Splenic Irradiation: A Concise Review of the Literature

Omer Sager*, Ferrat Dincoglan, Bora Uysal, Selcuk Demiral, Hakan Gamsiz and Murat Beyzadeoglu

University of Health Sciences, Gulhane Training and Research Hospital, Department of Radiation Oncology, Gntevfik Saglam Cad. 06018, Etilik, Kecioren Ankara, Turkey

Received Date: April 04, 2017, Accepted Date: June 03, 2017, Published Date: June 12, 2017.

*Corresponding author: Omer Sager, Department of Radiation Oncology, University of Health Sciences, Gulhane Training and Research Hospital, Gntevfik Saglam Cad. 06018, Etilik, Kecioren Ankara, Turkey, Tel: +90-312-304-4683; E-mail: omersager@gmail.com

Abstract

Massive symptomatic splenomegaly may be seen in various hematological malignancies and disorders such as myelofibrosis, myeloid metaplasia, chronic myelocytic leukemia, chronic lymphocytic leukemia, hairy cell leukemia, prolymphocytic leukemia, polycythemia vera, idiopathic thrombocytopenic purpura, multiple myeloma, myeloproliferative disorders, and lymphomas. Patients with splenomegaly may suffer from several symptoms which lead to deterioration of their quality-of-life. Despite the availability of several therapeutic options, most patients are not ideal candidates for potentially curative treatments and palliative approaches are commonly used in clinical practice. Splenic irradiation (SI) is a viable treatment option for patients with massive, symptomatic splenomegaly and offers effective palliation of symptoms. Recent technological advances in the discipline of radiation oncology allow for more refined treatment of these patients with incorporation of adaptive radiotherapy strategies and image guidance. Adaptive radiotherapy approaches may be used to account for changes in target volume during the course of SI. Image Guided Radiation Therapy (IGRT) techniques offer the potential for reduced normal tissue exposure by optimization of treatment margins. Optimization of the therapeutic ratio may be achieved through more focused radiation delivery by use of image guidance and “shrinking field” technique. Since the dominant pattern of toxicity is hematological, close monitoring of blood indices is required to ensure prompt management. Individualization of treatment with respect to palliation achievement or toxicity occurrence should be considered. Herein, we present a concise review of the literature regarding the use of SI in the management of symptomatic splenomegaly.

Keywords: Splenic Irradiation (SI); Symptomatic Splenomegaly; Image Guided Radiation Therapy (IGRT)

Introduction

The spleen is a unique organ with several supportive roles in the human body. As part of the lymphoid system, the spleen is involved in cellular and humoral immunity. Besides acting as a filter for the blood, it also takes part in defense against pathogens. The cause of splenomegaly is mostly benign (infections, inflammatory diseases, trauma, infiltrative diseases, cirrhosis and portal hypertension), however, various hematological malignancies and disorders such as myelofibrosis, myeloid metaplasia, chronic myelocytic leukemia, chronic lymphocytic leukemia, hairy cell leukemia, prolymphocytic leukemia, polycythemia Vera, idiopathic thrombocytopenic purpura, multiple myeloma, myeloproliferative disorders, and lymphomas may also result in enlargement of the spleen [1–3].

Splenomegaly may lead to impairment of essential functions as a consequence of filtering of normal blood cells along with the abnormal cells, and a resultant reduction of healthy cells in the blood may occur. Abundant number of trapped platelets and erythrocytes may cause major impairment with even damage of the spleen itself. Patients with massive splenomegaly may suffer from abdominal distention and severe epigastric pain, discomfort and tenderness in left upper quadrant, indigestion, early satiety and a feeling of fullness due to stomach compression, weakness and weight loss, dyspnea, abdominal bloating, cytopenias and related complications such as hemorrhages or myocardial infarctions [1–3]. These manifestations may also be ascribed to underlying conditions which lead to splenomegaly, however, even a case with renal failure due to pressure of the left kidney by the enlarged spleen has been reported in the literature [4]. All these manifestations deteriorate the quality-of-life significantly and thus require prompt management. Decision making for treatment should take into consideration several parameters including age, co-morbidities, clinical symptoms, blood indices, and general health status of the delicate patients who may be exhausted with previous treatments.

