Case report:

Acute Promyelocytic Leukemia in a 17yr Male presenting as Intracerebral Haemorrhage

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ABSTRACT

Acute promyelocytic leukemia (APML), once highly fatal, has emerged as the most curable subtype of acute myeloid leukemia in adults. Early mortality most often is due to a severe catastrophic bleeding, often intracerebral in location. Here we report a 17year male patient presented with status epilepticus having high leukocyte count (3,28,000/mm^3) and low platelet count(34,000/mm^3).Peripheral blood & bone marrow was showing good no. of atypical promyelocytes. CT scan of brain revealed an intracerebral haemorrhage with laboratory profile of prolonged prothrombin time and activated partial thromboplastin time, the presence of D-dimer and decreased fibrinogen concentration. The patient was diagnosed as Acute Promyelocytic Leukemia with Intracerebral haemorrhage. The patient died on the same day. APML is the notorious subtype of acute myeloid leukemia which causes fatal intracranial haemorrhage which has high mortality and morbidity. Clinically significant coagulopathy is present in 70%– 80% of APML patients at the time of diagnosis. Early detection and aggressive correction of coagulopathy may prevent the catastrophic event. Prompt image study for locations and types of ICH can predict outcomes.

Key Words : Acute Promyelocytic Leukemia, DIC, Intracerebral Haemorrhage

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BACKGROUND

Acute promyelocytic leukaemia (APML) is a condition classically characterised by t(15,17) (q22,q21), with disseminated intravascular coagulopathy (DIC) being a major cause of death. Central nervous system involvement with APML commonly occurs in relapse; however, it is rarely seen at presentation, with only six reported cases in the literature[1]. Approximately 20 to 30% of patients died of hemorrhage, most often intracerebral in location, either at presentation or after the initiation of chemotherapy[2,6]. the bleeding diathesis became a major focus of research because the outcome of patients with APL appeared to be more favourable compared with that of patients with other subtypes of AML.

CASE REPORT

A 17year male without a significant medical history was referred to our hospital in January 2013 complaining of repeated seizures for last 2 weeks. Later on he developed vomiting and photophobia. The haematological finding obtained was leukocyte count (3,28,000/mm^3), hemoglobin (5.6 g/dL), platelet count(34,000/mm^3), and differential white cell count was lymphocyte 11%, myelocyte 08%,promyelocyte 41%, myeloblast 40%. Bone marrow examination revealed more than 70% hypergranular promyelocytes with atypical features. Laboratory tests showed a prolonged prothrombin time (27 seconds) and activated partial thromboplastin time(41 seconds), the presence of D-dimer, a fibrinogen concentration of 84 mg/dL all of which were compatible with DIC. The CT scan of brain revealed two frontal areas of hyperattenuation, which was suggestive of hemorrhage. The patient was diagnosed as Acute Promyelocytic Leukemia with Intracerebral haemorrhage. He was transfused with fresh frozen plasma. The patient died on the same day.

Acute promyelocytic leukaemia is frequently associ-

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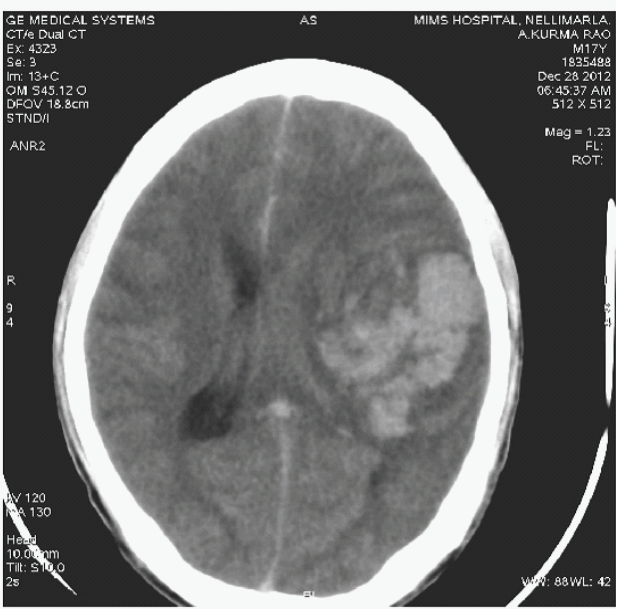
ated with clotting abnormalities and carries a high risk of intracranial haemorrhage[7]. CNS involvement

