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Eosinophilia with PDGFRB Gene Rearrangement and Isolated Del 5q; an Extremely Rare Presentation of Myeloid Neoplasm

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ABSTRACT

Introduction: Myeloproliferative neoplasms with PDGFRA, PDGFRB and FGFR1 rearrangements are reported to be very rare entities. Myeloid neoplasms with PDGFRB rearrangement have prominent eosinophilia, neutrophilia or monocytosis and presence of t (5;12)(q31~q33;p12-13) or variant translocation. **Case Report:** We report a 55 years old female patient who presented with eosinophilia along with predominant eosinophil precursors on bone marrow and concomitant isolated del (5q) and PDGFRB gene rearrangement which is an infrequent and rare finding. **Conclusion**: isolated acquired deletion of the long arm of chromosome 5 (del 5q) also known as 5q- syndrome, is a distinct hematologic disorder reported to be primary myelodys plastic syndrome which is found in females of middle age and usually presents with macrocytic anemia, oval macrocytes, with white blood cell counts normal or reduced, platelet counts normal or elevated and bone marrow exhibitery throid hypoplasia with megakaryocytes showing hypolobated nuclei
Key words: Del 5q, Eosinophilia, PDGFRB rearrangement.

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INTRODUCTION

Myeloproliferative neoplasms with PDGFRA, PDGFRB and FGFR1 rearrangements are rare entities with reported incidence of <1/100,000.[1]Golub and Gilliland in 1994 first described the ETV6–PDGFRB fusion genes in patients with chronic myelomonocytic leukemia with eosinophilia andt(5;12).[2] Since then, a number of fusion partners for PDGFRB have been described, however most of them being onlycasereports.[3] The diagnostic criteria for a myeloproliferative neoplasm with PDGFRB rearrangement include prominenteosinophilia, havingmonocytosis or neutrophilia and presence of t(5;12)(q31~q33;p12-13) or variant translocations.4 It frequently presents with peripheral blood monocytosis mimicking chronic myelomonocytic leukemia with concomitant eosinophilia.[3,4] On cytogenetic analysist (5;12)(q31~q33;p12-13) or variant translocations are found.3On the other hand in 1974 Berghe and colleagues reported a distinct hematologic disorder i.e. isolated acquired deletion of the long arm of chromosome 5 del(5q) which found in middle aged females having macrocytic anemia and erythroid hypoplasia with non-lobulated megakaryocyte nuclei on bone marrow.[5-7] Subsequently Boult wood and Wains coat proposed the definition of the 5q- syndrome as primary myelodysplastic syndrome (MDS) with del(5q) as the sole cytogenetic abnormality without excess of blasts and having low risk of transformation to acute leukemia.[8]

CASE REPORT

A 55 year old female presented with history of cough for 01 week duration and increased frequency of micturition for 5 days. Her physical examination was unremarkable. On systemic examination chest was clear, abdomen was soft, non tender and there was no visceromegaly or lymphadenopathy. Complete blood counts showed hemoglobin 142 g/L, white cell count 51x10^9/L, and platelet count 251x10^9/L. Peripheral blood film revealed normocytic normochromic blood

