

# The Gulf Journal of Oncology



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**5<sup>th</sup> Combined Gulf Cancer Conference**  
Sharjah, United Arab Emirates

**CONTINUUM OF CARE  
IN CANCER CONTROL  
& MANAGEMENT**

Awareness & Prevention | Early Detection & Screening | Diagnosis  
Treatment | Palliative Care | Survivorship | Research

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NOV 2022**

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The Official Journal of the Gulf Federation For Cancer Control

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## Case Report

# Childhood Early T Cell Precursor Acute Lymphoblastic Leukaemia with t(12;17) (p13;q21) Translocation – A Rare Entity or Part of ETP/Myeloid Mixed Phenotype Acute Leukaemia

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## Abstract

The translocation t(12;17) (p13; q21) is a rare cytogenetic event most commonly described in pre-B– acute lymphoblastic leukaemia and acute myeloid leukaemia. We identified a child with an immunophenotype of Early T Cell Precursor Acute Lymphoblastic Leukaemia ETP– ALL having t(12;17) (p13; q21) translocation as the primary karyotypic anomaly. The association of t(12;17) (p13;

q21) with ETP–ALL has not been described previously in literature. The possibility of it being a novel genetic abnormality or a part of the newly described entity of ETP/myeloid MPAL is being discussed. Detection of such abnormalities can alter the prognosis of ETP–ALL.

**Key words:** ETP–ALL , t(12;17) (p13;q21) translocation, ETP– MPAL

## Introduction

Early T cell Precursor Acute Lymphoblastic Leukemia (ETP–ALL) is a relatively new entity of acute lymphoblastic leukaemia (ALL), described in the WHO classification of tumours of hematopoietic and lymphoid tissues (2017), characterised by negative T cell surface markers CD1a and CD8 ; and also absent expression of CD5 with aberrant positivity seen in one or more myeloid or stem cell markers ( CD34, CD13, CD33, HLA– DR , CD117, CD65, CD11b etc) <sup>(1)</sup>. The presence of myeloperoxidase (MPO) expression in ETP–ALL characterises it under T/ myeloid mixed phenotype acute leukaemia (MPAL). Recently, many authors have described a new provisional entity of ETP/myeloid MPAL <sup>(2,3)</sup>.

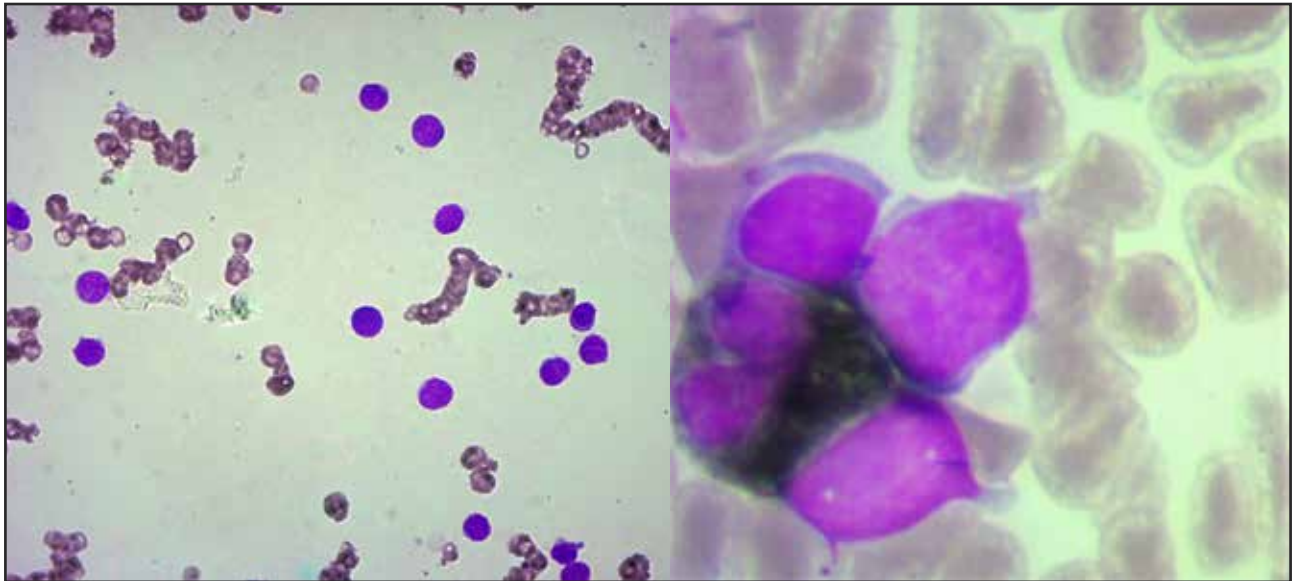
The role of cytogenetic abnormalities in the prognosis of ALL is well established and recurring chromosomal abnormalities are present in as many as 80% of all cases of ALL. However, t(12;17) (p13;q21) is a very rare translocation and is mainly described in ALL pre–B immunophenotype, acute myeloid leukaemia (AML) and acute mixed lineage leukaemia<sup>(4)</sup>.

