

## CASE REPORT

### Adult Type – Chronic Myeloid Leukemia in Childhood: A Case Report.

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#### Abstract:

*Background:* In pediatric patients, chronic myeloid leukemia (CML) accounts for 2 to 5% of all the leukemia's but has an incidence of less than 1 case per 1,00,000 population younger than 20 years of age per year. CML is a clonal hematopoietic stem cell disorder. As per WHO classification, CML is included in Myelodysplastic/Myeloproliferative disorder. Adult type - CML is extremely rare in childhood.

*Case history:* We report one such a case of Adult type of CML in an 11 year old male patient with chief complaints of abdominal distension since 1 month and cough with fever since 4-5 days. The clinical differential diagnosis was malaria, storage disorder or tropical splenomegaly. Though biological behaviour and prognosis are identical to that of adult type, we are reporting this case because of its extremely uncommon incidence.

**Key Words:** Chronic myeloid leukemia (CML), adult type CML, childhood leukemia.

#### Introduction:

Chronic myeloid leukemia (CML) is uncommon in childhood, accounting for only 2-5% of all leukemias [1]. CML is a clonal hematopoietic stem cell disorder. It has

incidence of less than 1 case per 1, 00,000 population younger than 20 years of age per year [2, 3]. Two distinct forms have been described, namely - the juvenile and adult type [4, 5]. Philadelphia (Ph) chromosome is rarely seen in children [4]. The Manchester Children Tumor Registry has reported only 9 cases in 23 years [4, 6].

The most of our knowledge of CML has been derived from studies in the developed countries. We report one such rare case of adult type - CML in an 11 year old patient due to its unusual incidence.

#### Case Report:

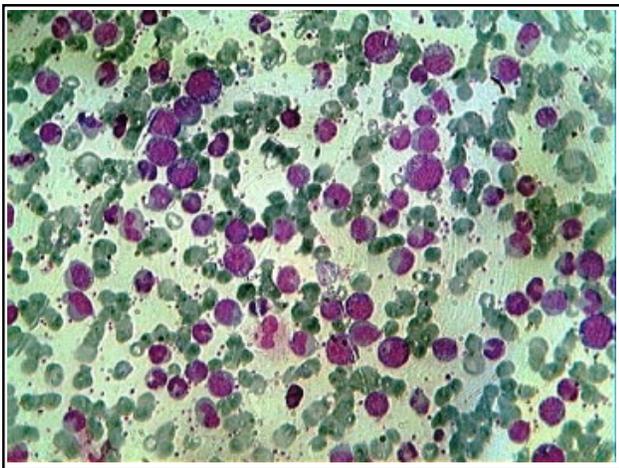
Eleven year male child came to the pediatric OPD in our hospital with chief complaints of abdominal distension since 1 month and cough with fever since 4-5 days. The patient was well immunized as per schedule. There was no history of consanguineous marriage of parents. On examination, the patient was averagely built and averagely nourished. Local examination revealed hard and distended abdomen. Liver was palpable 7 cms and huge splenomegaly was noted of 20 cms. In systemic examination – respiratory system revealed reduced air entry on right side. The patient was admitted in pediatric ward with differential diagnosis of malaria, storage disorder or tropical

splenomegaly.

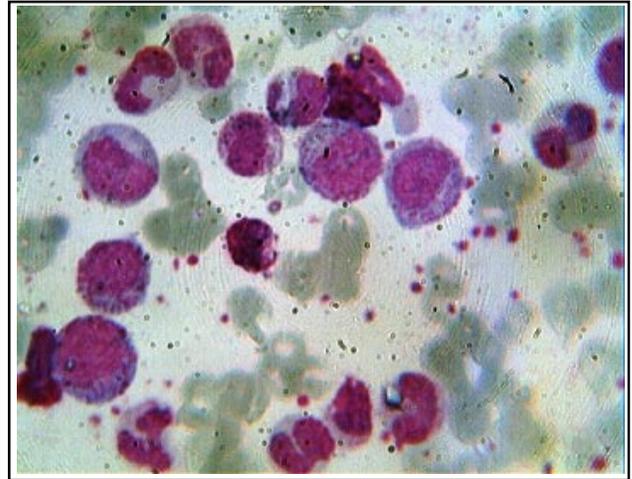
Routine hemogram was carried out, which revealed Hb – 10.7 gm/dl with markedly elevated Total leukocyte count of 2, 46,000/Cumm ( $246 \times 10^9$ / lit). A peripheral differential count revealed shift of myeloid series up to myeloblasts. Basophilia and eosinophilia was noted. (Polymorphs + Band forms = 47%, Metamyelocytes = 22%, Myelocyte = 10%, Promyelocytes = 02%, Blasts = 01%, Lymphocytes = 03%, Eosinophils = 07%, Monocytes = 03%, Basophils = 05%) (Fig. 1, 2). Platelet count was increased with 8.85 lac/Cumm ( $885 \times 10^9$ / lit). On peripheral smear examination, the diagnosis of - Chronic Myeloproliferative disorder suggestive of CML (adult) type was given.

