	15-35
Differential count (%)		
Neutrophil	07	40-70
Lymphocytes	3	22-44
Blasts	34	0
Metamyelocytes	19	0
Myelocytes	26	0
Promyelocytes	03	0
Basophils	6	1
Monocytes	2	4-11
Prothrombin rate (%)	45	70-100

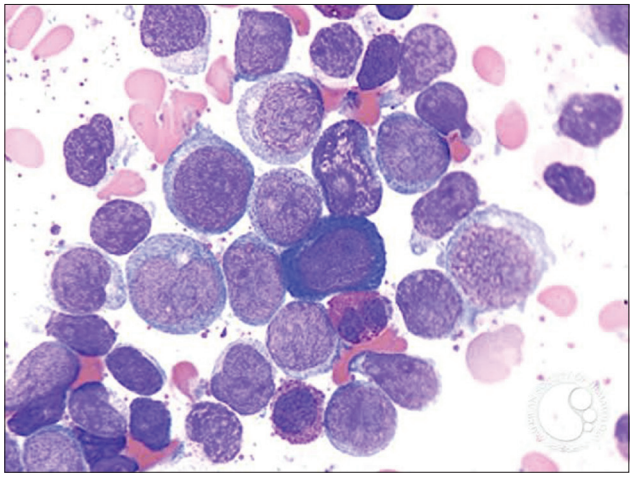

Figure 1: Blood picture showing myelocytes, metamyelocytes and basophils

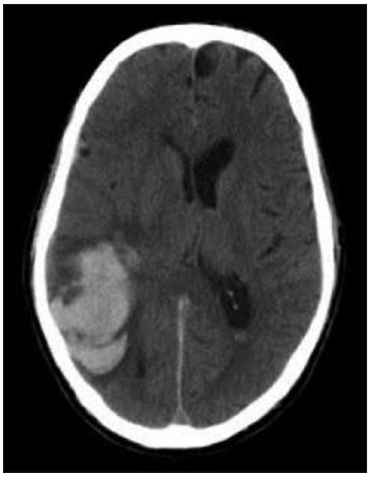

Figure 2: CT Scan of Brain showing parenchyma hematoma with associated edema causing midline shift

neurological deficit, changes in mental status leads to carry out non-contrast CT scan of head which shows the ICH. Our case had similar presentation. Hence the cause of ICH must be elucidated.

CML accounts for approximately 15% of adult leukemia. It is a rare myelopoliferative disease. The incidence of CML is 1.5 per 100,000 people per year and the age adjusted incidence is higher in men than in women (1.9 vs. 1.1).[4] The incidence of CML increases slowly with age until the middle forties, when it starts to rise rapidly. The only confirmed predisposing factor is exposure to ionizing radiation and cigarette smoking accelerated the progression to blast crisis.[5] CML has a triphasic clinical course: an initial indolent chronic phase (CP), which is present at the time of diagnosis in ~83% of patients with a median duration of 3–5 years; an accelerated phase lasting 6–18 months, in which neutrophil differentiation becomes progressively impaired and leukocyte counts are more difficult to control with myelosuppressive medications; and a terminal blast crisis (BC), a condition resembling acute leukemia lasting 3–6 months in which myeloid or lymphoid blasts fail to differentiate.[6]

CML is a disease characterized by specific cytogenetic marker, the Philadelphia chromosome, which results from a balanced translocation of segments between chromosome 9 and 22. One quarter of patients present with blastic phase (BC), without the pre-existing chronic phase being diagnosed[7] as in our present case discovery of the CML was immediately in the blast crisis so far as not reported in the literature.

