

# CASE REPORT

---

## CLINICO HEMATOLOGICAL PROFILE OF ACUTE MEGAKARYOBLASTIC LEUKEMIA: REPORT OF FIVE CASES

Rajendra Kumar Nigam<sup>1</sup>, Rajnikant Ahirwar<sup>2</sup>, Reeni Malik<sup>3</sup>, Ritu Jaipuria<sup>4</sup>, Rubal Jain<sup>5</sup>

### HOW TO CITE THIS ARTICLE:

Rajendra Kumar Nigam<sup>3</sup>, Rajnikant Ahirwar, Reeni Malik, Ritu Jaipuria, Rubal Jain. "Clinico hematological profile of acute megakaryoblastic leukemia: report of five cases". Journal of Evolution of Medical and Dental Sciences 2013; Vol. 2, Issue 43, October 28; Page: 8318-8323.

**ABSTRACT:** Acute Megakaryoblastic Leukemia (AMKL) is a rare entity accounting for 1-2% of all Acute myeloblastic Leukemia (AML) (1). It is known as a distinct entity since a very long time but still difficult to diagnose correctly due to lack of distinct clinical features and morphological criteria. Here we present the clinical, morphological, cytochemical features of five cases of AMKL. Certain morphological features such as presence of abnormal platelet count, giant platelets and cytoplasmic blebbing in blasts were found to be important pointers towards the diagnosis.

**KEYWORDS:** Acute Megakaryoblastic leukemia AML-M7

**INTRODUCTION:** Acute megakaryoblastic leukemia (AML) is defined as more than 20% (WHO Classification) & more than 30%(FAB Classification) of blasts of megakaryocytic lineages in the peripheral blood & bone marrow aspirate as determined by morphology & immune flow cytometry (1). AMKL is a rare entity & accounts for 1-2% of all AML (1) & 1 % of all leukemias during childhood & has an incidence of 0.5 per million per year. (1)

The clinical profile and morphological criteria can be confused with acute lymphoblastic leukemia ALL-L1. Acute myeloid leukemia, AML-M0. It may arise de novo or may be secondary to chemotherapy, or progress from myeloproliferative neoplasms (MPN) and /or myelodysplastic syndrome (MDS)(2,3).

Symptoms may be nonspecific-asthenia, pallor, fever, dizziness, and respiratory symptoms. More specific symptoms are bruises &/or excessive bleeding, DIC, neurological disorders and gingival hyperplasia. Splenomegaly is not seen in de-novo cases but is a feature of AML –developing from Chronic Myelogenous leukemia (CML) (4).

Diagnostic methods include blood analysis, bone marrow aspirate for cytochemical, immunological & cytogenetical studies and CSF investigations.

It has a bimodal peak of distribution (in adults and children 1-2 years of age).

Children with Down syndrome have a higher incidence of AMKL (5). Overall outcomes remain poor but outcome in AML with Down syndrome is +/- 70 %.(6)

Here we present five cases of AMKL with their clinico haematological, morphological; cytochemical features and discuss diagnostic difficulties/clue to arrive at definitive diagnosis.

**MATERIAL AND METHOD:** All acute megakaryoblastic leukemias diagnosed in the department of pathology, Gandhi medical college Bhopal, in the period of 2003-2012., were included in the study. A total of five cases were retrieved. The clinical history and other details were taken from the case files.

Leishman stained peripheral smears, and bone marrow aspirate smears were examined. Bone marrow biopsy was not available.

# CASE REPORT

In Cytochemistry – Myeloperoxidase and PAS was done.  
Immunophenotyping and immune cytochemistry were not available.

**RESULTS:** Clinico haematological profile of our five cases is summarized in table 1&2.

Features	Case I	Case II	Case III	Case IV	Case V
1. Age/Sex	17 yrs/M	3 Yrs/F	9 yrs/M	22 Yrs/M	14 yrs/F
2. Clinical features	Pallor, fever	Pallor, fever, dyspnoea, pedal edema, facial puffiness	Fever with rash chickenpox	Fever weakness, melena	Pallor, altered sensorium
3. Hepatosplenomegaly	-	+	-	-	-
4. Lymphadenopathy	-	-	-	+	-
5. HBsAg positive	-	-	-	+	-
6. LDH					Markedly raised
7. Hb gm/dl	3.8	2.9	3.0	3.7	3.9
8. TLC cells/cumm	3,000	39,000	6,200	4,500	4,400
9. Blasts	28	82	58	35	85
10. Morphology of blasts					
a. Cytoplasmic blebbing	+	+	+	+	+
b. Cytoplasmic vacuolation	-	+	+	+	+
c. Nuclear clefting	-	+	-	-	-
d. Auer rods	-	+	-	-	-
e. Platelet budding	-	+	+	-	+
11. Platelet count /cumm	Less than 10,000	1,10,000	40,000	9,00,000	Less than 10,000
12. Giant platelet				+, aggregates	

**Table 1: Clinical features and Hematological parameters**

CSF was done in two out of five cases & was negative for blasts.