We report a child with ETP– ALL who had a t(12;17) translocation which has never been described in this condition. The possibility of it being a novel genetic abnormality or a part of the newly described entity of ETP/ myeloid MPAL is being discussed.

## Case Report

A 6–year–old girl presented to us with intermittent fever and petechial bleeding of 2 weeks duration. Her physical examination revealed bilateral cervical lymphadenopathy and hepatosplenomegaly. The past medical history and family history were unremarkable. Peripheral blood findings showed the following: b level – 6.5 g/dL; leukocyte count – 18.780 x 10<sup>9</sup>/L (18,780/ μL); and platelet count – 25 x 10<sup>9</sup>/L (25,000/μL) with 10% neutrophils, 36% lymphocytes, 46% blasts. Serum LDH was 1110 IU/L and there was no evidence of tumour lysis. On the basis of these findings we suspected acute leukaemia and a bone marrow examination was conducted. Bone marrow morphology was suggestive of acute lymphoblastic leukaemia which was negative for MPO stain. [Figure1]. CSF cytology was negative for malignant cells.

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**Figure 1:** Bone Marrow Smears showing acute lymphoblastic leukaemia  
(a) MPO negative lymphoblasts (with neutrophils as positive internal control) (b)

Immunophenotyping showed moderate positivity for CD117, CD11b, CD4, CD7, HLA DR, cy CD3 and dim positivity for CD3 and TdT. The cells were negative for CD5, CD1a and CD 8 which was suggestive of an ETP-ALL [Figure 2].

Giemsa-banded karyotype by GTG banding technique showed 46,XX, del(5)(q13),t(12;17)(p13;q21)[15]/46,XX[5]. Fifteen of the 20 metaphases analysed were abnormal and showed deletion on the q arm of chromosome 5 at band 5q13 along with translocation involving the p arm of chromosome 12 and q arm of chromosome 17 at bands 12p13 and 17q21 [Figure 3]. Cytogenetics by qualitative polymerase chain reaction did not show any other genetic abnormalities.

In view of the very rare translocation detected, immunohistochemistry with MPO stain was done on the bone marrow biopsy to rule out any evidence of myeloid series; which was negative. The bone marrow biopsy also did not have any evidence of dysplasia.

