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Original Article

Acute Promyelocytic Leukemia: Clinico-Demographic Profile

Nadia Altaf, Shahtaj Khan,Khizer Abdullah and Lihaz Gul
Department of Pathology,Hayatabad Medical Complex, Peshawar.

Abstract:
Acute promyelocytic leukemia is a unique subtype of acute Myeloid Leukemia about which there is limited data from Pakistan. The aim of the present study is to evaluate itsclinico-demographic profile along with risk stratification at a tertiary care hospital in Pakistan.
Materials and Methods: A retrospective study was performed in which 28 cases of acute promyelocytic leukemia diagnosed at Pathology department of Hayatabad Medical Complex Peshawar, Pakistan between June 2014 and July 2018 were enrolled for analysis. All data were documented and statistical analysis was performed by SPSS-23 software.
Results: Median age of the patients was 21 (range 2-65) years. Male to female ratio was3:1 .Hypergranular variant (92.8%) was more common as compared to microgranular type (7.14%). Majority of patients had complaints of fever (71.4%), bleeding (53.5%) and generalized weakness (14.2%). Pallor (64.2%) was the predominant finding on physical examination followed by petechial and purpureal rashes (46.4%). Mean Hemoglobin was 8.3 (range 5.3-12.2) g/dl. The mean total leukocytes count was 39.6 (range 1.3-121) x 10^9/ Land mean platelet count was 40 (range 7-78) x 10^9 /L. Most patients fall into high riskgroup (60.7%) on risk stratification followed by intermediate risk (32.1%) and low risk (7.1%).
Conclusion: Clinical features and risk stratification results of our study are comparable with the published data.In the present study pallor was the most commonpresentation. Risk stratification showedpredominance of high-risk score.
Keywords: Acute promyelocytic leukemia, Myelocytic Leukemia, t15;17, M3, all trans retinoic acid (ATRA)

Introduction

Acute promyelocytic leukemia (APL) is a clonal expansion of promeylocytic leukemic cells owing to a distinct translocation between chromosomes 15 and 17, defined in the FAB classification as M3. APL cases can easily be recognized on morphology, as the APL cells have a very typical morphological appearance.[1]
APL accounts for approximately 10% of AML cases in adults and is regarded as the most curable subtype of AML.[2]In 1985 It was found that all trans retinoic acid (ATRA) is successful in specifically targeting the PML-RARa oncogene. It brings about complete remission in 90% of patients and 70% of the patients are potentially cured.[3] Arsenic oxide discovered in 1992 is the second mile stone agent used in the management of APL.[4]
In developing countries such as Pakistan, patients came across to local physicians first and are then referred to tertiary care hospitals lately due to which there is a delay in diagnosis and initiation of treatment.[5]
Early death is one the major causes of induction failure in APL and results from causes such as hemorrhage, differentiation syndrome and infection. Intracranial hemorrhage is a notorious cause of death while resistance to therapy is an uncommon cause of induction failure.[6]
Hemorrhage in APL are commonly due to diffuse activation of coagulation, hyperfibrinolysis and non-specific proteolytic activity and have been reported to occur efore diagnosis of APL and initiation of treatment.[7]
Current guidelines regard APL is a medical emergency, is to be managed with immediate therapeutic actions based upon morphological and clinical suspicion.Genetic confirmation is desirable.[8]

Author for Correspondence:
Dr Nadia Altaf
Consultant hematologist
Email: nadia.altaf12@gmail.com

Materials and Methods

This was a retrospective study conducted in the Pathology department of Hayatabad Medical Complex, a tertiary care hospital in Peshawar. Diagnosed cases of APL were enrolled for analysis between June 2014 and July 2018.As there was no intervention and there was no breech of patient privacy formal ethics board approval was not sought. Data was analyzed using software SPSS version 23.

Demographic findings such as age, gender and medical history were noted. 3 ml of blood was collected in EDTA tube and hematological parameters were performed by hematology analyzer (Ruby cell dyne). Bone marrow aspirations and biopsies were performed under aseptic techniques. Cytogenetics (conventional G band karyotype) analysis were done where ever possible.

Patients were stratified according to Gruppo ItalianoMalattieEmatologicha dell Adult (GIMEMA) and PETHEMA studies into 3 groups i.e. low risk, intermediate risk and high risk.

Low risk : Leukocyte count less than or equal to 10 x 10^9/ L and platelet count >40x 10^9/L.

Intermediate risk : Leukocyte count less than or equal to 10 x 10^9/ L and platelet count <40x 10^9/L.

High risk: : Leukocyte count > 10 x 10^9/ L regardless of platelet counts.