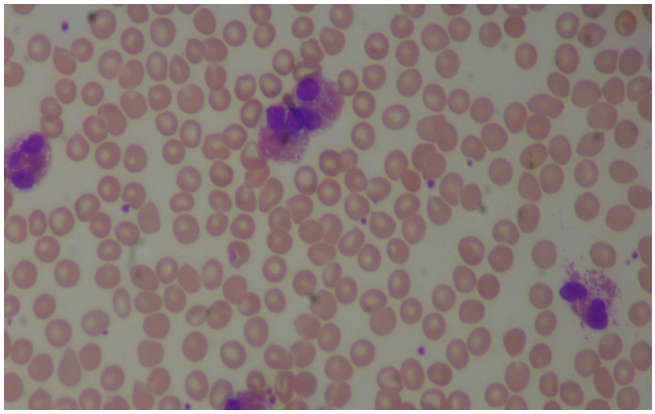

Figure I: Peripheral Blood Film

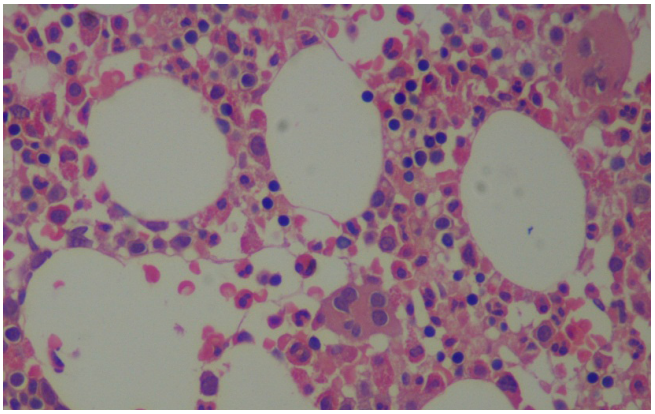

Figure 2: Bone Marrow Trephine Biopsy

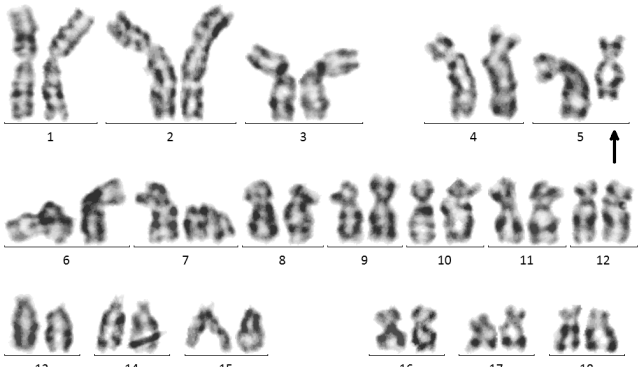

Figure 3: Bone Marrow Cytogenetics (Out of 20 metaphases analyzed, 06 cells(30%) showed del(5q33) where as 14 cells(70%) showed 46 number of chromosomes with normal female karyotype {46,XX,del(5q33)(06)/46,XX(14)})

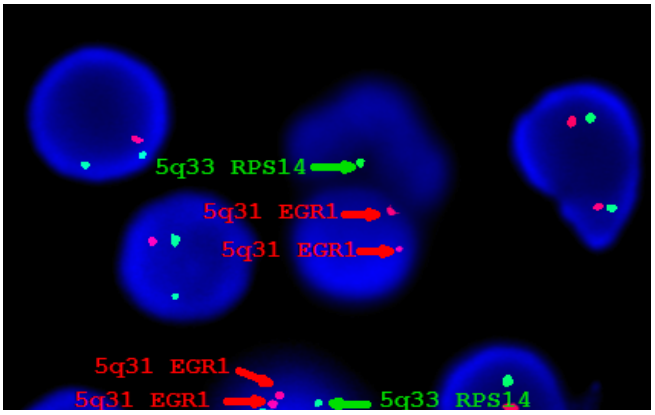

Figure 4: FISH Analysis for del 5q (Total 25 inter-phase nuclei were analyzed out of which 12 cells showed normal signal pattern whereas 13 cells showed evidence of del 5q31.2/5q33 locus)

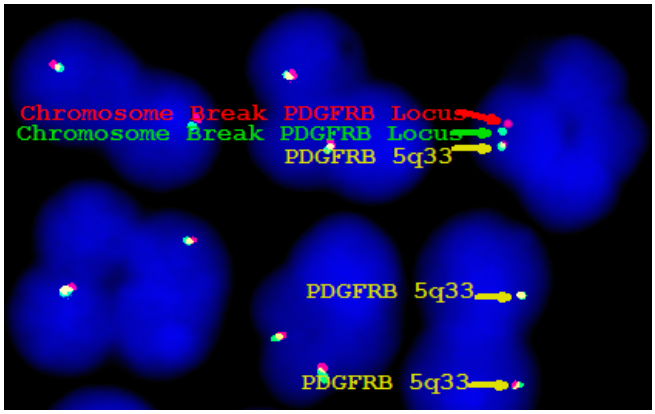

Figure 5: FISH Analysis for PDGFRB gene rearrangement (Total 326 inter-phase nuclei were analyzed out of which 120 cells (37%) showed evidence of PDGFR-B gene rearrangement whereas 206 cells (63%) showed normal signal pattern)