Management options for symptomatic, massive splenomegaly in patients with hematological malignancies and disorders include stem cell transplantation, chemotherapeutics, immunomodulatory drugs, JAK inhibitors, erythropoiesis-stimulating agents, radiotherapy, and splenectomy [1–3,5,6]. Despite the availability of several therapeutic options, most patients are not ideal candidates for potentially curative treatments and palliative approaches are commonly used in clinical practice [1–3,5,6].

Splenic irradiation (SI) has been used for more than a century as a viable treatment option for patients with massive, symptomatic splenomegaly [7]. As an intriguing topic of interest, radio resistance has been shown after total body irradiation (TBI) as a myeloablative and immunosuppressive regimen [8,9]. After TBI, lymphoid tissues such as the spleen may serve as reservoirs of CD 4 (+) lymphocytes [8,9]. In this regard, overcoming this radio resistance may have implications for improving the affectivity of immunosuppressive regimens. Intensified chemotherapy regimens, dose-escalated irradiation protocols with or without total nodal irradiation, or anti-T monoclonal antibodies may be considered to overcome the radio resistance [9]. Clearly, there is a lot of room for improvement in understanding of the immune system. Recent technological advances in the discipline of radiation oncology allow for more refined treatment of the patients with incorporation of adaptive radiotherapy strategies and image guidance. Herein, we present a concise review of the literature regarding the use of SI in the management of symptomatic splenomegaly.

Indications

SI has been used in the palliation of symptomatic splenomegaly for patients with various hematological malignancies and disorders such as myelofibrosis, osteomyelosclerosis, myeloid metaplasia, chronic myelocytic leukemia, chronic lymphocytic leukemia, hairy cell leukemia, prolymphocytic leukemia, polycythemia Vera, idiopathic thrombocytopenic purpura, multiple myeloma, myeloproliferative disorders, and lymphomas [1–3,5,6,10–13].

SI is typically used for patients with massive, symptomatic splenomegaly who are not ideal candidates for splenectomy.
Mechanism of action is not completely understood, nevertheless, SI can induce both local and systemic effects which may result in systemic remissions besides local palliation. Proposed mechanisms for these effects include low-dose hypersensitivity, radiotherapy-induced apoptosis, immune modulation, and radiation-induced cytokine release and abscopal effect [2,5,14–20].

In this context, using lower radiotherapy doses may be important for avoiding excessive radiation-induced toxicity. The concept of SI with lower doses has been supported by several studies in which palliation of symptoms with lower doses of SI has been accomplished [3,10–13,17]. Close monitoring of hematological parameters during the course of SI is critically important for early detection and prompt management of radiation-induced toxicity. In an effort to avoid excessive radiation-induced toxicity, treatment interruption or cessation should be considered for patients receiving SI if toxicity is detected. Discontinuation of SI may also be taken into consideration when effective palliation is achieved. Radiation-induced toxicity may also be minimized by treating only a part of the spleen or by taking into account the changes in splenic size with frequent imaging of patients during the SI course. Recent technological advances in the discipline of radiation oncology allow for more refined treatment of the patients with incorporation of adaptive radiotherapy strategies and image guidance. From the technical aspect of radiotherapy, margins used for internal motion and setup uncertainties may be optimized by incorporating modern radiotherapy techniques and image guidance along with motion assessment if technology is available [1–3]. Breathing maneuvers may be used in compliant patients to improve accuracy and precision of SI [21–24].

**Treatment Techniques and Dose-Fractionation Schemes**

Although SI has a long history in symptomatic splenomegaly management, its utility in clinical practice has somewhat waned with introduction of more effective systemic treatments. Reaching a consensus on optimal dose-fractionation schemes is hardly achievable given the low number of patients referred for SI and significant heterogeneity in patient characteristics, diagnosis, and prognosis. There are no prospective randomized trials comparing SI techniques and dose-fractionation schemes partly due to limited use of SI in clinical practice. Also, wide diversity among patient and treatment characteristics in different studies hampers comparative assessments. Given that SI is primarily used to provide effective palliation without toxicity, achieving an optimal therapeutic ratio requires treatment individualization without being dependent on a uniform dose-fractionation scheme for SI of patients with different underlying diseases.

