# Bilineage involvement of the fusion gene in a patient with FIP1L1-PDGFRA positive chronic eosinophilic leukemia and T-cell lymphoblastic lymphoma: A CASE REPORT

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## INTRODUCTION

**There are successful attempts treating FIP1L1-PDGFRA positive chronic eosinophilic leukemia (CEL) with low dose imatinib mesylate. However, FIP1L1-PDGFRA fusion gene can induce both proliferation and differentiation of eosinophils, neutrophils, monocytes, lymphocytes and mast cells. A recent report noted three cases with association of FIP1L1-PDGFRA positive CEL and T-cell lymphoblastic lymphoma (T-LBL).**

## CASE:

**A 42 years-old man addmitted to the hospiltal.**

### Clinical presentation:

- **General fatigue**
- **Hepatosplenomegaly**
- **Cervical and axilar lymphadenopathy.**

### Peripheral blood:

- **Leucocytosis 51 x $10^9$/l**
- **Marked eosinophilia 22 x $10^9$/l**
- **Evated promyelocytes and myelocites**
- **No blasts.**

### Hystological findings:

- **Bone marrow biopsy exhibited diffuse eosinophilic hyperplasia with iron deposition, II° reticulin fibrosis and secondary/reactive mastocytosis and minor population of CD3+ TdT+ precursors (<5%): histological features compatible with diagnosis of chronic eosinophilic leukaemia (CEL) with possible minimal T-LBL. The flow cytometry was recommended. (*Figure 2*).**
- **Cervical lymph node biopsy showed T-LBL.**
  - **Immunophenotype: TdT+; CD34-; CD1a+; CD117-; CD3+; CD2+ ; CD4+; CD5+; CD7+; CD10+/-; CD79a-/+; MPO-. (*Figure 1*).**

### Treatment:

**6 cycles of ACVBP chemotherapy was administered resulting**

- **complete remission of T-LBL**
- **decrease of eosinophil counts to upper normal range.**

**However, eosinophilia progressed again to more than 51 x $10^9$/l in a couple of months after completion of chemotherapy.**

### Molecular diagnostics:

- **G-band karyotyping showed no abnormalities and BCR-ABL was absent in the peripheral blood.**
- **FIP1L1-PDGFRA transcripts (*Figure 4*) by RT-PCR were identified in**
  - **Peripheral blood and bone marrow (*Figure 3*).**
  - **Lymph nodes affected by T-LBL (*Figure 3* ).**

### Final diagnosis:

**FIP1L1-PDGFRA positive chronic eosinophilic and T-lymphoblastic lymphoma.**

### Follow up:

- **Blood and bone marrow counts normalized after the initiation of imatinib mesylate 100 mg/d.**
- **2 years after the final diagnosis the patient is alive in complete clinical, hematological and molecular remission *(Figure 5)* on imatinib 100 mg/d.**

## CONCLUSION

- **FIP1L1-PDGFRA positive CEL in conjunction with T-cell LBL suggests a bilineage cell involvement probably arising from an early hematopoietic progenitor.**
- **Identification of FIP1L1-PDGFRA in cases of T-LBL with concurrent eosinophilia is essential in selecting the targeted tyrosine kinase therapy.**