Bone marrow aspiration from sternal puncture was carried out under all aseptic precautions, which revealed hypercellular bone marrow with myeloid predominance. Granulocyte series showed all forms with increased

**Fig 1: Photomicrograph of blood smear of patient showing marked leucocytosis with shift of myeloid series (Giemsa stain, x 400).**

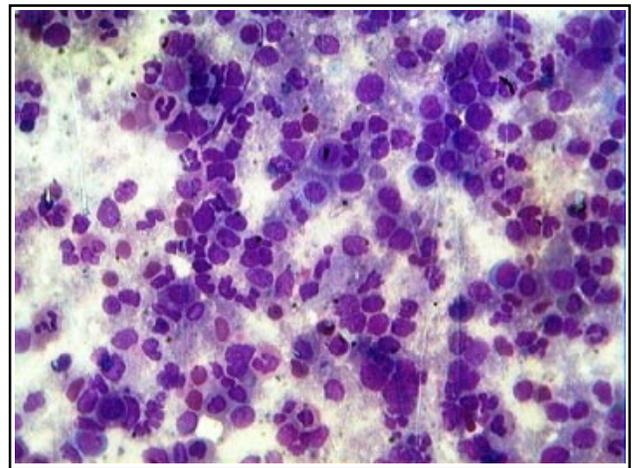


**Fig 2: Photomicrograph of blood smear of patient showing basophilia, shift of myeloid series and thrombocytosis (Giemsa stain, x1000).**



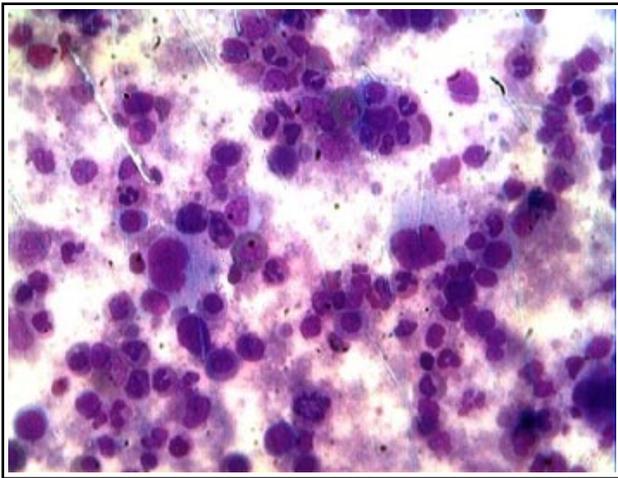
metamyelocytes, band forms and myelocytes (30%). Erythroid and lymphoid series were suppressed. Megakaryocytes were increased in number with micromegakaryocyte predominance (Fig. 3, 4). With above peripheral smear and bone marrow findings, final diagnosis of adult type - CML was given.

**Fig 3 : A bone marrow aspirate smear shows hyper-cellular marrow with myeloid predominance (Giemsa stain, x400).**



Cytogenetics [Philadelphia chromosome (Ph)] was carried out, which was positive. Thus diagnosis of Adult type of CML in 11 year old male patient was confirmed and patient was on chemotherapy with regular follow up.

**Fig 4: Bone marrow aspirate shows marked leucocytosis with shift of myeloid series with micromegacaryocytes (Giemsa stain, x1000).**



### Discussion:

Amongst childhood leukemias, chronic myeloid leukemia (CML), is a rare entity with an annual incidence of one case per million children [7]. Adult type of CML in children is even rarer and is characterized by Philadelphia chromosome [t (9:22)] positivity [8]. BCR – ABL fusion gene is better prognostic variant in children and accounts for 3-5% of childhood leukemias [9].

