www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i4.10

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Case Report

BCR-ABL1 Fusion Gene Positive Chronic Myeloid Leukemia - Chronic Phase in Childhood

Authors
Guddi Rani Singh[1], Rawi Agrawal[1], Bipin Kumar[2], Ajeet Kumar[1], Amit Kumar Sinha[1], Suryajit Kumar Singh[1]
[1]Senior Resident, Department of Pathology, IGIMS, Patna
[2]Professor and Head, Department of Pathology, IGIMS, Patna

Abstract
Philadelphia chromosome (Ph1)-positive Chronic Myelogenous Leukemia (CML) in a child below the age of 10 years is extremely rare. We have reported such a case in a 9 year old female child. Peripheral blood smear and bone marrow revealed features of CML and karyotypic study showed(Ph1) positivity. Biologic behaviour and prognosis are similar to that of adult-type of CML. we are reporting this case because of its extremely uncommon incidence.
Key Words: *Chronic myeloid leukemia (CML), adult type CML, childhood leukemia.*

Introduction

Philadelphia chromosome (Ph1)-positive Chronic Myelogenous Leukemia (CML) in childhood is rare, constituting about 3% of childhood leukemias [1]. In children below 10 years, it is even rarer. Only modem of information is available in the form of case reports [2,3]. Diagnosis of such cases can be made from peripheral blood smear examination, supported bykaryotypic study. Though biologic behaviour and prognosis are identical to that of adult type, we are reporting this case because of its extremely uncommon incidence[1,2] Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm that originates in a abnormal pluripotent bone marrow stem cell. The median age at diagnosis is in the 5th and 6th decades of life (WHO, 2008). CML occurring in children is a rare diagnosis, accounting for less than 10% of all CML and less than 2% of all pediatric leukemias (Hara et al, 2010, Singhal et al, 2010, Aperley, 2009, Radhakrishnan et al, 2009, Suttorp et al, 2009) {1,2,3,4,5}. 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]. We report one such rare case of adult type - CML in an 9 year old patient due to its unusual incidence.

Case Report

9 year female 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..On General examination, the patient was thin built. Local examination revealed hard and distended abdomen. On USG Liver was palpable 7 cms and huge splenomegaly was noted of 20 cms (Fig 1). 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.

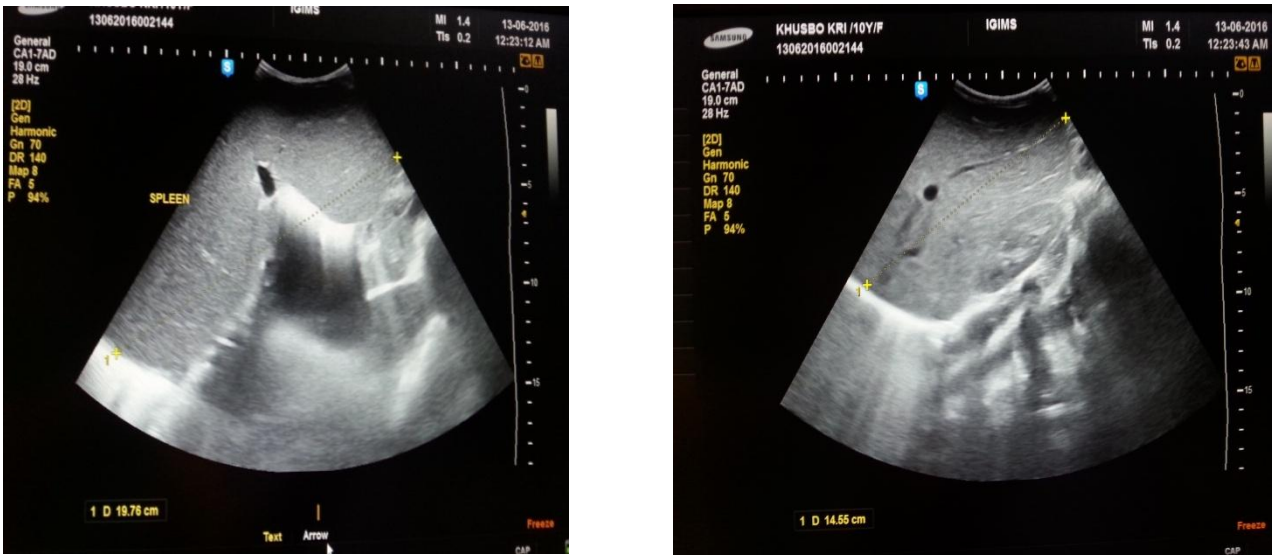

Fig 1. USG of abdomen showing liver 7cm and spleen 20 cm enlarged.

