Journal of
Hematology & Thromboembolic Diseases

OPEN ACCESS Freely available online

Case Report

Spontaneous Resolution of Monosomy and Treatment Related Myelodysplastic Syndrome in a Breast Cancer Survivor

Kamble R*, Mukherjee A, Shagufta N, Scholoff A, Gloria O and Carrum G

Department of Center Cell and Gene Therapy, Baylor College of Medicine and Houston Methodist Hospital, Texas, USA

ABSTRACT

Monosomy 7 is a frequent karyotypic abnormality in de novo or therapy-related MDS (t-MDS). The overall prognosis of patient with monosomy 7 remains poor. However, a small number of case reports from pediatric literature describe spontaneous resolution of Myelodysplastic Syndrome (MDS) with monosomy 7. Herein we document first report of spontaneous remission of t-MDS with monosomy 7 in an adult patient.

Key words: Monosomy 7; Myelodysplastic syndrome; Breast cancer

CASE REPORT

A 58-year-old female from the West Indies developed right T2N2AM0, stage IIIA breast cancer in August 2014 [1-3] that was HER-2neu and ER/PR positive. She completed pegfilgrastim supported neoadjuvant chemotherapy (pertuzumab 840 mg IV × 1 then 420 mg IV, trastuzumab 4 mg/kg × 1 then 2 mg/kg, Docetaxel 75 mg/m2 and carboplatin with AUC-6 every 3 weeks × 6 cycles) in January 2015. A right breast lumpectomy in February 2015 revealed residual disease (4 mm) and she underwent external Beam Radiation (XRT) to the right breast in May 2015. She completed adjuvant herceptin in September 2015. All chemotherapies were administered without dose delay or dose reduction [4]. While on adjuvant letrozole, at the tail end of herceptin therapy, she presented in August 2015 with fatigue and pancytopenia (Table 1). In September 2015, she required 2 units of packed red cell transfusion for hemoglobin of 5.9 gm/dL and hematocrit of 17.6%. Her cytopenia progressed to white cell count of 1.2 (absolute neutrophil count 400) and platelets of 43,000. A repeat Complete Blood Count (CBC) following week revealed White Cell Count (WBC) of 1.46 (absolute neutrophil count 800), hemoglobin 9.3 and platelets of 81,000. Blood tests for B12, folate deficiency, hemolysis, iron deficiency and Paroxysmal Nocturnal Hemoglobinuria (PNH) profile was negative CT scan of abdomen did not reveal splenomegaly [5] for the continued pancytopenia

Table1: Cytopenia, marrow dysplasia and monosomy 7 following completion of cytotoxic chemotherapy in January 2015.

Month/year	WBC	ANC	Hb	Platelets	BM	Cytogenetics
Apr-15	3.7	2000	10.1	299	NA	NA
Jun-15	5.5	4000	10.3	191	NA	NA
Aug-15	2.4	1100	8.9	81	NA	NA
Sep-15	1.2	400	6.9	43	NA	NA
Oct-15	1.46	800	9.3	81	MDS	Monosomy 7 in 35% cells
Nov-15	3.9	2200	11.5	226	NA	NA
Dec-15	3.8	2300	11.4	187	NA	NA
Feb-16	5.5	4000	11.9	200	NA	NA
May-16	8.2	7000	11.8	242	No MDS	Monosomy 7 in 5% cells
Aug-16	7.5	4600	11.3	288	NA	NA
Dec-16	6.1	4400	11.3	268	No MDS	Monosomy 7 in 0% cells
Mar-17	7	5600	12.4	293	NA	NA
Jun-17	6.7	5000	11.1	310	NA	NA
Jan-18	6.3	4500	12.1	320	NA	NA
Jun-18	6.7	4000	12.2	307	NA	NA

Note: WBC=White Blood Count (x109/L), ANC=absolute neutrophil counts, Hb=hemoglobin (gm/dL), Platelets (x109/L); **BM**= Bone Marrow Morphology.

***Corresponding author:** Kamble R, Department of Center Cell and Gene Therapy, Baylor College of Medicine and Houston Methodist Hospital, Texas, USA, Telephone: +923315671659, E-mail: kamble@sbcglobal.net

Received November 14, 2018; **Accepted** December 26 2018; **Published** January 02 2019

Citation: Kamble R, Mukherjee A, Shagufta N, Scholoff A, Gloria O, Carrum G (2019). Spontaneous Resolution of Monosomy and Treatment Related Myelodysplastic Syndrome in a Breast Cancer Survivor. J Hematol Thrombo Dis 2019, 7:298.

of 3 months duration, she underwent a bone marrow biopsy in October 2015 that revealed monosomy 7 and myelodysplastic changes in hypercellular marrow (85%) showing dysplastic changes in the erythroid and megakaryocytic lines and 2% blasts. Cytogenetic analysis revealed monosomy 7 in 7 cells of 20 cells examined (35% cells) and Fluorescent in-situ Hybridization (FISH) analysis showed deletion of 7q in 50% of the cells analyzed. Table 1 show to illustrate serial blood counts, cytogenetics and bone marrow morphology. Diagnosis of intermediate risk MDS (R-IPSS score- 4.5) necessitated a consultation for allogeneic hematopoietic transplantation. However, after 4 months of persistent pancytopenia, she began to recover blood counts with resolution of both cytopenia and monosomy 7 Morphologic improvement in MDS preceded cytogenetic improvement [6,7] (Table 1).