A diagnosis of early precursor T-ALL was made based on the reports and she was started on induction chemotherapy with BFM IC 2009 protocol. She received protocol based treatment with steroids, vincristine, daunorubicin and L-asparaginase until Day 29 of the protocol. Poor prednisolone response (PPR) was documented on day 8 with blast count of more than 5000/mm<sup>3</sup> in the peripheral blood. PPR according to our protocol was defined as a blast count number more than 1000/mm<sup>3</sup> in the peripheral blood on day 8 of the protocol. Blasts were cleared from peripheral blood only by Day 24 of protocol. She passed a mass per vaginum while urination on Day 26 of the protocol which

could not be retrieved for histopathological examination. This expulsion of the mass resulted in significant perineal injury. Child developed pancytopenia, perineal infection, gram negative septicaemia with carbapenem resistant *Pseudomonas aeruginosa*, septic shock and multi organ failure. She succumbed to neutropenic sepsis on day 35 of the treatment phase.

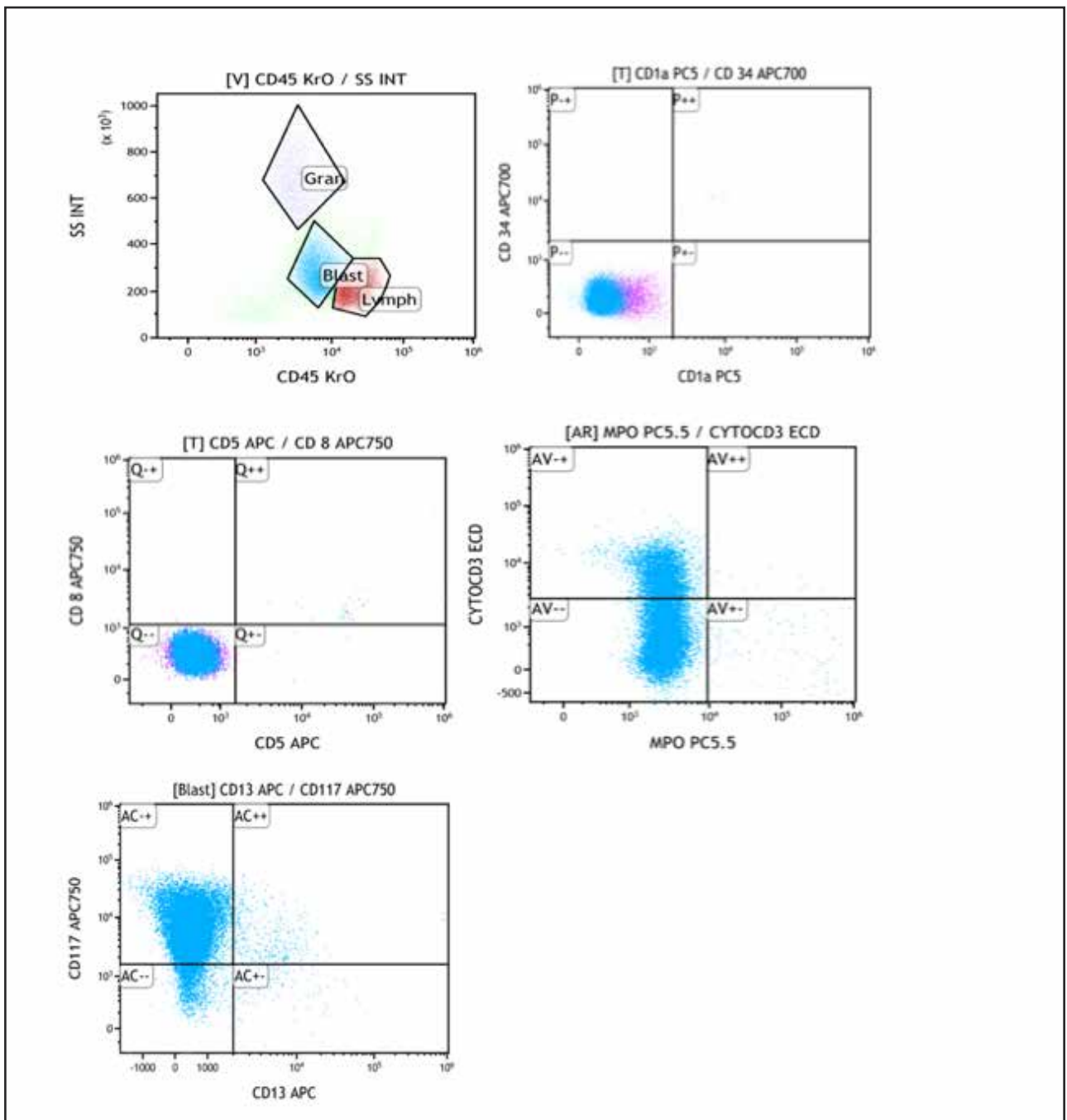
## Discussion

ETP-ALL was first described by Coustan-Smith E et al from St Jude Children's Research Hospital in 2009 as a high risk T-cell ALL with very poor prognosis and distinctive genetic profile. Genetic expression profiling revealed over-expressed genes which included CD44, CD34, KIT, GATA2, CEPBA, SPI1, ID2 and MYB, and under-expression of CD1, CD3, CD4, CD8, RAG1, NOTCH3, PTCRA, LEF1, TCF12, LAT, LCK, TCF7, ZAP70<sup>(5)</sup>.

ETP-ALL is a neoplasm that is composed of T-cells representing recent immigrants from the bone marrow to the thymus, indicating only limited early T-cell differentiation. They account for 5–10% of adult ALL and 10–13% of paediatric T-ALL<sup>(1)</sup>.

By definition, the staining for MPO is negative in ETP-ALL. The expression of MPO classifies it under T/myeloid MPAL. Patel B et al in 2016, had proposed a new entity ETP-myeloid MPAL in addition to already existing ETP-ALL after immunophenotyping and molecular profiling; which is a borderland between ETP-ALL/AML in addition to more typical cases of T-ALL/AML<sup>(2)</sup>. Mutations in FLT3-ITD and DNMT3A were described to be characteristics of this subset.

