Letter to the editor

Myelodysplastic syndrome accompanied by basophilia and eosinophilia with
t(5;12)(q31;p13)

Yukitaka Katsura\textsuperscript{a}, Kazumi Suzukawa\textsuperscript{a,b,*}, Toru Nanmoku\textsuperscript{c}, Noriko Nemoto\textsuperscript{a}, Takayuki Machino\textsuperscript{a}, Naoshi Obara\textsuperscript{a}, Yasushi Okoshi\textsuperscript{a}, Harumi Yamamoto Mukai\textsuperscript{a}, Yuichi Hasegawa\textsuperscript{a}, Hiroshi Kojima\textsuperscript{b}, Yasushi Kawakami\textsuperscript{b}, Toshiro Nagasawa\textsuperscript{a}.

\textsuperscript{a}Department of Clinical and Experimental Hematology, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Ibaraki, Japan
\textsuperscript{b}Department of Clinical Pathology, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Ibaraki, Japan,
\textsuperscript{c}Central Laboratory, Tsukuba University Hospital, Ibaraki, Japan

\textsuperscript{*}Corresponding author Kazumi Suzukawa
Department of Clinical and Experimental Hematology, Major of Advanced Medical Applications, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tennoudai, 1-1-1, Tsukuba, Ibaraki 305-8575, Japan
Telephone/FAX: +81-029-853-3054
E-mail: suzukazu@md.tsukuba.ac.jp
The t(5;12)(q31-35;p12-13) translocation is rare among cytogenetically categorized myeloid diseases. Here we describe a case of MDS with basophilia followed by leukocytosis, basophilia and eosinophilia with t(5;12)(q31;p13).

A 44-year-old man was referred to Tsukuba University Hospital due to severe anemia and thrombocytopenia in August 2005. Peripheral blood showed hemoglobin 4.5 gm/dl with MCV 109 fl, platelets 73 × 10⁹ l⁻¹ and white blood cells 4.9 × 10⁹ l⁻¹ with 23% basophils, 3% eosinophils and 0% blasts. Bone marrow was slightly hypocellular marrow with trilineage dysplasia. Cytogenetic examination of the bone marrow cells revealed 46,XY. A diagnosis of MDS-RAEB2 was made according to the WHO classification. Two months later, his white blood cell (WBC) count gradually increased with emerging eosinophilia. Peripheral blood showed white blood cells 27.5 × 10⁹ l⁻¹ with 54% basophils, 29% eosinophils and 0% blasts. Bone marrow was hypercellular with relative increase of immature cells. Cytogenetic examination of his bone marrow cells revealed 47,XY,t(5;12)(q31;p13), +8[5]/46,XY[15]. We tried short-term administration of Imatinib in our case but saw no response. We next started administration of hydroxyurea. The
WBC count temporarily increased to maximum of $87.3 \times 10^9$ l$^{-1}$, and then gradually decreased. Three months later, he received unrelated allogenic bone marrow transplantation following a myeloablative preparation regimen of cyclophosphamide (120mg/kg) and total body irradiation (12Gy) in March 2006. Currently, he is healthy with negative test for t(5;12)(q31;p13).

Recently, human long fatty acyl CoA synthetase gene, ACS2, on 5q31 was identified as a fusion partner of ETV6 in acute myeloid leukemia (AML) and MDS cases with t(5;12)(q31;p13)[1]. We also performed RT-PCR for ETV6-ACS2 from the bone marrow cells following the published method [1] and an amplified DNA fragment was detected (fig.1A). DNA sequencing of the DNA fragment revealed an out-frame fusion of exon 1 of ETV6 gene to exon 1 of ACS2 gene (fig.1B). Expressions of interleukin-3 (IL-3) or interleukin-5 (IL-5) were detected in the bone marrow cells of our case while no expression was seen in controls (fig.1C,D), which may be related to the cause of eosinophilia or basophilia as previously suggested [2, 3].

