Leukemia Research Reports 10 (2018) 37–40

Contents lists available at ScienceDirect

Leukemia Research Reports

journal homepage: www.elsevier.com/locate/lrr

Lenalidomide induced durable remission in a patient with MDS/MPN-with ring sideroblasts and thrombocytosis with associated 5q- syndrome

Ahmed Alshaban[a], Osvaldo Padilla[b], Alexander Philipovskiy[a], Javier Corral[a], Meghan McAlice[a], Sumit Gaur[a,*]

[a] Department of Medicine, Texas Tech University Health Sciences Center Paul L. Foster School of Medicine, El Paso, TX, USA
[b] Department of Pathology, Texas Tech University Health Sciences Center Paul L. Foster School of Medicine, El Paso, TX, USA

ARTICLE INFO

Keywords:
MDS/MPN
Ring sideroblast
Thrombocytosis
5q
Lenalidomide

ABSTRACT

We describe a patient with MDS/MPN with ring sideroblasts and thrombocytosis who had deletions of long arm of chromosome 5 (5q-) and chromosome 20 (20q-). Molecular studies showed an exon 9, frame shift mutation in the calreticulin (CALR) gene, and absence of mutations in JAK2, MPL, SETBP1 or SF3B1.

Treatment with lenalidomide resulted in durable clinical remission which has lasted 2 years.

1. Introduction

Refractory anemia with ringed sideroblasts and thrombocytosis (RARS-t) was a provisional entity under myelodysplastic/myeloproliferative neoplasms (MDS/MPN) unclassifiable in the 4th edition of the WHO classification of myeloid malignancies [1]. Based upon a better understanding of the underlying molecular pathogenesis, the recent 2016 update of the 4th edition include RARS-t as a MDS/MPN overlap subtype, now called MDS/MPN with ringed sideroblasts and thrombocytosis(MDS/MPN-RS-T) [2]. Mutations in the spliceosome gene, SF3B1, occurs in up to 80% of these patients and co-exists with mutations in JAK2 (~50%), TET2 (~25%), ASXL-1 (20%), DNMT3A (~15%) and CALR (0–12.5%) [3].

We describe a patient with features of MDS/MPN-RS-T, who was found to have a deletion in the long arm of chromosome 5 and chromosome 20. Molecular studies showed a frame shift mutation in the CALR gene. Treatment with lenalidomide led to rapid normalization of peripheral blood abnormalities which have been durable for 2 years.

2. Case report

An 84-year-old white male was referred to us for anemia and thrombocytosis. He had a history of hypertension and dyslipidemia, for which he took enalapril and lovastatin. He lived and worked on a ranch in far west Texas. He had been fatigued for a few months. Physical exam showed mild conjunctival pallor. Liver and spleen were not palpable. Rest of the physical exam was unremarkable. Complete blood count (CBC) showed a white blood cell count of 9600/μl (4000–10,000) with a normal differential, hemoglobin of 9.9 g/dl (13.5–17.5) with MCV (mean corpuscular volume) of 108 fl (80–95). Platelet count was 986,000/μl (150,000-–450,000). Peripheral blood smear showed macrocytosis, moderate anisopoikilocytosis and marked increase in platelets. Prothrombin time and activated partial thromboplastin time were normal. He then underwent a bone marrow biopsy and aspirate. This showed a cellularity of 50%. Megakaryocytes were increased (Fig. 1). Myeloid erythroid ratio was normal. There was no increase in fibrosis. Blasts were 1–2%. Iron stain showed 15–20% ring sideroblasts (Fig. 2). Cytogenetic studies showed a deletion of the long arm of chromosome 5 in all twenty metaphases analyzed. Eleven of those cells also had a deletion of the long arm of chromosome 20 (Fig. 3). Molecular studies did not show JAK2 mutation or BCR/ABL rearrangement. A CALR exon 9, frame shift mutation (c1103_1130del37) was detected.

No mutations were detected in CSF3R, SRTBP1, MPL or SF3B genes.

Patient was initially started on hydroxyurea for cytoreduction. Once the results of cytogenetic studies became available, hydroxurea was discontinued and lenalidomide (10 mg) was initiated. After a transient period of worsening anemia, his CBC improved and by 3 months his peripheral blood counts were normal (Fig. 4). Fluorescent in situ hybridization and PCR studies on peripheral blood, performed 6 months after diagnosis, did not detect 5q deletion, 20q deletion or CALR mutation, suggesting molecular remission. At last follow up at 2 years, patient has continued to stay on lenalidomide and has a normal CBC.