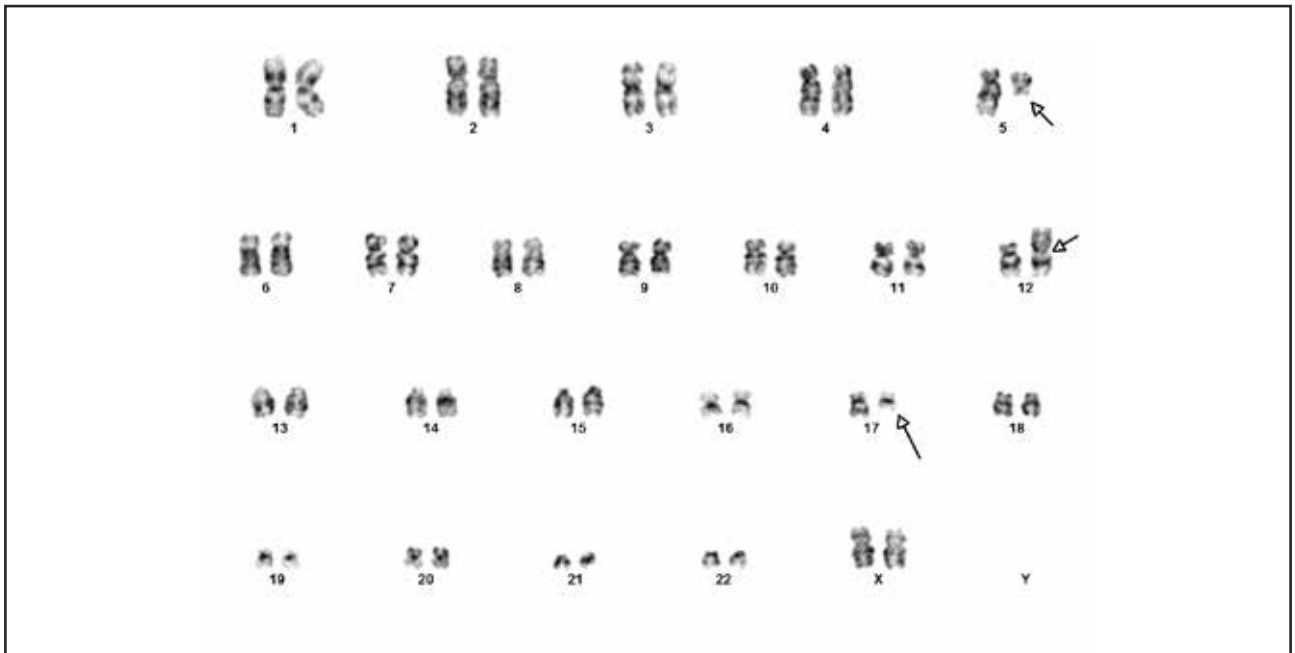




**Figure 2:** Flow cytometry analysis of peripheral blood. Blasts (blue) represent 80% of the total WBCs. They show dim expression for CD 45, subset positive for cy CD 3, positivity for CD 117, CD 4 and Tdt and are negative for CD 34, CD 1a, CD 5, and CD 8. This immunophenotype is typical of Early T cell precursor Acute lymphoblastic leukaemia.

The short arm of chromosome 12 is particularly prone to translocations in ALL and abnormalities are present in up to 25% of childhood ALL. The TEL gene is likely to be involved in these 12p abnormalities. However, t(12;17)(p13;q21) is a very rare translocation and only about 25 cases have ever been reported in literature<sup>(6)</sup>. The rearrangement is a zinc finger protein ZNF384 on chromosome 12 while the partner gene on chromosome 17 can vary from q11–21; most common being TAF15.

Most of the case reports on t(12,17) translocation are in precursor B–ALL and AML<sup>(7,8,9)</sup>. It has also been identified as a recurrent cytogenetic aberration in mixed phenotype leukemias in older individuals<sup>(10)</sup>. Lineage switch from pro–B ALL to AML in a case with t(12;17)(p13;q11)/TAF15–ZNF384 rearrangement has been described<sup>(11)</sup>. There is also a case report of the translocation in secondary acute myeloid leukaemia<sup>(12)</sup>. Most of the case reports are in adult patients while among the very few children



**Figure.3:** Giemsa–banded karyotype by GTG banding technique showing 46,XX,del(5)(q13),t(12;17)(p13;q21)[15]/46,XX[5]

described to have the rare translocation, most are in acute lymphoblastic leukaemia with B cell phenotype<sup>(13,14)</sup>. To the best of our knowledge this is the only case report of t (12;17) (p13; q21) in a case of childhood ETP–ALL. Whether this is a novel translocation or this represents a clone of myeloid blasts which may be characterised as ETP/myeloid MPAL needs further discussion. Our patient also had evidence of 5q deletion which is also a feature seen in acute myeloid leukaemia and MDS<sup>(15)</sup>.

Initial data suggested that adults and adolescents with ETP –ALL had a poor prognosis<sup>(16)</sup>; although emerging data from the UKALL and COG group suggests that they might have an intermediate prognosis with ALL regimens and might not require allogeneic transplant in the primary setting<sup>(17, 18)</sup>.

The prognostic significance of ZNF384/TAF15 translocation is not very clear<sup>(19)</sup>. But detection of such chromosomal abnormalities may suggest a biphenotypic nature of the disease and thus confer a poor prognosis to the otherwise better prognosis of ETP –ALL ; signifying the importance of identifying poor prognostic translocations<sup>(20)</sup>.

The limitation of our report is that we could not confirm the translocation by Fluorescent in situ Hybridisation (FISH).The mass passed per vaginum could have represented a chloroma /granulocytic sarcoma suggesting a biphenotypic lineage but could not be examined histopathologically.

## Conclusion

We report a 6 year old child with ETP–ALL having a rare t (12,17) translocation. The rarity of the particular phenomenon and whether it can be part of the ETP/MPAL spectrum is discussed.

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