We have summarized the published reports of hematological disorders accompanied by t(5;12)(q31;p12-13) (Table 1). A remarkable male preponderance (14/15) can be seen. Only two cases (case 8 and case 16) were
accompanied by basophilia (Table 1, [1, 4]). On the other hand, 15 of 18 cases (83%) were accompanied by eosinophilia (Table 1, [1-13]). ETV6:ACS2 fusion gene was identified in seven cases. Eight cases seem to be classified as MDS / MPD by WHO criteria. These cases may be typified as a distinct subgroup of myeloid disorders. Another nonrandom translocation which involves the short arm of the chromosome 12 and the long arm of the chromosome 5 is the t(5;12)(q33;p13) [14]. The translocation juxtaposes the ETV6 gene with the platelet-derived growth factor receptor β (PDGFRβ) gene. It is of clinical importance that imatinib mesylate is effective for patients with rearrangement of the PDGFRβ gene [15]. Our patient received a course of imatinib without response. It is important to determine the precise breakpoint or identify the fusion gene in hematological malignancy with t(5;12) to ensure an appropriate choice of therapy.

We experienced a rare case of MDS with t(5;12)(q31;p13) with basophilia and eosinophilia. Further studies are needed to understand the precise mechanism of disease by the translocation or the resultant fusion gene.
References


Figure captions

**Fig. 1.** (A) RT-PCR amplification of *ETV6-ACS2* fusion. Lane 1: 50bp ladder marker; lane 2: bone marrow at initial presentation in August 2005; lane 3: bone marrow with basophilia and eosinophilia in December 2005; lane 4: bone marrow after alloBMT in April 2006. (B) DNA sequencing of the RT-PCR product revealed a fusion between *ETV6* exon 1 and *ACS2* exon 1. Arrows indicate the breakpoint. Lower line represents putative coding region of *ETV6-ACS2* fusion[1]. (C,D) RT-PCR of *IL-3* (C) and *IL-5* (D) genes. Lane 1: 50bp ladder marker; lane 2: bone marrow at initial presentation in August 2005; lane 3: bone marrow with basophilia and eosinophilia in December 2005; lane 4: bone marrow after alloBMT in April 2006; lane 5 and 6: bone marrow from lymphoma patients without involvement. Transcription of *IL-3* was detected as a 169 bp fragment. The 394 bp fragment is due to an amplification of contaminated genomic DNA[2].
## Table 1: Cases of myeloproliferative disorders with t(5;12)(q31;p12-13)

