

## CASE REPORT

### Acute promyelocytic leukaemia with a novel translocation t(16;17)(q12;p13): a case report

Hilal BHAT, Sajad GEELANI, Masrat RASHID\*, Tariq BHAT\*\*, Mudasir QADRI\*\*\*, Nusrat BASHIR\*\*\*\*, Fahim MANZOOR\*\*\*\*, Shuaeb BHAT\*\*\*\*, Fayaaz RATHER\*\*\*\*\* and Javid RASOOL

*Department of Clinical Hematology, Sheri-kashmir Institute of Medical Sciences (SKIMS), Srinagar, Jammu and Kashmir (J&K), India, \*Department of Pharmacology, VP Chest Institute Delhi University, New Delhi, India, \*\*St. Elizabeth's Medical Centre, Department of Cardiovascular Medicine Boston, USA, \*\*\*Department of Internal Medicine, Sheri-kashmir Institute of Medical Sciences (SKIMS), Srinagar, Jammu and Kashmir (J&K), India, \*\*\*\*Department of Hematology, Sheri-kashmir Institute of Medical Sciences (SKIMS), Srinagar, Jammu and Kashmir (J&K), India, \*\*\*\*\*Department of Cardiology SKIMS, Srinagar J&K India*

#### Abstract

Acute promyelocytic leukaemia (APML) is characterised by the t(15;17)(q22;q21), that results in the fusion of the promyelocytic leukaemia (PML) gene at 15q22 with the retinoic acid  $\alpha$ -receptor (RARA) gene at 17q21. The current case report describes a 13-year-old male with APML, who was negative for PML/RARA fusion signal but reported to have an atypical translocation t(16;17). To the best of our knowledge this is the first case report of APML responsive to ATRA with such a translocation.

**Keywords:** Novel translocation, acute promyelocytic leukaemia, fusion genes

#### INTRODUCTION

Acute promyelocytic leukaemia (APML) presents with typical features that differentiate it from other acute myeloid leukemias and warrants prompt treatment strategies. These features include haemorrhagic syndrome, disseminated intravascular coagulation (DIC) and translocation between chromosomes 15 and 17, resulting in the formation of two reciprocal fusion genes - promyelocytic leukaemia (PML)/retinoic acid  $\alpha$ -receptor (RAR $\alpha$ ) on chromosome 15 and RAR $\alpha$ /PML on chromosome 17. These fusion genes are sensitive to differentiating agents, such as all-trans retinoic acid (ATRA), and novel anti-apoptotic agents, including arsenic trioxide.<sup>1,2</sup> In addition to this most common translocation, some patients with APML do have other rare translocations.

#### CASE REPORT

A 13-year-old student presented to our hospital with bleeding gums. 5 days before the presentation he was seen by a local dentist for mild bleeding

gums and dental caries. A dental extraction was planned. Soon after local anaesthetic was given, he started bleeding profusely and was transferred to our hospital. On examination, he was conscious and pale. He was afebrile and hemodynamically stable. He had no purpura or petechial rash. There was no palpable lymphadenopathy. Systemic examination revealed mild splenomegaly.

#### Pathology findings

A peripheral blood film revealed a haemoglobin level of 6.5 g/dl (normal range 11.5-14.0 g/dl), platelet count of 44  $\times 10^3/\mu\text{l}$  (normal range 150-400  $\times 10^3/\mu\text{l}$ ), total white cell count of 5.46  $\times 10^3/\mu\text{l}$  (normal range 4.5-12.5  $\times 10^3/\mu\text{l}$ ) with 70 per cent leukaemic promyelocytes and 6 percent blasts with Auer Rods suggestive of acute promyelocytic leukaemia (APML). Bone marrow aspiration confirmed APML with marrow smears showing about 90 percent hypogranular promyelocytes with suppression of the other haematopoietic cells (Fig. 1). Special staining of marrow smears revealed strong positivity for SBB and Myeloperoxidase

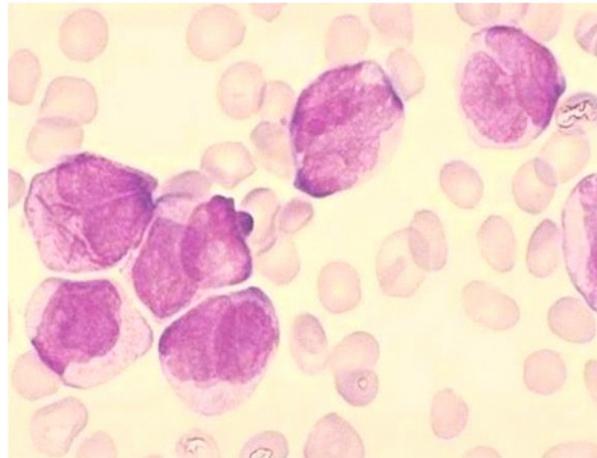


FIG. 1: Bone marrow aspiration showing hypogranular promyelocytes (100x Leishman stain)

and negativity for PAS. Immunophenotyping revealed that abnormal cells were HLADR+, CD34+, CD117+ CD33+, CD38+, cMPO+, confirming the myeloid phenotype. A diagnosis of AML, M3 variant was made according to the French-American-British Group criteria.

