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A RARE CASE OF MYELODYSPLASTIC SYNDROME DUE TO LOSS OF CHROMOSOME Y.

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ABSTRACT
Myelodysplastic syndrome (MDS) represents a heterogeneous hematopoietic stem-cell disorder that results in abnormal cellular maturation and peripheral blood cytopenias. MDS is characterized by progressive bone marrow failure, which can lead to bleeding, infections, and complications secondary to anemia. Approximately 40% to 45% of patients diagnosed with MDS progress to acute myeloid leukemia (AML), which confers a poorer prognosis. MDS may develop de novo without underlying risk factors or may be secondary, occurring after exposure to chemotherapeutic agents or ionizing radiation. Here we present a case of MDS in 78 year old gentleman with fever of unknown origin (FOUO).

KEYWORDS: Myelodysplastic syndrome (MDS) represents a heterogeneous hematopoietic stem-cell disorder that results in abnormal cellular maturation and peripheral blood cytopenias.

INTRODUCTION
Approximately 35% to 40% of patients diagnosed with MDS progress to acute myeloid leukemia (AML), which confers a poorer prognosis. MDS may develop de novo without underlying risk factors or may be secondary, occurring after exposure to chemotherapeutic agents or ionizing radiation. Cytogenetic abnormalities have been observed in at least 50% of patients with primary myelodysplastic syndrome (MDS). The most frequent abnormalities are loss or gain mutations, as opposed to the balanced translocations more common in acute myeloid leukemia (AML). Good prognosis includes patients with normal karyotypes and deletion of the Y chromosome (-Y), and Del (5q) or Del (20q) as single abnormalities; Poor prognosis includes patients with complex karyotypes or monosomy 7, and intermediate prognosis includes patients with most other chromosomal abnormalities.

CASE REPORT
78-year-old gentleman with history of multiple TIAs (on aspirin and clopidogrel), HTN, hyperlipidemia, COPD, BPH and diastolic dysfunction. He was admitted to hospital 12/29/19 - 1/10/20 due to fever, and while admitted developed AKI (creatinine level 6.17), treated empirically with antibiotics for sepsis syndrome. He was readmitted again 1/16/20 - 1/22/20, with recurrent fever (39.6 on admission), mild confusion, elevated creatinine (2.36), hemoglobin (9.8), markedly elevated BNP. Troponins were positive with negative ischemic change on ECG and was diagnosed in decompensate diastolic heart failure and has been diuresed. Extensive infectious disease workup was negative for fever. We thought perhaps fever was drug related due to hydralazine due to its temporal relationship and he developed rash during his hospitalization which was also thought due to Hydralazine possibility of sweet syndrome/ versus adult onset still disease. Hydralazine was stopped, and so far he has not had recurrent fever and feels well. A 24-hour urine collection for Bence Jones proteins have been completed proteins showed free kappa 410 mg/24 hr, free lambda 29, K/L ratio 14.1, but CT C/A/P without contrast negative for bone lytic lesions and normal calcium level. Random urine protein electrophoresis and immunofixation were also negative for monoclonal protein. . His creatinine has been trending down despite diuresis, 1.53 on 1/23/2020 but Hb is still below 10. With the suspicion of multiple myeloma is a cause of anemia, bone marrow biopsy obtained. The marrow was morphologically normal, with no dysplasia or plasma cell neoplasm, but karyotype showed loss of Y chromosome in 90% of cells, highly suggestive of hematologic dysplasia. Flow cytometry was normal. Cytogenetic 45, X,-Y (27)/46, XY (3). MDS FISH negative. NGS testing was requested (Foundation Heme), but was declined by insurance. He started ESA therapy with Aranesp 300 mcg
Serum EPO:- 23.4 (2/21/20).

2/26/20: Aranesp 300 mcg; 3/20/20: Aranesp 300 mcg

Date	1/22/2020	1/23/2020	2/13/2020	2/26/2020	3/20/2020	4/30/2020
Hemoglobulin	8.8	8.4	9.1	8.8	9.5	11.7
WBC	7000	6400	7800	6700	6800	6700
ANC	5.8	5.6	5.8	6.7	5.2	5.1
Platelets	166000	168000	246000	292000	281000	222000
Creatinine	1.66	1.53	1.29	1.58	1.37	1.42
Mcv	96	97	98	97	99	97

DATE	FERRITIN
10/29/2019	198
01/04/2020	793
01/16/2020	534
01/20/2020	654
03/20/2020	294

CASE DISCUSSION

Chromosomal deletions and monosomies are frequently seen in MDS. Most of the malignant diseases of myeloid lineage are characterized by single chromosomal abnormalities like translocation; however MDS is typically associated with cytogenetic deletions like Chromosome Y, 5q, 7q, 20q and 12p. MDS and loss of the Y chromosome are both observed in older patients. Currently loss of the Y chromosome in >75% of the cells from unstimulated cultures is used as the cut off to suggest the possibility of existence of a neoplastic process. The recent characterization of the molecular abnormalities underlying the biology of MDS should provide objective biomarkers to confirm the diagnosis of MDS in cases with loss of the Y chromosome as the sole abnormality. Molecular profiling may be informative in confirming the diagnosis of MDS in cases suspected of MDS with loss of the Y chromosome as the sole abnormality.

CONCLUSION

In this patient with the deletion of Y chromosome mylodysplastic syndrome, we identified rare and phenotypically distinct deletion of Y chromosome in 90% of cells which highly suggestive of hematologic dysplasia. The marrow was morphologically normal, with no dysplasia or plasma cell neoplasm and flow cytometry is also normal. Deletion of chromosome Y is considered a good-risk karyotype. However there is controversy that loss of a Y chromosome is an age-related phenomenon.

CONSENT

Written informed consent was obtained from the patient for publication of this case report.

COMPETING INTERESTS

The authors declare that they have no copeting interests.

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