* Corresponding author.
E-mail address: sumit.gaur@ttuhsc.edu (S. Gaur).

https://doi.org/10.1016/j.lrr.2018.08.001
Received 11 June 2018; Received in revised form 7 August 2018; Accepted 16 August 2018
Available online 24 August 2018

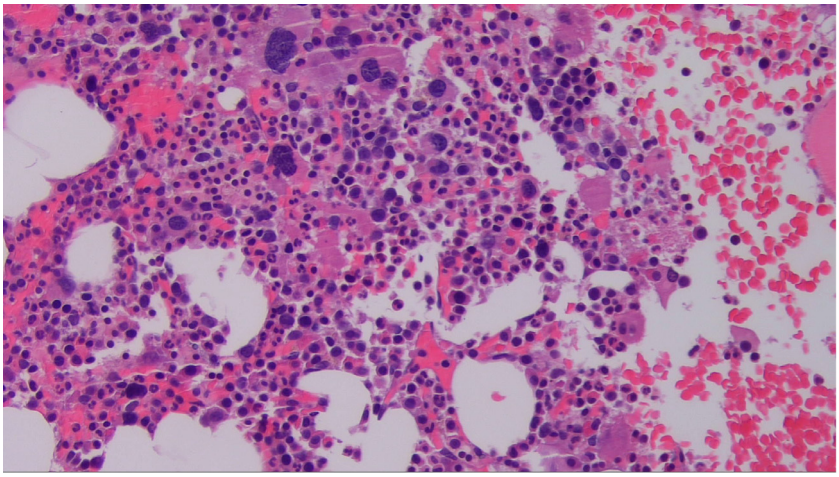

Fig. 1. Bone marrow biopsy showed 50% cellularity with increased megakaryocytes.

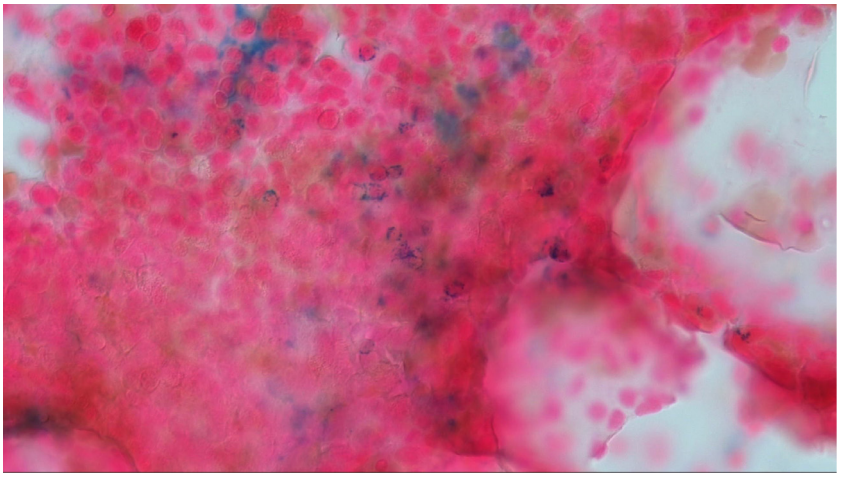

Fig. 2. Bone marrow biopsy iron stain showed 15–20% ring sideroblasts.

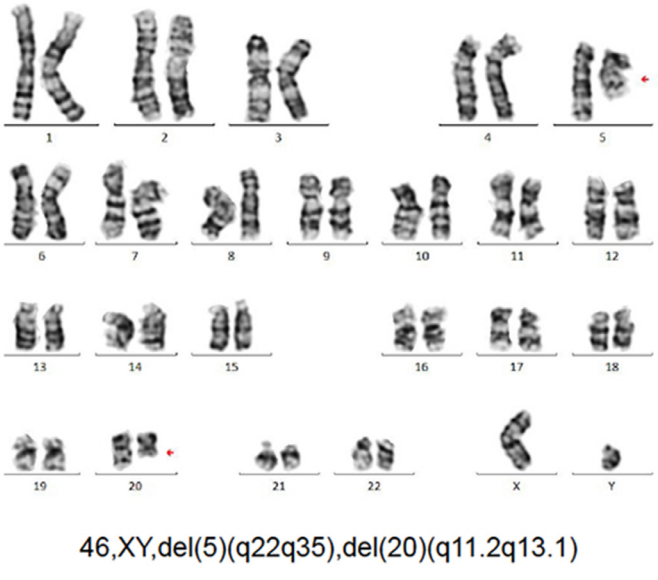

Fig. 3. Cytogenetics showed abnormal male karyotype, del(5q, del(20q).

3. Discussion

Disease's with features of both MDS and MPN have been termed MDS/MPN overlap syndrome.

Amongst the overlap syndrome, Refractory anemia with ringed sideroblasts and thrombocytosis (RARS-T) was initially included as a provisional entity by WHO in 2001. It was felt to have features of the MDS, refractory anemia with ringed sideroblasts and the MPN, essential thrombocytosis. The pathological hallmark of dysplasia was the presence of ringed sideroblasts detected by Prussian blue staining, in 15% or more of the erythroid progenitors. However, presence of ringed sideroblasts do not signify clonality, is sometimes reversible, and the percentage of RS do not correlate with prognosis. In addition RS can sometimes be seen in other myeloid disorders, including MPNs [4,5].

In 2006, Szpurka et al. found that 67% of patients with RARS-t had mutations in the JAK2 gene [6]. In addition to JAK2, mutations on CALR (3/24) and MPL have been described and probably contribute to the proliferative phenotype of MDS/MPN-RA-t [7–9]. It is possible that cases of RARS can transform to MDS/MPN-RA-T after acquiring mutations in these genes.

Since 2011, with the advent of next-generation sequencing in clinical practice, it has become obvious that a large proportion of cases with RARS-T have mutations in the genes encoding mRNA splicing factors, predominantly in the SF3B1 gene [10]. The detection of spliceosome mutation correlates with the morphological presence of RS, however its contribution to prognosis is controversial. The 2016 WHO revision