Anterior and posterior opposed treatment portals are commonly preferred in field arrangement for SI [1,25]. Total SI 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 in studies, which may be explained by different patient and treatment related factors including diagnoses, comorbidities, previous therapies, treatment cessation or interruptions due to toxicity or palliation achievement [1]. Dose per fraction and total SI dose may be kept at lower levels in selected patients to avoid toxicity, which has been supported by a study demonstrating remarkable improvement with a total SI dose as low as 100 cGy delivered in 4 fractions (25 cGy per each fraction) [17]. As mentioned previously, incorporation of adaptive radiotherapy approaches and recent advances such as image guidance may enhance the accuracy and precision of SI [1–3]. Adaptive radiation therapy allows redesigning of treatment plans with respect to changes in target volume during the radiotherapy course. In this regard, it is prudent to modify radiotherapy plans to take into account the reduction in splenic size during the course of SI, which is likely to occur in many patients. (Figure 1) shows axial computed tomography images of a patient before SI (A) and after 5 treatment fractions of SI (B).

Given that radiation-induced toxicity is correlated with the irradiated volume, the use of “shrinking field” technique for SI may have implications for improving the toxicity profile by decreased exposure of normal tissues. It may also be important when reirradiation of the spleen is considered. The use of image guided radiation therapy (IGRT) techniques improves accuracy and precision of radiotherapy by accounting for intrafractional and interfractional uncertainties during the fractionated radiotherapy course. Also, close monitoring of splenic size under image guidance aids in treatment adaptation to exploit the reduction in target volume.

**Figure 1:** Axial CT images of a patient: A) before SI, B) after 5 treatment fractions of SI. (CT: computed tomography; SI: splenic irradiation).
Outcomes

Outcomes of SI are assessed by using several endpoints such as pain relief, reduction in size of the enlarged spleen, improvement of cytopenias and symptoms associated with splenomegaly. Reported efficacy and toxicity outcomes in studies of SI show considerable diversity. This may be explained by divergent patient and treatment characteristics, indications, and outcome endpoints in different studies. Majority of patients receiving SI have terminal disease along with significant comorbidities. In this regard, it may be quite complex to differentiate between SI-induced toxicity and complications of the underlying disease. It is difficult to assess duration of response to SI and late toxicity due to short survival of most patients. Nevertheless, several studies have reported effective palliation of symptoms even with low doses of SI [3,10–13,17]. During the course of SI, close monitoring of blood indices should be performed to avoid excessive toxicity. Since reirradiation may be required and even modest doses of SI may induce profound cytopenias, treatment interruptions or cessation should be considered in the presence of toxicity occurrence or effective palliative achievement.

In a recent comprehensive systematic review, Zaorsky et al. reported that splenic size reduction was achieved in 72% of the SI courses [1]. Palliation of pain was achieved in 59% of the SI courses, and 70% of SI courses were effective in improving cytopenias.

In terms of toxicity, discrimination between complications of the underlying disease and SI-induced toxicity may be difficult. Nevertheless, toxicity of SI is mainly hematological and fairly manageable with supportive measures. To minimize radiation-induced toxicity, adaptive radiation therapy techniques and IGRT should be considered. Besides accounting for intrafractional and interfractional uncertainties during the SI course, image guidance also allows close monitoring of splenic size during treatment. Adaptation of SI plans with respect to changes in splenic size and using the “shrinking field” technique may improve treatment outcomes.

Conclusions

Splenic irradiation remains to be a viable treatment option for symptomatic, massive splenomegaly. Effective palliation may be achieved without excessive toxicity. Recent technological advances in the discipline of radiation oncology allow for more refined treatment of these patients with incorporation of adaptive radiotherapy strategies and image guidance. Adaptive radiotherapy approaches may be used to account for changes in target volume during the course of SI. IGRT techniques offer the potential for reduced normal tissue exposure by optimization of treatment margins. The therapeutic ratio may be optimized with more focused radiation delivery by use of image guidance and “shrinking field” technique. Since the dominant pattern of toxicity is hematological, close monitoring of blood indices is required to ensure prompt management. Individualization of treatment with respect to palliation achievement or toxicity occurrence should be considered. Prospective randomized studies are needed to further refine dose-fractionation schemes.

Conflict of Interest

Authors declare no conflict of interest.

References