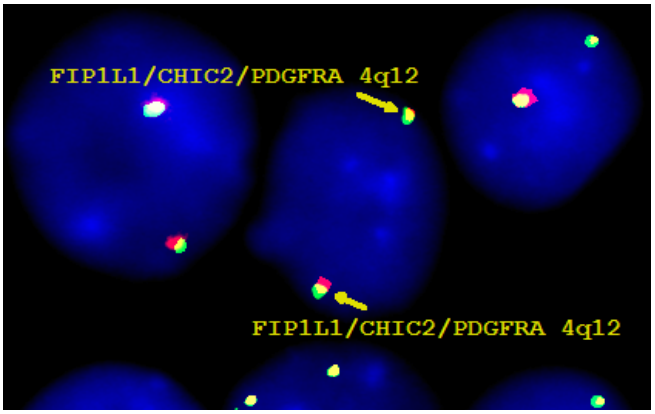

Figure 6a: FISH Analysis for FIP1L1/CHIC2/PDGFRA

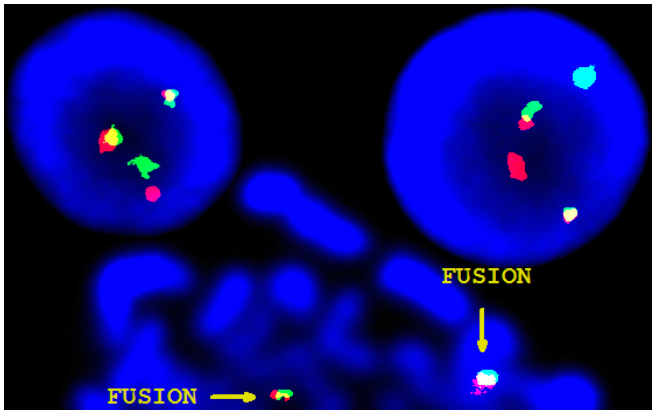

Figure 6b: FISH Analysis for BCR-ABL

picture, leukocytosis and absolute eosinophilia with 90% eosinophils (Figure 1). Bone marrow examination showed suppressed erythropoiesis and myelopoiesis and predominant population of eosinophil and precursors. Megakaryocytes were adequate, majority exhibiting dysplastic features like multinucleation (Figure 2). Renal and liver function tests were normal, urinalysis revealed 8-10WBC/HPF. X-Ray chest was unremarkable, serum Ig E levels were within normal range, echocardiography was normal, stool for ova and cyst was negative. Cytogenetic analysis was performed on overnight, 24-hrs un-stimulated and 72-hrs stimulated bone marrow cultures using standard procedures. The GTG (G-bands via trypsin using Giemsa) banding technique was applied, karyotypes were described according to the International System for Human Cytogenetic Nomenclature (ISCN) 2013, karyogram were made using Meta system. Out of 20 metaphases analyzed, 06 cells(30%) showed del(5q33) whereas 14 cells(70%) showed 46 number of chromosomes with normal female karyotype {46,XX,del(5q33)(06)/46, XX(14)} (Figure 3). For molecular cytogenetics fresh slides were used for FISH analysis using XL 5q31/5q33 locus-specific probe to see deletion in long arm of chromosome 5. Total 25 inter-phase nuclei were analyzed out of which 12 cells showed normal signal pattern whereas 13 cells showed evidence of del 5q31.2/5q33 locus (Figure 4). Using a LSI BCR/ABL dual color dual fusion translocation probe (metasystem), a total of 100 interphases + metaphases were analyzed, using a fluorescence Nikon Eclipse Ci microscope equipped with appropriate filters. Image capturing and processing were carried out using Cytovison imaging system (Leica, Richmond, USA). Total 326 inter-phase nuclei were analyzed out of which 120 cells (37%) showed evidence of PDGFR-B gene rearrangement whereas 206 cells (63%) showed normal signal pattern (Figure 5). FISH results were negative for detection of FIP1L1/CHIC2/PDGFRA 4q12, and BCR-ABL (Figure 6a and 6b). Treatment was started with prednisolone at a dose of 0.5 mg/kg/day for 15 days after which her blood counts revealed hemoglobin 149 g/L, white cell count 12x109/L, and platelet count 381 x 10^9/L with 36 % eosinophils. She was also treated for her urinary tract infection. She is now given Imatinib 200 mg/day. Patient is stable and on regular follow up.

DISCUSSION

In our patient, the presence of concomitant del (5q) and PDGFRB gene rearrangement is an infrequent and rare finding. There was no peripheral blood monocytosis or basophilia and neither increase in bone marrow mast cells. The patient presented with preserved platelet counts and she did not have anemia though bone marrow megakaryocytes showed dysplastic features like multi nucleation, only few megakaryocytes were exhibiting monolobation. There was absence of splenomegaly. On cytogenetic analysis unlike translocations involving chromosome 5, isolated deletion 5q was seen. Isolated del (5q) is feature of MDS category of 5q- syndrome. In literature isolated del (5q) abnormality with concomitant JAK2 V617F mutation has been reported earlier,[9] but to best of our knowledge no case has been reported so far with concomitant PDGFRB gene rearrangement and isolated del (5q). Since 5q- alone has good prognosis, it is quite likely that she had it before she developed eosinophilia and 5q- was discovered accidently. However, since this has not been reported earlier we present this unusual combination of molecular abnormalities. If this 5q- has any prognostic advantage to this PDGFRB positive case is unclear and warrants more studies.

CONFLICT OF INTEREST

Nil

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