INTRODUCTION

Atypical chronic myeloid leukemia (aCML) is a rare disorder, classified among the group of myelodysplastic/myeloproliferative neoplasms by WHO in 2008. It is characterized and distinguished from chronic myeloid leukemia (CML), mainly on the basis of presence of myeloid dysplasia and absence of BCR-ABL1 fusion gene.1 It is primarily a disease of elderly population. The mean age of diagnosis is 70 - 80 years. The estimated incidence of aCML is only 1 - 2 cases for every 100 cases of BCR-ABL1 positive CML.2 It is much rarer among paediatric population with few case reports and no case of aCML has been reported in children less than 1 year of age.

The current diagnostic criteria of aCML, both for adult and paediatric population, include peripheral blood leukocytosis (WBC ≥ 13 x 10^9/L) with immature neutrophil precursors ≥ 10%, basophils < 2%, and monocytes < 10% of white blood cells (WBC), bone marrow showing myeloid hyperplasia with myelodysplastic features, < 20% blasts and absence of BCR-ABL1 fusion gene and PDGFR gene rearrangements.3 Eighty percent of aCML patients exhibit karyotypic abnormalities, most common of which are +8 and del (20q).4 The disease has a poor prognosis but some of the diagnosed patients are found to have CSF3R mutations which can lead to activation of JAK/STAT signalling pathway. Ruxolitinib is the targeted therapy against this mutation, which has shown promising results in aCML patients.5

Same mutation has been reported by Freedman et al. in 2016 in an 11-year girl diagnosed with aCML.6 We report a case of aCML in a 5-month baby.
precursors 6%. Genetic analysis for Philadelphia chromosome and BCR-ABL1 gene was planned. The Philadelphia chromosome was not detected on karyotyping; and fluorescent in situ hybridization (FISH) studies were negative for BCR-ABL1 gene. It was further repeated on reverse transcriptase-polymerase chain reaction (RT-PCR) which turned out to be negative for BCR-ABL1 gene. The JAK2 V617F mutation was not detected. Testing of CSF3R-T618I mutation could not be carried out because of its non-availability in Pakistan. On cerebrospinal fluid (CSF) cytology, no immature myeloid forms were seen. Hydroxyurea was started at the dose of 50 mg/kg/day at day 1 and it was escalated on day 3 to 75 mg/kg/day.

**DISCUSSION**

Atypical chronic myeloid leukemia, BCR-ABL1 negative, has not been described separately for paediatric patients, since very few children with this disease have been reported. The diagnostic criteria followed nowadays were established by WHO in 2008. Before this period, many cases of children with juvenile myelomonocytic leukemia (JMML) have been described in the category of atypical presentation of CML with absence of BCR-ABL1 gene, thus creating a lot of confusion about aCML in paediatric population. Clinically, the course varies, but commonly these patients present with symptoms related to anaemia or bleeding tendency due to thrombocytopenia and splenomegaly. After the establishment of diagnostic criteria for myeloproliferative (MPN) and myeloproliferative/myelodysplastic neoplasms (MPN/MDS) and with the advent of targeted therapies, the importance of genetic studies cannot be denied. The detection of BCR-ABL1 by FISH and by RT-PCR is available in Pakistan. The targeted therapy, that is the tyrosine kinase inhibitors (TKI) including imatinib, has been made available for CML, BCR-ABL1 positive patients both in public and private sectors of the country. But when we talk about aCML, it is an atypical and rare disorder which presents with a number of heterogeneous mutations; detection of all may not be possible in majority of the cases. The reported mutations in aCML adult patients are CALR, JAK, ETNK1, SETBP1, NRAS, IDH2, NUP98 and CBL. Same mutations have been looked for children being diagnosed with aCML with no difference from adult patients.

aCML has a poor prognosis with the reported median survival of 14 - 29 months. Fleischman et al. identified oncogenic mutations in CSF3R (GCSFR) in 60% of chronic neutrophilic leukemia (CNL) and atypical chronic myeloid leukemia (aCML) patients. Such mutations are responsible for the activation of JAK/STAT pathways. Ruxolitinib is a JAK inhibitor targeting the specific mutation and has shown wonderful response in adult aCML patients. In a recent case report, CSF3R mutation has been identified in paediatric aCML patients as well, responding well to ruxolitinib. However, there is no extensive study on the use of this drug in children.

Our index case has highlighted the facts that aCML can occur in infants as well, thus the genetic analysis for such neoplasms should be carried out. The presence or absence of specific mutations can be of prime importance in the selection of a drug and for the follow-up of the residual disease.

**REFERENCES**