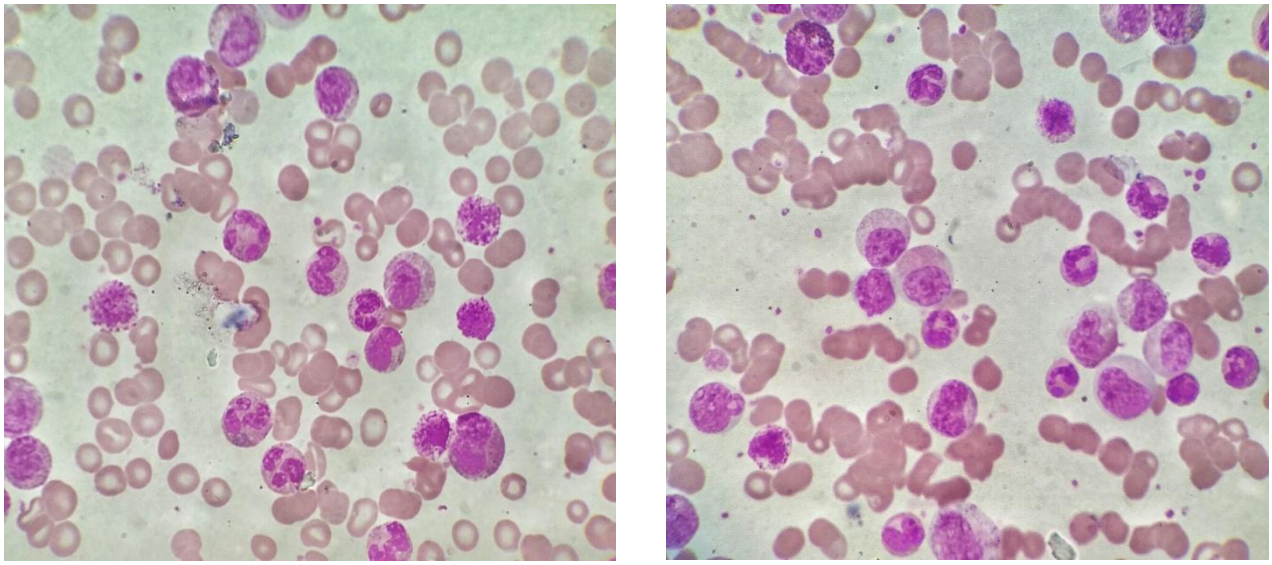

Fig 2. Showing PBS with basophils,myelocyte, metamyelocyte,and band form.

Routine hemogram was carried out, which revealed Hb. 6.6 gm/dl with markedly elevated Total leukocyte count of 2, 46,000/Cumm (246× 109/ lit). A peripheral differential count revealed shift of myeloid series up to myeloblasts. Basophilia and eosinophilia was noted. (Polymorphs + Band forms = 47%, Metamy-elocytes = 17%, Myelocyte = 15%,Promyelocytes = 02%, Blasts = 01%, Lymphocytes = 03%, Eosinophils = 06%,Monocytes = 03%, Basophils = 06%) . Platelet count was increased with 8.85 lac/Cumm (885 × 109/ lit). On peripheral smear examination, the diagnosis of – Chronic Myeloproliferative disorder suggestive of adult type CMl type was given (Fig 2).Bone marrow aspiration from posterior superior was carried out

under all aseptic precautions, which revealed hypercellular bone marrow with myeloid predominance. Granulocyte series showed all forms with increased myelocytes, Metamyelocytes and band forms. Erythroid and lymphoid series were suppressed. With above peripheral smear and bone marrow findings,final diagnosis of adult type - CML was given.cytogenetics [Philadelphia chromosome (Ph)] was carried out. BCR/ABL 1 fusion gene was detected in 80% of cells. So, the sample was positive for t $^{(9,22)}$. Thus diagnosis of Adult type of CML in 9 year old female patient was confirmed and patient was on chemotherapy with regular follow up. constitutes. Chemothera-peutic regim includes Hydroxyurea, interferon and. alpha, imatinib