| No. | Diagnosis       | Age/Sex | WBC (x10^9/L) | Hb (g/dL) | Platelet (x10^9/L) | Karyotype                                      | Detection of ETV6-ACS2 | Therapy                          | Follow-up (mons) | Status          | Ref. |
|-----|----------------|---------|---------------|-----------|-------------------|------------------------------------------------|---------------------------------|-------------------|-----------------------------|-----------------|----------------|-----|
| 1   | aCML           | 49/M    | NG            | increase  | NG                | NG, 46,XY,t(5;12)(q31;p12)                          | RT-PCR                        | NG                | NG                          | NG              |                | [2] |
| 2   | aCML           | 34/M    | NG            | increase  | NG                | NG, 46,XY,t(5;12)(q31;p12)                          | ND                             | NG                | 14+ alive            | NG              |                | [6] |
| 3   | aCML           | 53/M    | 49.0          | 0         | 0.88              | 56.6, 47,XY,t(5;12)(q31;p12),+10                    | ND                             | polychemotherapy     | 9 dead of sepsis     |                | [7] |
| 4   | aCML           | 40/M    | 46.9          | 12        | 1.2               | 6.8, 46,XY,t(5;12)(q31;p12)                         | ND                             | allo-SCT           | 14 dead             |                | [7] |
| 5   | HES (aCML?)    | 43/M    | 26.5          | 18        | NG                | NG, 46,XY,t(5;12)(q31;p12)                         | ND                             | HU,VCR,allo-SCT     | 48 dead of fungal infection |                | [8] |
| 6   | aCML/CMMoL     | 16/M    | 46.4          | 8         | 3                 | 12.0, 46,XY,t(5;12)(q31;p12)                        | ND                             | HU                | 31+ alive            | NG              | [9] |
| 7   | CMMoL          | 41/M    | 32.4          | 11        | 6                 | 202, 46,XY,t(5;12)(q31;p12)                        | RT-PCR                         | AraC              | dead of sepsis       | [1] |
| 8   | MDS            | 69/F    | 8.8           | 3         | 0                 | 37.5, 46,XX,t(5;12)(q31;p13)                       | ND                             | HU                | 84+ alive            | [3] |
| 9   | MDS            | 27/M    | 41.1          | 42        | NG                | NG, 46,XY,t(5;12)(q31;p12)                         | RT-PCR                         | NG                | 1 dead of sepsis      | [1] |
| 10  | MDS            | 8/F     | 33.7          | 62        | 1.0               | 322, 46,XY,t(5;12)(q31;p12)                        | ND                             | HU                | 48+ alive            | [11] |
| 11  | MDS            | 7/M     | 37.0          | 69        | NG                | NG, 46,XY,t(5;12)(q31;p12),-8,+12                  | ND                             | HU,FN             | 48+ alive            | [11] |
| 12  | EoL            | 59/M    | 136.0         | 94        | 1.3               | 116, 46,XY,t(5;12)(q31;p12)                        | ND                             | HU,BU             | 3 dead of brain stroke | [5] |
| 13  | AML            | 53/M    | 59.5          | 69        | 3                 | 59.5, 46,XY,t(5;12)(q31;p13)                       | RT-PCR                         | polychemotherapy    | 9 dead of eos. infiltration | [1] |
| 14  | MPD→EoL       | 50/M    | 20.9          | 10        | 3                 | 40, 46,XY,t(5;12)(q31;p12), t(19;21)(p13;q22)       | ND                             | BU,6TG            | 3 dead              | [12] |
| 15  | AML-relapse    | 30/M    | 41.1          | 42        | 2.4               | 13.4, 46,XY,t(5;12)(q31;p12)                       | ND                             | NG                | 1 dead of sepsis      | [13] |
| 16  | PV             | 29/M    | 11.2          | 16        | NG                | 21.0, 522, 46,XY,t(5;12)(q23;13p13)                 | FISH                           | HU                | 42+ alive            | [4] |
|     |                |         | 9.6           | 15        | 15                | 16.5, 484, 47,XY,t(5;12)(q31;p13),+8               | FISH                           | HU                | dead of hemorrhage    | [4] |
| 17  | PV/AML         | 31/F    | 18.2          | NG        | 13.0              | 278, 46,XY,t(5;12)(q23;13p13)                      | FISH                           | HU,Purinethol,AraC  | 11 dead of hemorrhage | [4] |
| 18  | MDS            | 44/M    | 22.7          | 30        | 42                | 5.5, 85, 47,XY,t(5;12)(q31;p13),+8                 | RT-PCR                         | HU,AraC,STI571, allo-SCT | 8+ alive | [Present case] |

**Abbreviations:** Eo, eosinophils; Baso, basophils; Mono, monocytes; NG, not given; aCML, atypical chronic myeloid leukemia; MDS, myelodysplastic syndrome; AML, acute leukemia; EoL, Eosinophilic leukemia; alloSCT, allogenic stem cell transplantation; IFN, interferon; HU, hydroxyurea; BU, busulfan; VCR, vincristine; ND, no determination.
Fig. 1

**A**

*ETV6-ACS2*

**B**

**ETV6**

```
P A Q C S I K S L S S H F W
CTGTGAGACATGTCTGAGACTCCTGCTCAGTGTAGCATTAAGAGTTTGTCCTCTCACTTCTGG
L * D M S B T P A Q C S I K S L S S H F W
```

**ACS2**

```
AGAAGATGCAGACACAGGAGATCCTGAGGA
```

**ETV6 exon1**

**ACS2 exon1**

**C**

*IL-3*

**D**

*IL-5*

```
CTGTGAGACATGTCTGAGACTCCTGCTCAGTGTAGCATTAAGAGTTTGTCCTCTCACTTCTGG
L * D M S B T P A Q C S I K S L S S H F W
AGAAGATGCAGACACAGGAGATCCTGAGGA
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