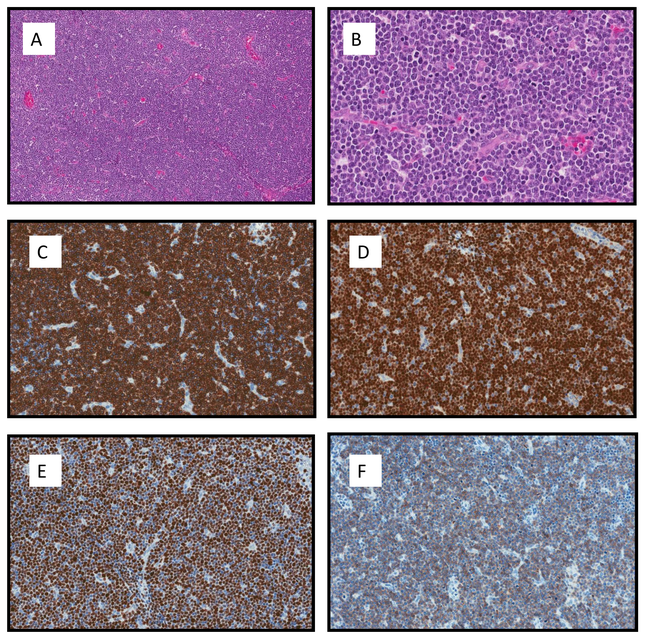


**Figure 1: A. HE, 10x. T-LBL: the diffuse infiltration of blastic cells with dense neovascularisation and poorly visible interstitial macrophages ("starry sky" pattern).**
**B. HE, 40x. T-LBL: the medium sized blastic cells with the scant cytoplasm, ovoid and slightly irregular and lobated nuclei and multiple mitoses.**
**C. CD3, 20x. The diffuse and strong cytoplasmic positivity of the tumor cells.**
**D. TdT, 20x. The diffuse and strong nuclear positivity of the tumor cells.**
**E. Ki67, 20x. High proliferative activity in the tumor cells (~90%).**
**F. CD1a, 20x. The diffuse and weak-moderate cytoplasmic positivity of the tumor cells.**

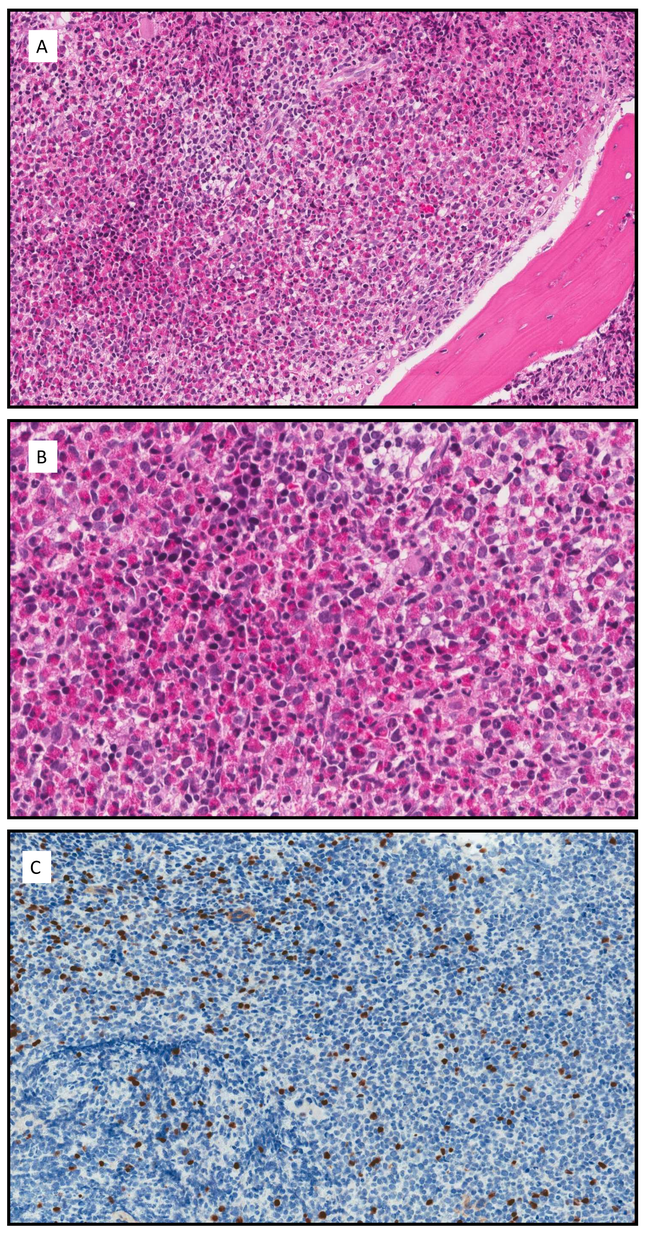


**Figure 2. A. HE, 20x. CEL: the hypercellular bone marrow with the prominent hyperplasia of the eosinophilic lineage.**
**B. HE, 40x. CEL: diffuse hyperplasia of the eosinophilic lineage with scattered erythroid islands and single megakariocytes.**
**C. TdT, 20x. The TdT+ (CD3+) precursor population in the bone marrow was elevated, but do not exceed 5% limit in the course of disease.**

