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Short Report

Acute Promyelocytic Leukaemia: An Experience with 6 Cases

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Abstract:

Background and objective: *Acute promyelocytic leukaemia (APL) is considered a distinct entity among the acute myeloid leukemias (AML). Our purpose is to see its clinical presentations and outcome with ATRA (all- trans retinoic acid).*

Materials and methods: *It is a retrospective descriptive study of 6 patients diagnosed by cytologic criteria between November 2008 and February 2011 in two tertiary care hospitals in Dhaka, Bangladesh. All specific information were recorded in standardized data sheet and analyzed manually.*

Results: *Mean (SD) age of patients was 28.6 (±7.84) years with equal gender distribution. Fever >101 F, weakness, easy fatigability, and bleeding manifestations were common presentations (100%). The other manifestations were bony tenderness, purpuric spots or DIC, but no lymphadenopathy and organomegaly were seen. Mean (±SD) Hb was 9.03 (±1.06) gm/dl, in 66% ESR was >50mm in 1st hr with 50% leukocytosis and 50% leucopenia but 100% thrombocytopenia.In the peripheral blood 40%-85% of the leukocytes were blast cells. Bone marrow was done in all cases which suggested AML-M3 (Acute promyelocytic leukemia) and cytogenetic diagnosis were done in 3 cases, which showed t(15;17)PML-RARA fusion protein positive. ATRA (all-trans retinoic acid) plus chemotherapy (daunorubicin ± cytarabine) achieved complete remission in 5 (80%) patients.*

Conclusion: *Modern treatment is highly effective if administered early.*

Keyword*: Acute promyelocytic leukaemia, PML/RARA fusion protein, All- trans retinoic acid (ATRA).*

Introduction:

Acute promyelocytic leukemia (APL) is a rare biologically and clinically distinct variant of AML accounting for only 15-18% of the total number of acute non lymphocytic leukemias.[1] The estimated incidence is approximately 6 cases per 10 million people per year with no apparent sex differences. The age of APL cases is younger than that of other acute myeloid leukemia (AML) .[2] APL represents a medical emergency with a high rate of early mortality, often due to hemorrhage from a characteristic coagulopathy. The introduction of all-trans retinoic acid (ATRA) and, more recently, arsenic trioxide (ATO) into the therapy of APL has revolutionized the management and outcome of this disease.[3] We present 6 (six) cases of APL with their clinical aspects and treatment outcome with ATRA.

Method:

It is a retrospective descriptive study of 6 patients diagnosed as APL between November 2008 to February 2011 in Shahid Suhrawardy Medical College Hospital and Sir Salimullah Medical College Hospital, two tertiary care hospitals in Dhaka, Bangladesh. All patients diagnosed on the basis of cytologic criteria were included. All specific information were recorded in standardized data sheet and analyzed manually.

Results:

Among the 6 patients, 3 were males (50%) and 3 females (50%). Mean (±SD) age was 28.6 (±7.84) years. All patients (100%) had continued fever >101° F for varying duration with bleeding manifestations (Table-I) and easy fatigability. All had moderate anaemia at diagnosis and purpuric spots

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over skin. 5 patients had bony tenderness but none had lymphadenopathy, organomegaly or features of DIC. Mean (±SD) Hb was 9.03 (±1.06) gm/dl, ESR was >50mm in 1st hr 4 (66.7%) patients. Three patients had leukocytosis while other had leucopenia but all showed thrombocytopenia with a mean (±SD) platelet count of 33000 (±16370.7)/cumm. 40%-85% of the leukocytes were blast cells. Bone marrow done in all cases suggested AML-M3 (Acute promyelocytic leukemia). Cytogenetic diagnosis was made in 3 cases by real time PCR and t(15;17)PML-RARA fusion protein was positive in all cases. Five patients (83.33%) were given ATRA (all-trans retinoic acid) plus chemotherapy (daunorubicin ± cytarabine). There was complete remission in 4 patients (66.67%) by 60 days which was evaluated by serial CBC with PBF and bone marrow examination and 1 patient died on 4th day of remission induction therapy. One patient denied maintainance therapy and died with a relapse. The remaining 3 patients are in good health on maintenance therapy.

Table-I

Bleeding manifestation

Bleeding manifestations	No of pt. (n=6)	Percentage (%)
Petechiae, purpura	5	83.33
Echimosis	2	33.33
Gum bleeding	4	66.67
Hematuria	1	16.67
Menorrhagia	1	16.67

Table-II

*Hematological findings **(N=6)***

Hematological findings	No of pt.	Percentage (%)
Hb (<10 gm/dl)	5	83.33
High ESR (>50mm in 1st hr)	4	66.67
Leucopenia (<3000/cumm)	3	50
Leucocytosis (>80000/cumm)	3	50
Low platelet(<60000/cumm)	6	100
Blast cells(60-85%)	6	100

Discussion:

This study takes the opportunity to report a few cases of a rare clinical entity- 'Acute Promyelocytic Leukaemia'. Age of presentation, gender equality and common presentations of pancytopenia related complications, i.e. weakness and easy fatigability, fever with infections of variable severity, and/or hemorrhagic findings such as gingival bleeding, purpura, ecchymoses, found in our cases are similar to other published case series.[4] As the efficacy of differentiation treatment based on retinoids derivatives is strictly dependent on the presence of the PML/RARA fusion in leukemia cells, most authors suggest genetic confirmation of this specific lesion but morphologic diagnosis of hypergranular (typical) APL is also highly predictive of an underlying PML/RARA rearrangement.[5] RT- PCR done in the 3 out of 6 cytologically diagnosed patients were all positive in the present series. The simultaneous administration of all-transretinoic acid (ATRA) and anthracycline-based chemotherapy (daunorubicine) is currently considered the standard induction therapy in newly diagnosed patients leading to complete remission (CR) rate greater than 90% and potential cure in up to 80%. Once in CR, the standard post remission therapy consists of 2-3 cycles of anthracycline-based chemotherapy followed by ATRA-containing maintenance therapy.[6-10] We treated 5 patients accordingly and one patient with conventional chemotherapy (daunorubicine+ citarabine). ATRA based treatment achieved 80% complete remission. Supportive measures consisted of fresh frozen plasma and blood transfusions to maintain the fibrinogen concentration and platelet count above 100 to 150 mg/dL and 30 to 50×10^9/L, respectively and was continued during induction therapy until disappearance of all clinical and laboratory signs of coagulopathy. The only death during induction was preceded by severe headache and convulsion, suggesting intracranial hemorrhage.The other patint died due to fatal relapse at home after refusing maintenance therapy. The patient who received conventional chemotherapy (daunorubicine+ citarabine) is in good health in consolidation phase

Conclusion: Despite the small sample size, the present study shows the diagnostic efficacy of cytological diagnosis and the antileukemic efficacy of ATRA with chemotherapy in APL, leading to a high rate of remission after induction therapy and the lack of relapses in those patients who completed induction and consolidation therapy.

Conflict of interest : None

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