None of the five cases had features of Down syndrome.

# CASE REPORT

Features	Case I	Case II	Case III	Case IV	Case V
Aspirate	Difficult	Difficult	Easy	Easy	Difficult
Cellularity	Hypocellular	Normocellular	Hypocellular	Normocellular	Hypocellular
Blasts	36	92	58	35	95
Morphology of blasts					
a. Cytoplasmic blebbing	+	+	+	+	+
b. Cytoplasmic vacuolation	-	+	-	+	+
c. Nuclear clefting	-	+	-	-	-
d. Auer rods	-	+	-	-	-
e. Platelet budding	-	+	+	-	+

Table 2: Bone Marrow Examination

Majority of cases were male, M:F =3:2.out of five cases, two were pediatric(3 year and 9 year),two adolescent(14 years and 17 years) and one adult(22 years).

Onset of all the five cases was presented with acute symptoms of marrow infiltration.

Four out of five were having fever, weakness and one patient had rash (Chickenpox),one had black colored stool and one had altered sensorium.

Two patients each with hepatosplenomegaly and lymphadenopathy were found.

Case IV an adult male with lymphadenopathy was HBsAg positive, and having history of blood transfusion.

Only one patient had markedly raised LDH levels.

All patients were anemic with hemoglobin was less than 4gm%. Moderate leucocytosis, and leucopenia was found in one patient each, although all patient had blasts in the range of 35-95% with typical morphology.

Thrombocytopenia was found in four cases and thrombocytosis in one patient.

LDH was markedly raised in case V.

Peripheral blood blast count was in the range of 28-85%. Blasts were large, pleomorphic, 3-4 times the size of small lymphocytes with moderate to abundant agranular basophilic cytoplasm. Nuclei were round to oval with 1-3 prominent nucleoli. Few blasts in all cases showed cytoplasmic blebbing (figure 1) and also characteristic platelet budding in three out of five cases (figure 2). Cytoplasmic blebbing in blasts of all cases, cytoplasmic vacuolation was seen in three cases, nuclear clefting in one, auer rod in one while giant platelets and aggregates of blasts were found in case IV.

Bone marrow was very difficult to aspirate in two cases probably because of fibrosis which is common complication in these cases, two normocellular and three were hypocellular .Blasts were in

# CASE REPORT

---

the range 35%-95% of all nucleated cells with morphology as seen in peripheral blood. Megakaryocytes were almost absent in 2 cases and markedly reduced in two.

Four out of five cases were PAS positive (cytoplasmic blebs) and all cases were MPO negative.

**DISCUSSION:** AMKL is a rare leukemia accounting for 7-10% of Childhood AML (7) & 1-2 % of adult AML (8, 9) and have a poor prognosis.

Patients with Down syndrome have increased incidence of AMKL & have a good prognosis.(7). AMKL can arise denovo or secondary to post chemotherapy or progress from myeloproliferative neoplasm or MDS (1, 2, 3) In our study one patient 22 yrs male who was HBV positive, presented with fever & malena, also had lymphadenopathy & normal total leucocyte count but have 35% blasts with typical morphology. Platelet count was 9,00,000/cumm, platelets aggregates were also seen.He was transfused blood 3 times in the past.

HCV is found with increased risk of haemopoietic malignancies -ALL,RAEB, NHL & AML HBsAg is reported controversially , having no relation with hemopoietic malignancies to increased risk of RAEB,CML with HBsAg Anti-HBcAg with AML(12) .However these increased risk are not statistically significant and number of cases are less so these findings need to be confirmed in larger case-controlled studies.

It is difficult to diagnose on the basis of morphology alone, needs immunophenotyping as gold standard, WHO classification needs cytogenetics too. However certain features like cytoplasmic blebbing, platelet budding, clustering of blasts may be useful for diagnosis (8 ).

MPO was negative in all cases, but cytoplasmic blebs were PAS positive.

**CONCLUSION:** AMKL is a rare leukemia. Importance lies in their correct diagnosis in view of its prognostic implication. Not all cases are related with Down syndrome. Although immunophenotyping & cytogenetics are the gold standard, it is not available in all centres in our country.

Careful search for features like cytoplasmic blebbing, platelet budding, clustering of blasts & cytochemical PAS positivity for cytoplasmic blebs can help in correct diagnosis of AMKL.

In view of the HBV positivity discovered in one out of five patients, it is mandatory to screen all the patients of anemia, & leukemia for transfusion transmitted infection to assess the morbidity pattern.

I would like to extend special acknowledgements to Dr. V.K. Bhardwaj, Mr. Atul Shrivastava, Dr. Suhas Kothari , and technical staff Mr. K.P. Verma.

