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Trends of Hematological Parameters During Splenic Irradiation: A Case Report

Sovan Sarang Dhar*, Minakshi Mishra, Satyabrata Kanungo, Adhar Amritt, Poornima Devi U, Nehla Haroon, Bikash Ranjan Mohapatra, Ashutosh Pattanaik, Bijaylaxmi Sahoo, Bijay Kumar Barik, Saroj Kumar Das Majumdar and Dillip Kumar Parida

All India Institute of Medical Sciences, Bhubaneswar, India.

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ABSTRACT

Splenomegaly resulting from either malignant or benign etiology is usually fraught with symptoms. Many of the symptoms are attributed to variable cytopenias encountered in individual scenario which necessitate some form of treatment to control splenic enlargement. Radiotherapy is an old and proven modality for management of symptomatic splenomegaly. The trends and patterns of different corpuscular parameters of blood following splenic irradiation though intriguing is sparse in published literature. In this case report we have plotted and analyzed the values of hemoglobin [Hb], Total Leukocyte Count [TLC], Absolute Neutrophil Count [ANC] and Platelet Count during a protracted course of radiotherapy in a young female with multiple co-morbidities for symptomatic splenomegaly to prove the safety as well as to identify the trend and pattern of changes in hematological parameters.

Keywords: Splenomegaly, Radiotherapy, Hemoglobin, TLC, ANC, Platelets

INTRODUCTION

Splenomegaly is encountered mostly with portal hypertension due to secondary etiologies such as infection, cirrhosis, and also from granulomatous inflammations, chronic hemolytic diseases, lipidoses, myeloproliferative diseases, haemophagocytic syndromes, splenic cysts/aneurysms/cavernous hemangiomas. Splenectomy though a straightforward solution to palliate symptoms apart from suitable systemic therapies is associated with significant complications (36%) and 6% post-operative mortality [1]. Associated cytopenias when improve by Splenectomy in known splenomegaly and normal/hypercellular bone marrow is known as Hypersplenism. Splenic irradiation first performed in 1903 has been in use to palliate symptoms when surgical Splenectomy is not advisable in both malignant as well as benign etiologies. A variety of total dose, dose/fraction, External Beam Radiotherapy [EBRT] techniques have been used for splenic irradiation. Radiation hypersensitivity, immune modulation, radiation-induced cytokine release and abscopal effect are the commonly proposed mechanism to validate the radio-biological aspects of splenic irradiation. Kinetics of cytopenias improvement following spleen EBRT is an unexplored area which may open up interesting trends and characteristics. Co-relating these with other clinical parameters can help in achieving a convincing picture of effects of splenic radiotherapy. The following case report is an observation of hematological parameters during the course of splenic radiotherapy in a diagnosed case of symptomatic splenomegaly with cytopenias.

CASE REPORT

Young female of age 32 years with known co-morbidity of rheumatic heart disease (post 10 years of Penicillin prophylaxis) and hypothyroidism (on regular medication, Thyroid Function Tests within normal limits) was evaluated for chronic left upper abdominal pain, heaviness and malaise. Clinical examination revealed a palpable tender splenomegaly approximate 12 cm below left costal margin in midclavicular line without palpable liver/ raised JVP. Abdomen ultrasonography suggested chronic liver disease [CLD] with portal hypertension [PH] and splenomegaly

Corresponding author: Sovan Sarang Dhar, Department of Radiotherapy, Senior Resident, All India Institute of Medical Sciences, Bhubaneswar, India, Tel: 8932018032; E-mail: sovan.sarangdhar@gmail.com

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which also was confirmed with contrast enhanced computed tomography of abdomen. Blood count revealed a picture of anemia, leucopenia, neutropenia as well as thrombocytopenia. Peripheral smear commented the anemia as normocytic and normochromic while aspiration cytology and biopsy found bone marrow to be normocellular. A diagnosis of CLD with Portal Hypertension and secondary splenomegaly was made. Splenectomy was disfavored owing to co-morbidities; instead management with irradiation in palliative intent was framed.

