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Status epilepticus and acute promyelocytic leukemia

Sunil Kumar Garg[✉], Pragya Garg

Dubai NMC Hospital, Dubai

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ABSTRACT

Neurological manifestations are rare as initial presentation in acute promyelocytic leukemia (APL). This case illustrates status epilepticus as initial presentation in this disease. Atypical cells on peripheral smear led to the diagnosis of leukemia.

1. Introduction

Central nervous system (CNS) involvement is a rare complication of APL and is encountered more frequently at the relapse stage than at presentation and only few cases have been reported in medical literature[1-5].

Most of the signs and symptoms of acute promyelocytic leukemia are seen in acute myelogenous leukemia (AML) and it includes fatigue, weakness and dyspnea due to low hemoglobin, easy bruising or bleeding due to thrombocytopenia and fever or infection related to leukopenia. Most patients with APL present with pancytopenia. APL differs from AML in that most patients present with coagulopathy and it has been described as disseminated intravascular coagulation with associated hyperfibrinolysis. In 40% of untreated patients pulmonary and cerebral hemorrhage can occur. However, a few present with thromboses.

2. Case report

A 26 year old previously well male presented to emergency department with history of recurrent seizure for last around one hour without regaining consciousness. He was intubated, ventilated and shifted to intensive care unit on midazolam infusion after loading with levetiracetam. His heart rate was 107 per minute regular, blood pressure 188/116 mmHg, respiratory rate 22 per minute and temperature 36 degree centigrade in emergency department. He was unconscious and pupils were semidilated and fixed. His serum electrolytes, renal and liver function values were within normal range. Complete blood counts revealed hemoglobin 16.2 g/dL, total white blood cell count 10 600, neutrophils 28%, lymphocytes 41%, monocytes 0.3%, eosinophils 0.5% atypical cells 23% and platelet count 158 000. EEG done in intensive care unit showed beta fast

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[✉]First and corresponding author: Sunil Kumar Garg, NMC hospital, Dubai.
E-mail: sucare12@yahoo.co.in

activity without any seizure discharges. His initial lactate values were elevated. CSF examination done on second day was normal but serum values of calcium, magnesium and uric acid were elevated.

His sedation was stopped after 24 hours but no improvement in sensorium noticed thereafter. EEG was repeated and it revealed generalised slowing. MRI brain showed multiple acute to subacute infarcts in bilateral thalami, mid brain involving both cerebral peduncles, pons, right corona radiata, right posteromedial temporal, right occipital cortex and right parahippocampal gyrus. In view of anticipation of prolonged ventilation tracheostomy was done and he was weaned off from ventilator.

Atypical cells in peripheral smear continue to increase steadily thereafter and reached more than 90% on seventh day of admission. He developed further worsening of neurological response on sixth day so he became completely unresponsive and developed apnea so put back on mechanical ventilation. At this stage CT brain revealed large hypodensity involving left temporoparietooccipital lobe exerting mass effect and CT neck angiography showed significant reduced calibre of left internal carotid artery and the left anterior and middle cerebral arteries were not contrast opacified. There was also evidence of eccentric filling defect in the left vertebral artery and distal basilar artery as well as its branches were not contrast opacified. He was given supportive management including antibiotics and antifungals because of later development of candidemia.

Morphology on Flow cytometry revealed approximately 75% blast cells and cytochemical MPO positivity. Finding of immunophenotyping includes blast cells (moderate SSC/dim CD 45) express CD 33 (heterogenous) and CD 117 (partial/dim). All other markers including HLA-DR negative. Confirmation of acute promyelocytic leukemia was done by cytogenetic analysis and demonstration of promyelocytic leukemia-retinoic receptor alpha rearrangement by reverse transcriptase PCR in the peripheral blood cells. Patient succumbed to his illness on 10th day of admission.

3. Discussion

Central nervous system involvement with APL commonly occurs in relapse; however, it is rarely seen at presentation, with only few reported cases in the literature. This case is the first to describe a patient with APL who presented with a status epilepticus as per our knowledge.

APL is a unique disease entity associated with distinctive morphology and chromosomal abnormality, and it is often accompanied by severe coagulopathy[6]. However, a few present with thromboses. In an observational cohort study of 379 patients with acute leukemia, the overall incidence of thrombosis was 6.3% and it was the presenting manifestation in 3.4% of all patients, with a higher rate among patients with APL (9.6%)[7]. Data regarding the risk factors for thrombosis emerged in a larger PETHEMA study. The overall incidence of thrombosis was 5.1% (39/759), with 6

out of the 26 patients who died before initiation of chemotherapy presenting with thrombotic events (three cerebral strokes, two pulmonary emboli, one acute myocardial infarction)[8].

Patient with acute promyelocytic leukemia can present with ischemic stroke and acute stroke can be associated with status epilepticus. Initial MRI brain done three days later revealed multiple acute to subacute infarct bilaterally. We initially attributed MRI changes to status epilepticus and atypical cells in peripheral smear as reactive. We believe initial MRI findings was not due to status epilepticus but was the cause of status epilepticus as we could not find other reason of status as CSF was also normal. Only when patient stopped seizing, atypical cells continue to rise and patient start developing fall in hemoglobin and platelets we thought of leukemia as the underlying problem.

Conclusions

Blood dyscrasias should not be overlooked in patients with the acute onset of neurological symptoms.

Conflict of interest statement

The authors report no conflict of interest.

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