The most common clinical signs of CML are weight loss, night sweats, malaise, sometimes marked exhaustion and prostration as predominant symptom. Symptoms resulting from splenomegaly, when it is marked, included feeling weight, dragging, or actual pain under the left costal margin. Actual pain over the spleen may occur after splenic infarction and may mimic an acute abdominal emergency.[6] Onset is usually insidious, symptoms often having been present for many months before diagnosis. In fact, clinical manifestations are mostly absent in chronic phase.[4] Priapisim is also described in rare cases. Approximately 85% of patients are diagnosed in the chronic phase; progression to the accelerated and blast phases (BC) generally takes 3–5 years. The median time to development of blastic phases approximately 36 months before the advent of interferon therapy, 48 months with interferon therapy and 5 years after allogenic bone marrow transplantation.[7] Recently the treatment with tyrosine kinase inhibitors can control the clinical features for years or even decades (10–20 years) in the majority of patients.[4,8] Blastic transformation may be suspected clinically because it is commonly associated with symptoms of anorexia, malaise, fatigue, night sweats, bone pain, and splenic discomfort. The onset of additional clinical findings, such as fever, lymphadenopathy, which is absent in the chronic phase of the disease, cachexia, pallor, sternal tenderness, progressively increasing splenomegaly and progressive immaturity of marrow and blood granulocytes, is of the blast phase. In most cases, the blast cells are myeloid, but in 20–30%, the blast cells have lymphoblastic features.[6,7] Some atypical presentation of CML was reported in literature with infiltration of nervous system. The nature of these manifestations depends on the site and the extent of the hemorrhage. Hemorhhage into the ocular funds may cause impairment of vision, while hemorrhage into the internal ear might cause deafness and tinnitus and vertigo.[7]

Leukostasis is clinically suspected when respiratory or neurological disorders appear in a patient with an important leukocytosis (more than 100,000/ml for CML). This leukostasis is much rare in the CML as compared to its rate in acute leukemia's.[3] The pathophysiological mechanism of ICH is not yet well determined; disorders of hemostasis would be implicated, as well as vascular microthrombosis by leukocytes[3] and it seems to occur in the accelerated or blastic phase more than in chronic phase.[9] While ICH is often identified in autopsy studies of leukemic patients or in patients diagnosed with acute leukemia, it is rare for ICH to be the presenting sign that ultimately leads to the diagnosis of leukemia[3] as far as in the knowledge of author. The prognosis at this stage is often fatal within the first 10 days. ICH is a grave prognosis indicator in either myelogenous or lymphoblastic leukemia and is second only to infection as the most common cause of death which is unresponsive to treatment.[3] Such is the case of our present report.

While our clinical report presents an additional case of spontaneous acute hematoma and describes its association with CML, it demonstrates some conclusion. First a careful clinical history and non-contrast head CT scan are often necessary for any patient presenting with symptoms suggestive of potential intracranial pathology and leads often to a diagnosis of ICH. Second, the presence of acute hematoma in the absence of head trauma should warrant further investigations like the practice to obtain basic blood workup that includes a complete blood count, peripheral blood film, a complete metabolic panel and coagulation studies for every patient admitted to emergency medicine practice.[10-12] The management of ICH in cases with coagulopathy is largely medical.[3] Current recommendations from the American Heart Association give consideration to surgical evacuation of hemorrhage that is located within 1 cm of the cortical surface and associated with substantial mass effect edema or midline shift.[3] This report highlights the importance of primary care physician in gaining familiarity with medications uncommonly used in the emergency medicine. The patient's rapid progression makes this a valuable example of how critical a role the primary care physician can play in the care and management of patients with ICH. In our case treatment was medical because the hematoma was located within more than 1 cm so he received transfusion of plasma regarding his low rate of prothombin time, and phenobarbital to seizures.

Conclusions

In conclusion, initial blast crisis of CML presenting as ICH, as emergency physicians we need to be aware of this diagnosis and maintain a high degree of suspicion for ICH. It should

be considered in the differential diagnosis of any situation in which sub-aracnoid hemorrhages or ICH, epidural and subdural hematomas[13] are detected prior to the diagnosis of leukemia with unknown etiology, particularly in the setting of hyperleukocytosis, and a characteristically abnormal peripheral blood smear. The author's hope is that this case will improve emergency medical practice by highlighting the emergent nature of complications of CML in blast crisis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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