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Leukaemia Section

Short Communication

t(5;12)(q33;p13) ATF7IP/PDGFRB

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Abstract

Ph-like ALL is characterized by several chromosomal translocations involving activating cytokine receptor or tyrosine kinase such as CRLF2, ABL1, JAK2, and PDGFRB (Robert K.G et al, 2014). Recent increasing evidences suggest that patients with Ph-like ALL bearing PDGFRB translocation are potentiated to respond to tyrosine kinase inhibitors. Thus, this translocation should be included within the molecular companion diagnostics to facilitate tailor-made cancer therapy.

Keywords

Ph-like acute lymphoblastic leukemia, tyrosine kinase inhibitor (TKI), PDGFRB

Clinics and pathology

Disease

Ph-like acute lymphoblastic leukemia

Clinics

The patient is an 8-year-old male with B-ALL. Initial cytogenetics analysis showed a 45, XY, -7, add (12) (p13). RNA sequence analysis identified a novel translocation of ATF7IP/PDGFRB (Kobayashi K.et al, 2013). He showed good response to standard risk ALL therapy, but he relapsed even in the continuation of the maintenance chemotherapy at 26 months after the diagnosis. He received 3 course of salvage therapies following by stem cell transplantation. Second generation dasatinib was commenced with the minimum residual disease (MRD) at day 60 post-transplant. The therapeutic response was prompt, with the disappearance of genomic-PCR based on MRD within 3 months, and he has maintained complete molecular remission for 12 months (Kobayashi K.et al, 2014).

Prognosis

As was shown in Ph-like ALL bearing PDGFRB translocation, i.e. EBF1/PDGFRB, t(5;12)(q33;p13) ATF7IP/PDGFRB translocation seems response to TKI.

Cytogenetics

Cytogenetics morphological

Banding cytogenetics revealed 45, XY, -7, add (12) (p13). The mRNA sequence analysis identified an in-frame transcript fusing exon 13 of ATF7IP with exon 11 of PDGFRB, i.e. t(5;12)(q33;p13).

Genes involved and proteins

PDGFRB

Location

5q33

Protein

PDGFRB is a frequent target of chromosomal translocation in a broad spectrum of hematological malignancies.

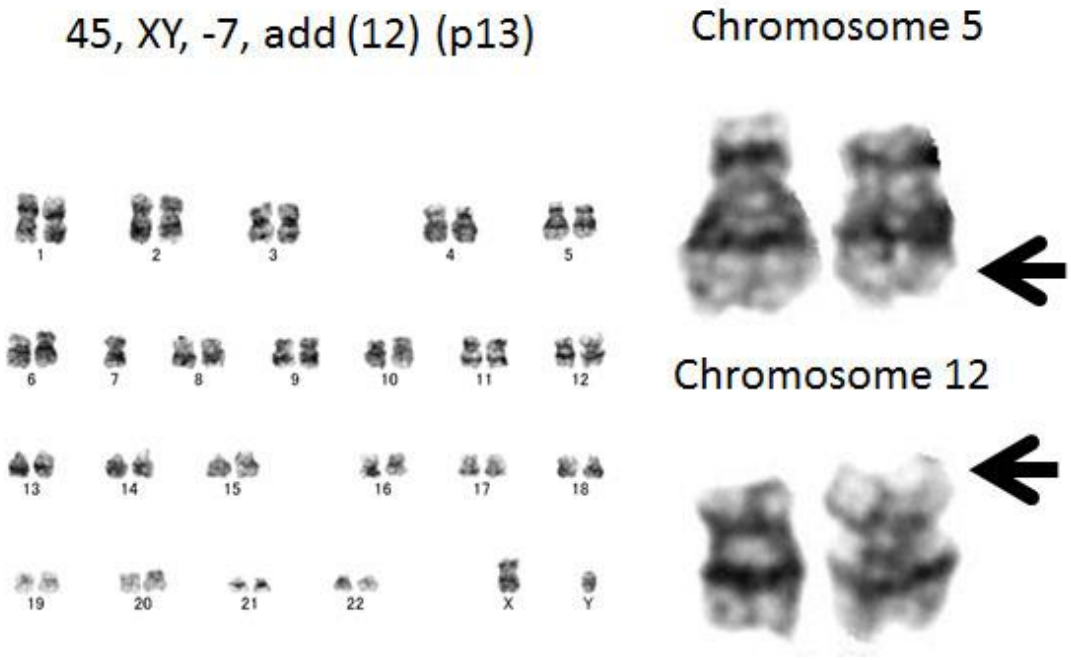
ATF7IP

Location

12p13

Protein

ATF7IP acts as transcriptional regulators and is frequently overexpressed in cancer cells modulating



telomerase TERT and TERC gene expression (Liu, L. et al, 2009).

Result of the chromosomal anomaly

Hybrid gene

Description

5' ATF7IP-3' PDGFRB

Fusion protein

Description

Forced expression of ATF7IP/PDGFRB, not wild-type PDGFRB, conferred growth factor independence to murine Ba/F3cells, indicating that coiled-coil domain from 5' ATF7IP- would favour subsequent constitutive activation of the PDGFRB tyrosine kinase domain.

References

Kobayashi K, Miyagawa N, Mitsui K, Matsuoka M, Kojima Y, Takahashi H, Ootsubo K, Nagai J, Ueno H, Ishibashi T, Sultana S, Okada Y, Akimoto S, Okita H, Matsumoto K, Goto H, Kiyokawa N, Ohara A. TKI dasatinib monotherapy for a patient with Ph-like ALL bearing ATF7IP/PDGFRB translocation. Pediatr Blood Cancer. 2015 Jun;62(6):1058-60

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