Patient was simulated in supine position immobilized with thermoplastic cast and non-contrast computed tomography slices of 2.5 mm thickness was obtained from carina upto true pelvis. Images **(Figure 1A)** were transferred and registered in Monaco treatment planning system (version5.11), planned using Volumetric Modulated Arc Therapy [VMAT] **(Figure 1B)** to a dose of 5Gy in 10Fractions,0.5 Gy per fraction delivered using 6 megavoltage X-ray by VERSA HD ™ –Elekta twice weekly.

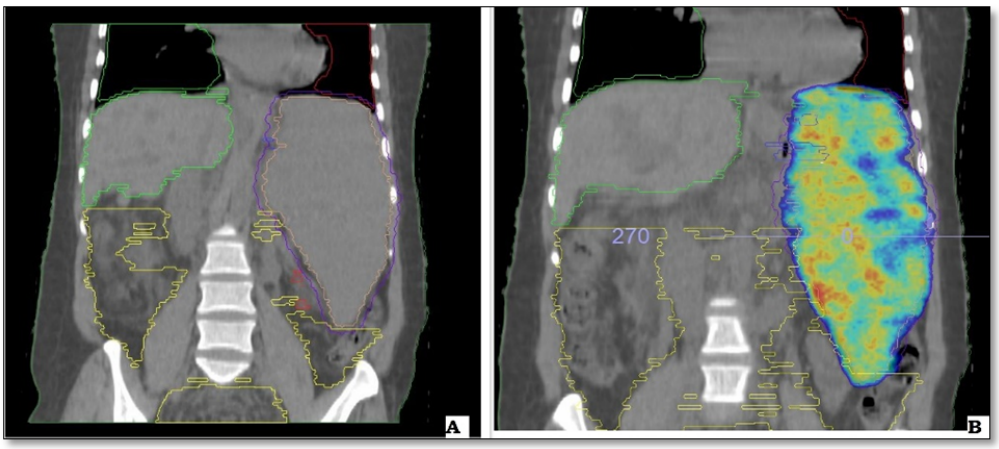

Figure 1. (A) Coronal image showing contoured enlarged spleen (blonde colour) with a margin(violet). (B) Coronal image showing dose distribution using VMAT planning technique.

Complete Blood Count (CBC) was recorded before start of radiotherapy. The values were designated as baseline (0 hours) and subsequently CBC was repeated at 12 hourly intervals to see changes with passage of time and repetition of radiotherapy fractions. It took 32days/768 hours from beginning to complete the planned dose of 5 Gy in 10fractions delivered in twice weekly schedule. A total of 45 readings as compared to planned 64 readings at 12 hourly intervals could be obtained owing to practical challenges in the period of lockdown and Corona virus disease (COVID19) pandemic.

Baseline value of hemoglobin recorded at the beginning of radiotherapy was 7.2 g/dl; which increased to 8.8 g/dl at 816 h after start of first fraction. An increase of 1.6 g/dl over 34 days following a linear trend as shown in **(Figure 2)**. The values of TLC and ANC **(Figure 3)** however followed a different pattern. Both decreased for a short time period followed by an increase; a pattern that repeated itself with each fraction of EBRT delivered. More interestingly the ANC

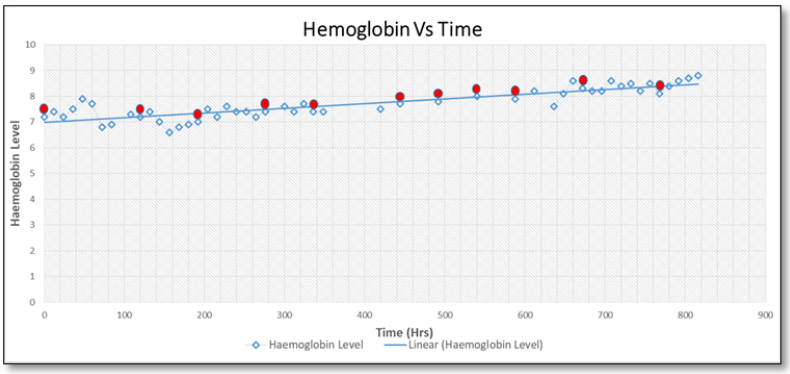

Figure 2. Hemoglobin Versus Time. X-axis shows time in hours. Hb value in gram/dl represented in Y axis. Plotted graph shows almost a linear increase (trend line blue color) in hemoglobin level with passage of time. The red dot represents individual radiation fraction.