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 [7]. BCR -ABL fusion gene is better prognostic variant in children and accounts for 3-5% of childhood leukemias [7]. CML in childhood presents as one of the two clinically distinct syndromes. i.e. .adult type CML (ACML) which is Philadelphia positive, and juvenile CML, also known as Juvenile Myelomonocytic Leukemia (JMML), which is Philadelphia negative. Diagnosis of such cases in chronic phase can be done by haematological investigations. CML occurring in children is called as adult form CML, which has the same clinical, morphologic and cytogenetic findings as adult Ph positive as in our case. Clinical features of adult type of CML in children are similar to that seen in CML occuring in adults as abdominal distension. Hepatomegaly, splenomegaly and generalized lymphadenopathy, anemia, hyperleukocytosis has been observed in all patients [4,7]. The mean spleen size has been 13cm and ranged from 8-22 cm as per Sinniah et al [8] as in our case. 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) [7]. Accelerated and blast phase has worst prognosis. Sinniah D et al [8] have reported only 5 cases of CML out of 168 cases of leukemia. Adult type CML remains poor and treatment needs re-evaluation [8]. Mshra A et al [9] reported similar findings for Ph positive CML in a child. Allogenic bone marrow transplant is the most successful therapy if a suitable HLA identical donor is available for chronic phase CML [5]. For patients without a suitable donor, control of the disease with chemotherapy (either hydroxyurea/busulphan or alpha interferon) is the best current alternative [5,10]. The same progress in the recent therapeutic strategy for older adults with haematological 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 [11].

Management of childhood CML in chronic phase is stem cell transplant [12]. Imatinib in childhood CML, controls leukocyte count in 1-2 weeks but with variable non haematological 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 in chronic phase. Thus our case is fulfilling the morphological and cytogenetic criteria required for diagnosis of adult type CML. This needs to be differentiated from the other form of myeloproli-ferative 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

neoplasm [12]. Hepatomegaly, lymphadenopathy, recurrent infections and bleeding are the hallmarks of JMML [1] with Leukocytosis with monocytosis [> 5000 / □l i.e. (> 5 × 109/ 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.

References

1. Hara Y, Kamura Y, Oikawa A, et al. Case of pediatric chronic myeloid leukemia with bilateral visual loss onset. Nippon Ganka Gakkai Zasshi. 2010; 114:459-463.
2. Singhal M, Makharia G, Bakhshi S. Childhood chronic myeloid leukemia with celiac disease. Pediatr Blood Cancer. 2010; 54:177-179
3. Apperley J. CML in pregnancy and childhood. Best Pract Res Clin Haematol. 2009;22: 455-474
4. Wechalekar AD, Parande CM Hematological malignancies in developing countries: is CML the commonest childhood leukemia? Leukemia. 2007; 21:2194-2197.
5. Suttorp M, Claviez A, Bader P, et al. Allogeneic stem cell transplantation for pediatric and adolescent patients with CML: results from the prospective trial CML-paed I. Klin Padiatr. 2009; 221:351-357.
6. Radhakrishnan S, Das P, Singh S, et al. Presentation of childhood CML mimicking bone sarcoma. Pediatr Blood Cancer. 2009;52:901-902
7. Vardiman JW, Melo JV, Baccarani M et al. Chronic myelogenous leukemia BCR-ABL1 positive. In: Swerdlow S; Campo E, Hariis NL, et al. WHO Classification of hematopoietic and lymphoid tissue, 4th ed. Switzerland: WHO Press, 2008:32-37.
8. Sinniah D, Ariffin WA, Shiong HW, Lin HP. Chronic myeloid leukemia in Malaysian children. Singapore Medical Journal. 1981;22 (6): 350-353.
9. Mishra A, Tripathi K, Mohanty L and Pujari S. Philadelphia Chromosome positive chronic myeloid leukemia in a child: A case report. *Indian Jr Hemat Blood Transfusion* 2010; 26 (3): 109-110.
10. Silliman CC, Tyson RW, Wei Q, et al. Philadelphia chromosome-positive leukemia in an adolescent boy after liver transplantation J Pediatr Hematol Oncol. 2003;25: 565-568.
11. Rabinowitz I, Larson RS. Chronic myeloid leukemia. In: Greer JP, Foerster J, Lukens JN, Rodgers GM (edi). Wintrobes clinical hematology. Lippincott Williams and Williams. 11th edition. Volume 2. 2004:2235-44.
12. Millot F, Traore P, Guihot J, Welken B, Leblane T, *et al.* Clinical and biological features at diagnosis in 40 children with chronic myeloid leukemia. Pediatrics. 2005; 116: 140-43.