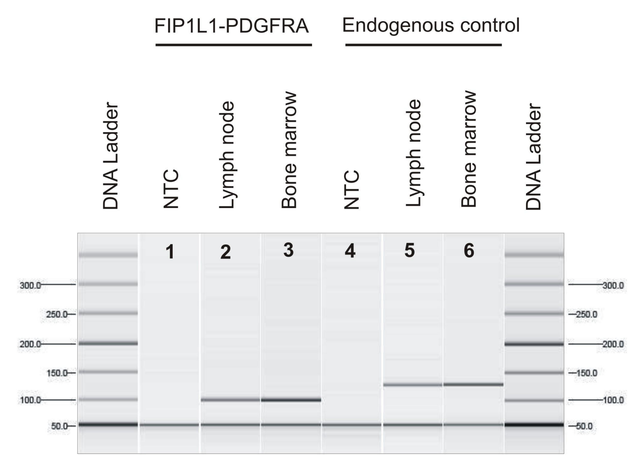


**Figure 3: RT-PCR analysis of *FIP1L1-PDGFRA* fusion transcripts in lymph node and bone marrow samples. Obtained PCR products (Lanes 2 and 3) correspond to a fusion of *FIP1L1* exon 10 and *PDGFRA* exon 12. *ABL* was used as an endogenous control (Lanes 5 and 6). The sizes of DNA Ladder are indicated.**

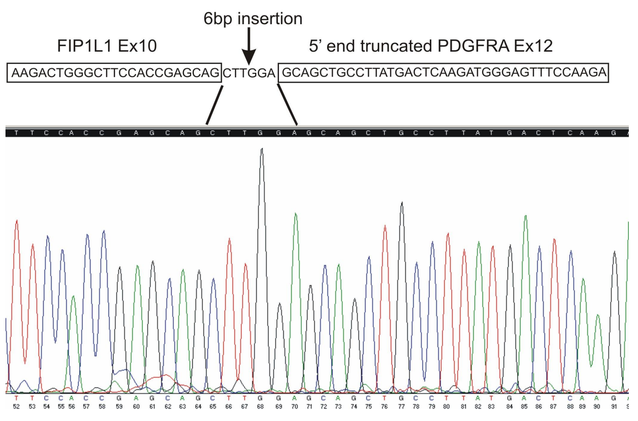


**Figure 4. Sequencing of PCR product. Sequence analysis of PCR product of rearranged *FIP1L1-PDGFRA* confirmed an in-frame fusion between *FIP1L1* exon 10 and 5'-end truncated *PDGFRA* exon 12 with intervening 6 nucleotides.**

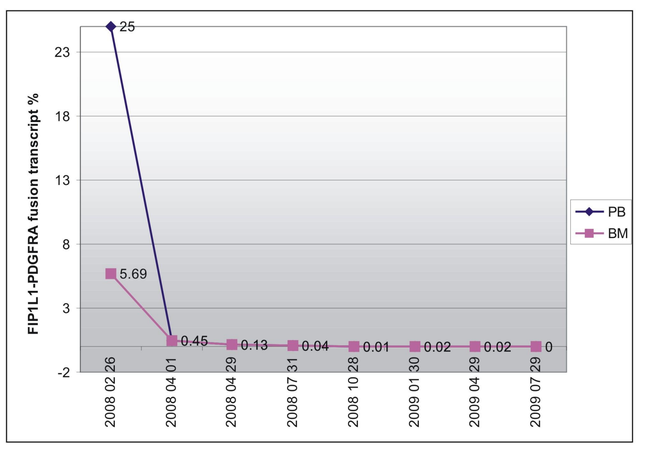


**Figure 5. MRD monitoring of *FIP1L1-PDGFRA* fusion transcripts in PB and BM. Quantification of *FIP1L1-PDGFRA* transcripts was performed as described elsewhere (Jovanovic, J. V. et al. Low-dose imatinib mesylate leads to rapid induction of major molecular responses and achievement of complete molecular remission in FIP1L1-PDGFRA-positive chronic eosinophilic leukemia, Blood 2007, Vol 109, No 11, p4635-4640). The rate of *FIP1L1-PDGFRA* fusion transcripts was normalized to the *ABL* gene. The relative quantities of *FIP1L1-PDGFRA* transcripts at different sampling intervals are indicated.**