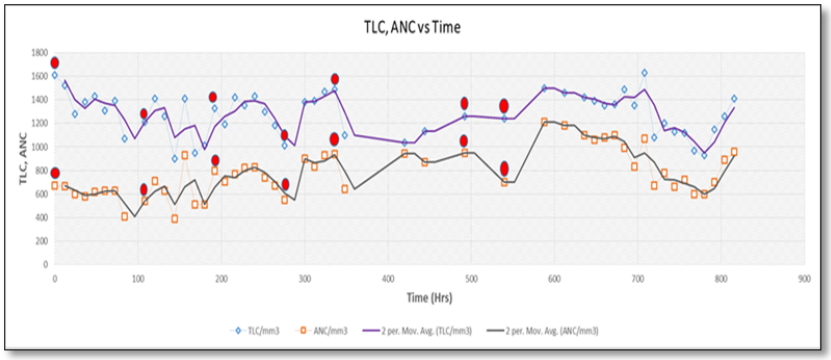

Figure 3. TLC, ANC versus Time. X-axis shows time in hours. TLC and ANC values represented in Y axis. Trend line of TLC (violet) and ANC (black) represent average of two consecutive readings. Plotted trend lines show a parallel trend between them. The red dot represents individual radiation fraction. The values at end of treatment is not much different than at the beginning.

curve followed the TLC curve in almost parallel manner throughout the course. After completion of the planned dose of EBRT the value of TLC and ANC however was not significantly higher as compared to baseline value.

The thrombocytopenia **(Figure 4)** measured at baseline (12500/mm^3) when followed over the course of treatment decreased (following individual fraction) and increased subsequently to again decrease following subsequent fraction followed by increase; a trend that repeated throughout the course. Platelet count at the end of 5Gy was more or less stayed around 15000/mm3, which had reached a nadir of <5000/mm^3 twice during the course accompanied by physical signs of petechiae and ecchymosis managed with transfusion of Random Donor Platelets [RDP].

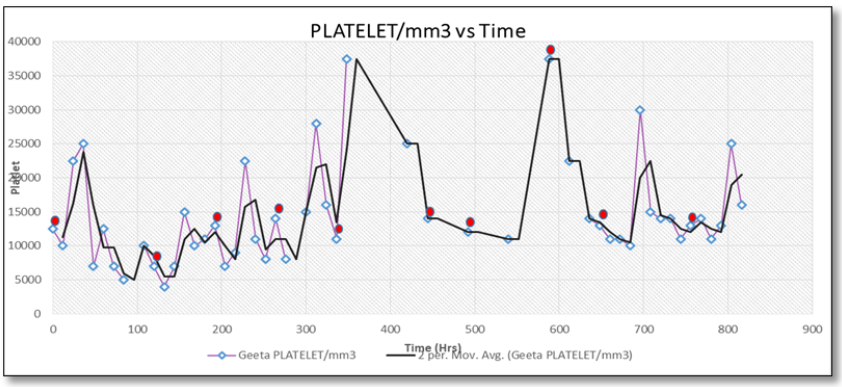

Figure 4. Platelets versus Time. X-axis shows time in hours. Platelets count represented in Y axis. Trend line shown as black line averaging consecutive 2 values. The red dot represents individual radiation fraction. The count at the end of treatment was near about baseline.