The incidence of leukemia among children younger than 15 years of age has shown a moderate increase in the past 20 years, with the trend primarily reflecting an increase in incidence of Acute Lymphoblastic Leukemia

(ALL) during this period [10]. The two major types of leukemia are ALL comprising nearly three-fourth and acute non-lymphoblastic comprising 19%. [10] CML is very rare in this age group.

CML in childhood presents as one of the two clinically distinct syndromes – i.e. “adult type CML (ACML) which is Ph(1)– positive, and juvenile CML, also known as Juvenile Myelomonocytic Leukemia (JMML), which is Ph(1)– negative.” Diagnosis of such cases in chronic phase can be done by hematological investigations. CML occurring in children is called as adult form CML, which has the same clinical, morphologic and cytogenetic findings as adult Ph positive CML.

We report one such a case of Adult type CML on peripheral smear and bone marrow, in an 11 year old male patient.

Clinical features of ACML are similar to that seen in CML occurring in adults as abdominal distension. Hepatomegaly, splenomegaly and generalized lymphadenopathy, anemia, hyperleukocytosis has been observed in all patients [4, 11]. The mean spleen size has been 13 cm and ranged from 8-22 cm as per Sinniah et al [4].

Three phases have been described for CML. Most patients are diagnosed in the first phase, called the chronic phase with median duration of 4-5 years. It can develop over time into the second- accelerated phase (6-8 months) and third- blast crisis phase (3-9 months) [5]. Accelerated and blast phase has worst prognosis.

Sinniah D et al [4] have reported only 5 cases of ACML out of 168 cases of leukemia in 13

year review. These cases have been treated with busulphan and intrathecal methotrexate. Median survival in all cases has been 30 months due to acute leukemia transformation and septicemia. They have stated that outlook for ACML remains poor and treatment needs re-evaluation [4]. Mishra A et al [11] reported similar findings for Ph positive CML in a child. Hehlmann R et al in 1994 have given comparison of survival of CML patients on busulphan and hydroxyurea as 45 and 58 months respectively [4].

Allogenic bone marrow transplant is the most successful therapy if a suitable HLA identical donor is available for chronic phase CML [9]. For patients without a suitable donor, control of the disease with chemotherapy (either hydroxyurea/busulphan or alpha interferon) is the best current alternative [5, 9, 12].

The same progress in the recent therapeutic strategy for older adults with hematological malignancies has also seen in younger adults. One of the BCR-ABL tyrosine kinase inhibitors, imatinib mesylate, is active for elderly Ph-positive Leukemias including ALL and CML [13]. Management of childhood CML in chronic phase constitutes – Hydroxyurea, interferon – alpha, imatinib, and stem cell transplant as per Robert I [14]. Imatinib in childhood CML, controls leukocyte count in 1-2 weeks but with variable non hematological side effects. [14]

Our patient has presented with abdominal distension and with hugely enlarged spleen i.e. 20 cms. Routine hemogram, Peripheral smear, Bone marrow and Ph chromosome (BCR - ABL) confirms the diagnosis of adult type

CML. Thus our case is fulfilling the morphological and cytogenetic criteria required for diagnosis of adult type CML. Patient is on chemotherapy and on regular follow up.

This needs to be differentiated from the other form of myeloproliferative disorder like Juvenile Myelomonocytic Leukemia (JMML). The term JMML is presently used to include all leukemias of childhood, formerly classified as Juvenile CML, Chronic Myelomonocytic Leukemia and infantile Monosomy 7 syndrome [5]. The disease mimics morphologically and clinically most closely to CML, but has unique biological characteristics. According to WHO classification, JMML is one of the bridging MDS/MPD category of myeloid neoplasms [12]. JMML represents 18-36% of MDS in children and about 2% of hematologic malignant neoplasms. It occurs predominantly in infants and young children less than 2 years [1]. Hepatomegaly, lymphadenopathy, recurrent infections and bleeding are the hallmarks of JMML [1] with Leukocytosis with monocytosis [ $> 5000 / \mu\text{l}$  i.e. ( $> 5 \times 10^9 / \text{L}$ )]. Eosinophilia and basophilia are observed in minority of the patients [1, 12]. JMML is Ph chromosome negative with aggressive clinical course. [1] These features have been absent in our case.

We have diagnosed the adult CML on routine peripheral smear examination and supported by bone marrow and cytogenetic study. Though biological behaviour and prognosis are identical to that of adult type, we are reporting this case because of its extremely uncommon incidence in childhood.

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