DISCUSSION

Such spontaneous resolution of monosomy 7 has not been previously reported in adults [7]. So far the 2 oldest patients reported are 19 years old [4-6] those reported from pediatric population is summarized in the overall incidence of MDS/AML in breast cancer patients following treatment with chemotherapy and radiation therapy is approximately 0.29%. The median time to develop MDS/AML was 3.06 years (Range=0.41-12.95 years) [8]. Furthermore, granulocyte colony-stimulating factor (G-CSF) administration has been linked to the development of monosomy 7 in severe congenital neutropenia and aplastic anemia [9]. It has been suggested that pharmacologic doses of G-CSF increase the proportion of preexisting monosomy 7 cells. The abnormal response of monosomy 7 cells to GCSF can be explained by the expansion of undifferentiated monosomy 7 clones expressing the class IV GCSFR, which is defective in signaling cell maturation [10] (Table 2). It remains unclear whether our patient developed monosomy 7 clone secondary to chemotherapy or G-CSF or she had a preexisting clone. From the reported pediatric literature several hypotheses have emerged to explain transient abnormal hematopoiesis. It is postulated that aberrant clone may be unable to maintain its proliferative advantage as clonal loss of one copy of a critical 7q tumor suppressor gene may ultimately regress in absence of a "second hit". Another proposed hypothesis is self-limiting clonal aberration because it did not develop from stem cell pool [2]. Yet another plausible explanation is extrapolated from patients with severe aplastic anemia who develop MDS in context of immunosuppressive therapy [9,10]. Recovery of immune effector function following completion of chemotherapy may account for disappearance of malignant clone.

Table2: Reported monosomy 7 associated spontaneous MDS remission.

Author	Patients	Age/Sex	MDS type	CR duration
Mamtadakis 1999	4	8 months, male	t-MDS	108 months
Parker 2008	1	15 months, male	t-MDS	14 months
Renneboog 1996	1	8 years, male	t-MDS	67 months
Scheurlen 1994	1	10 years, male	t-MDS	95 months
Laver 1997	2	3 years, male	t-MDS	30 months
De novo	2	19 years, male	t-MDS	12 months
Yang 2017	1	14 months, male	t-MDS	4 months

CONCLUSION

This report highlights importance of recognition and stringent follow-up without therapeutic intervention in select t-MDS.

REFERENCES

1. Greenberg PL, Tuechler H, Schanz J. Revised international prognostic scoring system for myelodysplastic syndromes. Blood. 2012;120:2454-2465.
2. Mantadakis E, Shannon KM, Singer DA. Transient monosomy 7: A case series in children and review of the literature. Cancer. 1999;85:2655-2661.
3. Parker TM, Klaassen RJ, Johnston DL. Spontaneous remission of myelodysplastic syndrome with monosomy 7 in a young boy. Cancer Genet Cytogenet. 2008;182:122-125.
4. Renneboog B, Heimann P, De Mulder A, Jannsen F, Ferster A. Spontaneous remission in a patient with therapy related myelodysplastic syndrome (t-MDS) with monosomy 7. Br J Haematol. 1996;92:696-698.
5. Scheurlen W, Borkhardt A, Ritterbach J, Huppertz HI. Spontaneous hematological remission in a boy with myelodysplastic syndrome and monosomy 7. Leukemia. 1994;8:1435-1438.
6. Laver JH, Yusuf U, Cantu ES, Barredo JC, Holt LB, Abboud MR. Transient therapy-related myelodysplastic syndrome associated with monosomy 7 and 11q23 translocation. Leukemia. 1997;11:448-450.
7. Yang G, Rowsey R, Wang J, Ketterling RP, Fisher R. Transient monosomy 7 associated with bicytopenia in a 9 month old boy Report of a case and review of the literature. Hemato. 2017;2:24-30.
8. Kaplan HG, Malmgren JA, Atwood MK. Increased incidence of myelodysplastic syndrome and acute myeloid leukemia following breast cancer treatment with radiation alone or combined with chemotherapy: A registry cohort analysis 1990-2005. BMC Cancer. 2011;11:260.
9. Socie G, Henry AM, Bacigawpo A, Hows JTA, Ljungman P, McCann SR , et al. Malignant tumors occurring after treatment of aplastic anemia. European bone marrow transplantation-severe aplastic anaemia working party. N Engl J Med. 1993;329:1152-1157.
10. Sloand EM, Yong AS, Ramkissoon S, Solomou E, Bruno TC, Kim S, et al. Granulocyte colony-stimulating factor preferentially stimulates proliferation of monosomy 7 cells bearing the isoform IV receptor. Proc Natl Acad Sci USA. 2006;103:14483-14488.