DISCUSSION

Splenomegaly and associated symptoms such as upper abdominal/left flank pain, early satiety, malaise, bleeding, and features of cytopenias require intervention apart from addressal of primary etiology. Symptoms caused are by either the mass effect or sequestration of blood elements owing to congestive splenomegaly [2]. Spleen radiotherapy is carried out using external beam technique with variable total dose, dose per fraction and treatment schedules. Available literature suggests total doses in the range of 0.15-30.5 Gy and fraction doses in the range of 0.1-2.5 Gy have been used respecting the radiation sensitivity of spleen, primary etiology, co-morbidities and dose at which palliation is achieved [3]. The said patient had grade-3 anemia/neutropenia and grade-4 thrombocytopenia at baseline apart from upper abdominal pain and malaise secondary to CLD and PH other than existing co-morbidities [4]. Though young she was planned for a total splenic irradiation dose of 5Gy in 10 fractions delivered twice weekly owing to the concerns for adverse events mainly

hematological [5]. The EBRT technique used was VMAT for better conformation of doses to spleen rather than surrounding structures.

It was interesting to observe the hemoglobin value increasing almost in a linear trend following each fraction of EBRT to a total increase of 1.6 g/dl in 34 days. In a case series reported by Liu et al. [6] it was reported that the hemoglobin level didn't raise after splenic irradiation (12Gy/8Fractions, 5 fractions per week) in any of the patients (0/5) with Liver cirrhosis and portal hypertension[6]. While Bruns et al. reported improved hemoglobin in 3 out of 5 patients with splenomegaly (benign etiology) treated to a total dose of 3Gy in 0.5Gy per fraction delivered 2-3 times per week [7]. In our study the trendlines of both TLC and ANC followed the average values of two consecutive readings and it was seen that following each radiotherapy fraction the TLC values dipped for a brief duration ranging from 12-72 h followed by an increase; duration of which ranged from 12-24 h. The graph of ANC closely hugged that of TLC and the variation too graphically appeared similar **(Figure 3)**. Liu et al. [6] reported decline in TLC count in 3 out of 5 patients at the end of follow up (in one case count wasn't reported), Bruns et al. [7] suggested decrease in TLC count in 2 out of 5 patients. Reported benefit in platelet count were noted in all 5 patients by Liu et al. whereas 3 out of 5 patients in series by Burns et al. Our platelet count analysis suggested a decrease in count (median 3000/mm^3) following each time the fractional dose is delivered (median time 12 h from dose) followed by a hike. The nadir value of platelet reported were 4000/mm^3 which was manifested in the form of petechiae and ecchymosis but no episodes of life-threatening hemorrhagic event was noted. Platelets were transfused only when the counts went below 5000/mm^3. The last collected count of platelet/ANC (48 h after last fraction of EBRT) were 3500/mm^3, 290/mm^3 higher than baseline. The maximum decrease in different corpuscular parameters following each fraction of radiotherapy as compared to value at the time of delivery of dose occurred at a median time of 30.1-35.5 h. Mean, median, standard deviation, range of blood parameters are reported in **Table 1**.

Table 1. Statistical analysis of changes in blood parameters with time.

Statistical Parameters	Maximum TLC value decrease following each fraction of EBRT	Time to maximum TLC Value decrease following each fraction of EBRT in hours	Maximum ANC value decrease following each fraction of EBRT	Time to maximum ANC value decrease following each fraction of EBRT in hours	Maximum Platelet value decrease following each fraction of EBRT	Time to maximum platelet value decrease following each fraction of EBRT in hours
Mean	328	58.3	245	48	7000	29
Median	188	30.5	138	35.3	8836	30.1
Standard Deviation	320	72	260	60	3000	12
Range	500	72	440	84	25,500	72

Available literature in splenic irradiation suggests a partial or complete benefit for symptoms/lab abnormalities was obtained in 85-90% of treated patients [8]. In our study the patient was completely relieved of pain accompanied by 4cm decrease in size of splenomegaly (as measured in maximum cranio-caudal direction by CT image) and improvement in both anemia as well as thrombocytopenia. Except for transient decrease in platelet counts and resulting ecchymosis no other skin/gastrointestinal/infectious complications occurred during the course of splenic irradiation in the said patient.

CONCLUSION

Splenic irradiation is a safe and effective method to improve splenomegaly and resultant hypersplenism as a result of benign etiology even in patient with multiple co-morbidity. The dynamics of change in different blood parameters may be represented by linearly increasing hemoglobin, waning and waxing TLC, ANC and platelets following a certain trend. Validation of these trends will need observation in higher number of patients and using different radiotherapy dose/fractionation scheme.

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