*Conventional cytogenetics:* A karyotype analysis at diagnosis revealed 20 metaphases of which 20 were analysed and 5 were karyotyped. There was

a reciprocal translocation between the long arm of one of the chromosome 16 and the short arm of one of the chromosome 17, involving the region q12 and p13 respectively. In addition, there was a marker chromosome of unknown origin in 90 percent of cells studied. The remaining 10 percent of cells showed a normal karyotype. The karyotype was designated as 47,XY,t(16;17)(q12;p13) (Fig. 2). Real time-RT PCR for PML/RAR $\alpha$  translocation (quantitative) was

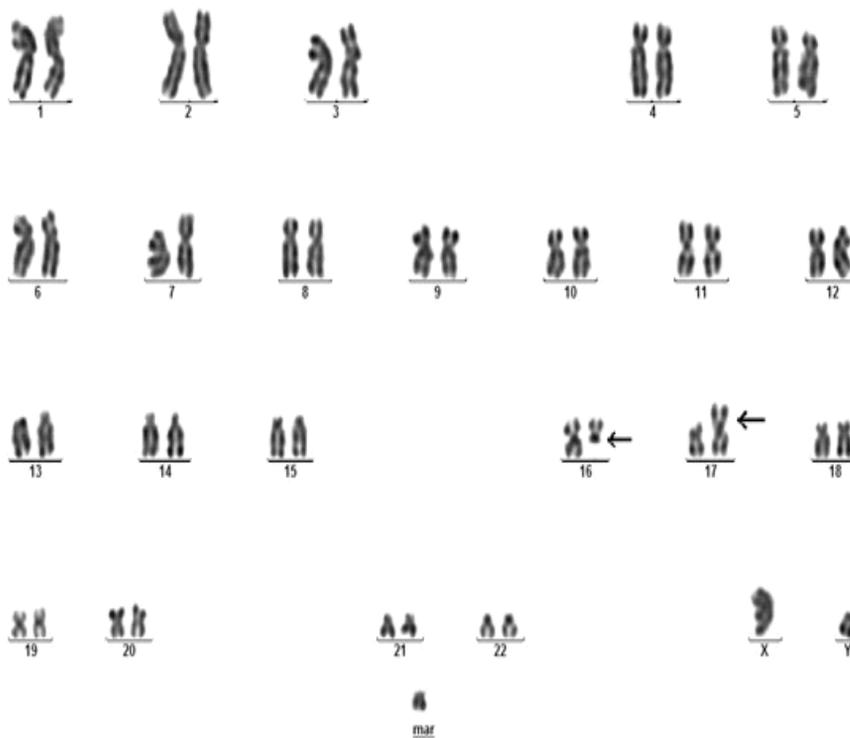


FIG. 2: Cytogenetics showing 47,XY,t(16;17)(q12;p13)

determined. However, the hybrid transcript for PML/RAR $\alpha$  quantified using minor groove binder real time RT-PCR assay showed no signal for PML-RAR $\alpha$  transcript in the leucocytes of the specimen. PML/RAR $\alpha$  translocation qualitative assay using RT-PCR and Gel Electrophoresis was also performed but hybrid transcript for PML/RAR $\alpha$  was not detected in the leucocytes including bcr1, bcr2, and bcr3 forms of the hybrid transcripts.

A final diagnosis of AML-M3 was made and the patient was put on IC-APL 2000 regimen with ATRA. Presently patient is on induction chemotherapy and has shown significant response.

## DISCUSSION

Acute promyelocytic leukaemia is a distinct type of acute myeloid leukaemia characterised by maturation arrest at the promyelocytic stage of the myeloid maturation. The presentation of this type of leukaemia is somewhat explosive with bleeding manifestations and DIC. Fortunately, the prognosis changed dramatically after the introduction of retinoic acid and arsenic trioxide. Nevertheless, bleeding still remains the most important complication of APML. Almost all the patients of APML possess the translocation t(15;17). This balanced translocation gives rise to a fusion gene PML-RAR $\alpha$ , the product of which blocks the differentiation of myeloid cells beyond promyelocytes. This results in accumulation of promyelocytes with granules therewith that produce typical features of this kind of acute leukaemia. However not all patients of APML have this typical translocation but some cases of other translocations are also now firmly established. These translocations involve the chromosome 17. They include notably t(5;17)(q35;q21) forming *NPM/RARA*, t(11;17)(q23;q21) producing *PLF/RARA* fusion and t(11;17)(q13;q21) generating *NUMA/RARA*, t(17;17)(q11,q21) producing *STAT5b-RARA*.<sup>3-5</sup> Response to ATRA appeared to be as good as a typical APML.

### Conclusion

To the best of our knowledge, this is a first report of a new translocation between chromosome 16 and 17 t(16;17)(q12;p13) which presented with all the typical features of APML but was negative for PML-RAR $\alpha$  fusion gene. Advanced study on these genes is likely to aid the elucidation of the oncogene or tumour suppressor gene associated with this translocation.

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