## REFERENCES:

1. Atlas of Genetics and Cytogenetics in Oncology and Haematology ([atlasgeneticsoncology.org/Anomalies/M7ANLLID1100.html](http://atlasgeneticsoncology.org/Anomalies/M7ANLLID1100.html))
2. S. T. Pullarkat, J. W. Vardiman, M. L. Slovak, et al., "Megakaryocytic blast crisis as a presenting manifestation of chronic myeloid leukemia," *Leukemia Research*, vol. 32, no. 11, pp. 1770-1775, 2008

## CASE REPORT

3. K. Hino, S. Sato, A. Sakashita, S. Tomoyasu, N. Tsuruoka, and T. Koike, "Megakaryoblastic transformation associated with disseminated intravascular coagulation in the course of polycythemia vera: a case report," *RinshoKetsueki*, vol. 33, no. 4, pp. 500–506, 1992 (Japanese).
4. [Blood journal.hematology library.org/cgi/content/abstract/78/3/748](http://bloodjournal.hematologylibrary.org/cgi/content/abstract/78/3/748).
5. B. J. Lange, N. Kobrinsky, D. R. Barnard et al., "Distinctive demography, biology, and outcome of acute myeloid leukemia and myelodysplastic syndrome in children with Down syndrome: Children's Cancer Group Studies 2861 and 2891," *Blood*, vol. 91, no. 2, pp. 608–615, 1998.
6. Verschuur A. Acute megakaryoblastic leukemia. *Orphanet Encyclopedia*. May 2004.
7. U. H. Athale, B. I. Razzouk, S. C. Raimondi, et al., "Biology and outcome of childhood acute megakaryoblastic leukemia: a single institution's experience," *Blood*, vol. 97, no. 12, pp. 3727–3732, 2001
8. L. Pagano, A. Pulsoni, M. Vignetti, et al., "Acute megakaryoblastic leukemia: experience of GIMEMA trials," *Leukemia*, vol. 16, no. 9, pp. 1622–1626, 2002
9. M. S. Tallman, D. Neuberg, J. M. Bennett, et al., "Acute megakaryocytic leukemia: the Eastern Cooperative Oncology Group experience," *Blood*, vol. 96, no. 7, pp. 2405–2411, 2000.
10. Lesley A Anderson, Ruth Pteiffer, John L Warren et al, " Hematopoietic Malignancies Associated with Viral and Alcoholic hepatitis" *Cancer Epidemol.Biomarkers Prev*. Nov 1,2008,17:3069-3075
11. O.P.Ghai 7th edition 2009, pp3, CBS Publishers and Distributors PVT Ltd.
12. Gentile G, Mele A, Monarco B, et al. " Hepatitis B and C viruses, Human T – cell lymphotropic virus type I and II , Leukemias : a case control study. The Italian Leukemia study Group." *Cancer Epidemol. Biomarkers Prev* 1996;5:227-30.

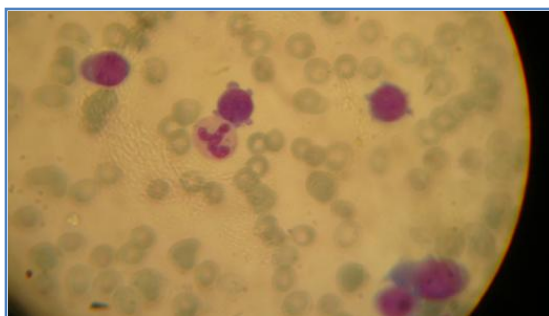


Figure 1-Blasts showing cytoplasmic

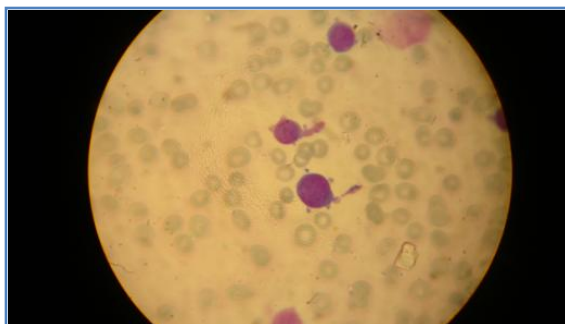


FIGURE 2-Blasts showing characteristic platelet budding

# CASE REPORT

---

## **AUTHORS:**

1. Rajendra Kumar Nigam
2. Rajnikant AHIRWAR
3. Reeni Malik
4. Ritu Jaipuria
5. Rubal Jain

## **PARTICULARS OF CONTRIBUTORS:**

1. Professor, Department of Pathology, Gandhi Medical College, Bhopal, Madhya Pradesh.
2. PG Student, Department of Pathology, Gandhi Medical College, Bhopal, Madhya Pradesh.
3. HOD, Department of Pathology, Gandhi Medical College, Bhopal, Madhya Pradesh.
4. PG Student, Department of Pathology, Gandhi Medical College, Bhopal, Madhya Pradesh.

5. PG Student, Department of Pathology, Gandhi Medical College, Bhopal, Madhya Pradesh.

## **NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:**

Dr. Rajendra Kumar Nigam,  
C-116, Shahpura,  
Bhopal, Madhya Pradesh,  
India - 46209.  
Email - dr.rajendranigam@gmail.com

Date of Submission: 12/10/2013.  
Date of Peer Review: 15/10/2013.  
Date of Acceptance: 19/10/2013.  
Date of Publishing: 24/10/2013