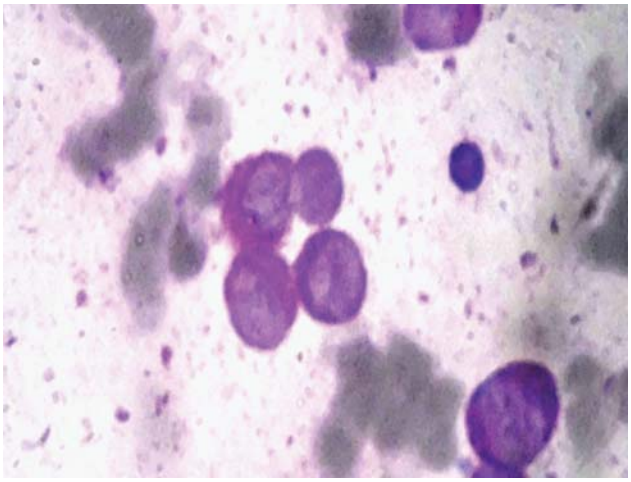
CT Scan of Brain showing Intracerebral Haemorrhage



in APML is extremely rare at presentation but not infrequent at relapse, and associated factors include raised white cell count (>10 x 10^9/l), prior CNS haemorrhage, microgranular variant and bcr3 PML/RAR type[8,9]. Past studies have revealed that fatal intracranial hemorrhage (40%) is the leading cause of death from cytotoxic chemotherapy[10] , although current treatment that combines all-trans-retinoic acid (ATRA) and conventional chemotherapy has much improved the prognosis.

Routine coagulation tests reveal prolongation in the PT and aPTT, low fibrinogen levels, and elevation in the D-dimer and fibrin degradation products (FDPs) in most but not all patients with APL[11]. These observations suggests that the bleeding diathesis is due to disseminated intravascular coagulation.The pathogenesis includes consumptive coagulopathy and procoagulant activity, fibrinolysis, proteolysis & increased angiogenesis. The use of ATRA to treat APL, especially in combination with chemotherapy, in patients with coagulopathy has improved the survival rate[12-15]. Few case supports that high-risk patients, in particular those who have intracranial haemorrhage and high white cell count at presentation, should have diagnostic lumbar puncture performed earlier once the coagulopathy has resolved. This approach may allow earlier detection and treatment of occult CNS disease and consequently reduce the risk of future relapse.

Bone Marrow showing good no. of hypergranular promyelocytes with prominent nucleoli(Leishman stain)



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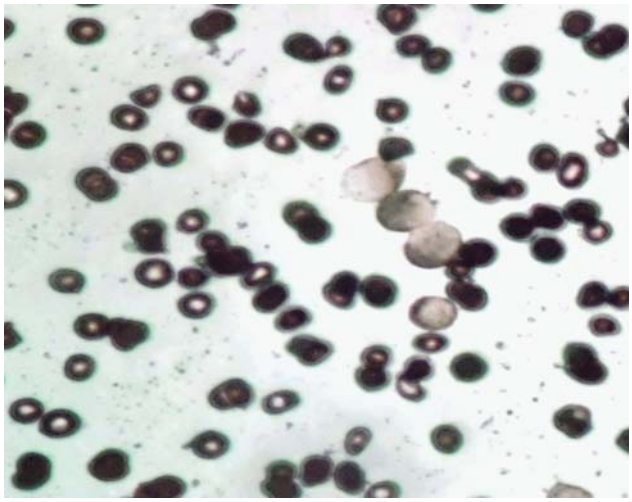

CONCLUSION:

Acute promyelocytic leukemia (APL), once highly fatal, has emerged as the most curable subtype of acute myeloid leukemia in adults. Cure is now expected in 70 to 90% of patients when treatment includes ATRA combined with anthracycline based chemotherapy. Early mortality most often is due to a severe and often catastrophic bleeding, often intracerebral in location, and remains a major cause of treatment failure. The most important therapeutic strategy is early institution of ATRA at the first suspicion of the diagnosis (without waiting for genetic confirmation) and aggressive blood product.

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