Results

28 patients were diagnosed as APL. Median age was 21 (range 2-65) years. There were 21 males (75%) and 7 females (25%) out of 28 patients. Male to female ratio was 3:1.

Majority of patients had complaints of fever (71.4%), bleeding (53.5%) and generalized weakness (14.2%). Pallor (64.2%) was the predominant finding on physical examination followed by petechial and purpural rashes (46.4%).

Laboratory parameters are shown in table 1. Mean Hemoglobin was 8.3 (range 5.3-12.2) g/dl. The mean total leukocytes count was 39.6 (range 1.3-121) x 10^9/ L and mean platelet count was 40 (range 7-78) x 10^9 /L. Hypergranular variant (92.8%) was more common as compared to microgranular type (7.14%).

Risk stratification shows predominance of high risk score (60.7%) followed by intermediate risk (32.1%) and low risk (7.1%).

Table 1. Laboratory parameters of APL patients.

Parameters	Mean (range)
Hemoglobin g/dl	8.31 (5.3-12.2)
White blood cell (x 10^9 /L)	39.6 (1.3-121)
Platelets (x 10^9/L)	40 (7-78)

Discussion

Acute promyelocytic leukemia was previously considered one of the most fatal subtypes of AML, due to arrest at the promyelocyte stage during differentiation showing characteristic chromosomal translocation t(15;17). It is now the most curable among all the subtypes of AML. The outcome of AML has changed tremendously due to understanding of molecular pathogenesis and advent of ATRA.[9]

28 cases of APL were followed at our center including their clinicohematological and risk stratification profiles. Data on APL patients from Pakistan is limited.

In our study the median age was 21 (range 2-65 years). Previous studies in Pakistan have reported median age of 32 and 41 years which is higher as compared to our study.[5,10] Studies from India and Egypt showed median age of 30 and 29 years respectively which is again bit higher in comparison with our findings.[11,12] However in all the studies it has been found that APL is a leukemia of younger age group.

In the present work there was male gender predilection which was also found in India while study conducted in Southern Pakistan showed female predominance which is similar to study findings fromMalaysia.[10,11,13] Another study in Pakistan showed no gender predilection same as in Italy.[14]

In our study majority of patients had complaints of fever (71.4%), bleeding (53.5%) and generalized weakness (14.2%). A study by Sultan S et al from Pakistan showed bleeding (80.7%) as the predominant complaint followed by fever (76.9%) and generalized weakness (30.7%).[10] Similar to our results reported were also seen in India showing fever (72%) followed by bleeding (69.7%) and weakness (34.8%).[11]

Pallor (64.2%) on physical examination was the predominant finding in our study followed by petechial and puerperal rashes (46.4%). Pallor was also a main clinical sign seen in India.[11]Study in Southern Pakistan revealed petechiae (61.5%) as the predominant finding followed by pallor (30.8%) which is more or less similar to our findings.[10]

Risk stratification in our study showed predominance of high risk score (60.7%) in comparison to other studies. (Table 2)

In the present study hypergranular variant (92.8%) was the most frequent morphological type followed by microgranular variant (7.14%). Our results are consistent with earlier reports from Pakistan.

Table 2: Comparison of risk stratification results among various countries

Study	Country/ Year	Low risk	Intermediate risk	High risk
Karim F et al.[5]	Pakistan/2014	23.1%	26.9%	50.0%
Khorshid O et al.[12]	Egypt/ 2011	16%	49%	34%
Bajpai J et al.[11]	India/2011	30.23 %	46.51%	23.25 %
Sultan S et al.	Pakistan/ 2015	19.2%	65.4%	15.3%
Present study	Pakistan/2018	7.1%	32.1%	60.7%

In conclusion the clinical features and risk stratification results of our study are comparable to published data. Pallor was the common presentation in our study. Risk stratification showed predominance of high risk score. Early diagnosis and immediate treatment under standard treatment chemotherapy protocols is essential in patients with APL. Limitation of the study is that most of the patients were having low socioeconomic status and so due to financial constraints genetic testing was not possible to be done in all of them

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CONTRIBUTION OF AUTHORS	
Author	**Contribution**
Nadia Altaf	A,B,C,D,E,F
Shahtaj khan	A,B,C,E
Khizar Abdullah	B,C,E,F
Lihaz Gul	B,D,E

KEY FOR CONTRIBUTION OF AUTHORS:

A. Conception/Study Designing/Planning
B. Experimentation/Study Conduction
C. Analysis/Interpretation/Discussion
D. Manuscript Writing
E. Critical Review
F. Facilitated for Reagents/Material/Analysis