Technical Innovations & Patient Support in Radiation Oncology 3–4 (2017) 23–29

Contents lists available at ScienceDirect

Technical Innovations & Patient Support in Radiation Oncology

journal homepage: www.elsevier.com/locate/tipsro

Case reports and case series

Treatment of symptomatic splenomegaly with low doses of radiotherapy: Retrospective analysis and review of the literature

Carolina de la Pinta [a], Eva Fernández Lizarbe [a,*], Ángel Montero Luis [b], José Antonio Domínguez Rullán [a], Sonsoles Sancho García [a]

[a] Ramón y Cajal University Hospital, Madrid, Spain
[b] HM Madrid, Spain

ARTICLE INFO

Article history:
Received 23 May 2017
Received in revised form 9 July 2017
Accepted 9 August 2017

Keywords:
Splenomegaly
Radiotherapy
Adaptative
Low doses

ABSTRACT

Objectives: To evaluate the effectiveness of low doses of radiation therapy for symptomatic splenomegaly in malignant and benign diseases.
Patients and methods: 5 patients with symptomatic splenomegaly were treated with low doses of radiation in our centre (January 2008–December 2016). 4/5 patients had malignant neoplasia (acute myeloid leukemia, non Hogdkin lymphoma and prolymphocytic B cell leukemia) and splenomegaly was caused by extramedullary hematopoiesis. 1/5 patient had benign disease (HBV liver cirrhosis) and splenomegaly was caused by vascular ectasia. Median age was 73 years (range 61–86 years). There were 4 females and 1 male. These patients had exclusively splenic pain or abdominal discomfort in 20%, exclusively cytopenias 40% and both 40%. Patients needed radiation therapy for symptomatic control. Dose per fraction was 0.5 Gy every two days; total dose initially prescribed 10 Gy. IGRT were performed in all patients to ensure an appropriate position and to adapt the treatment volume to the changes in the spleen volume along the treatment. Median craneocaudal length size of the spleen was more than 26 cm (range 15.2–34.9 cm).
Results: Median radiation doses were 4.85 Gy (range 2.5–10). Median craneocaudal spleen size reduction was 4.6 cm (0–8 cm). Splenic pain and abdominal disturbances improved in all patients. Median increase of haemoglobin and platelets levels was 1.6 mg/dl and 27.950 cells respectively in the first week after the end of radiotherapy.
One patient had to interrupt her treatment due to grade II neutropenia. No other toxicities were described. With a median follow-up of 39 months (16–89 months), only one recurrence was described at 24 months and consisted of thrombocytopenia. The patient received a second course of radiotherapy with excellent response.
Conclusion: Low doses of radiation therapy for treatment of symptomatic splenomegaly were effective, with a low rate of side effects. Splenic pain and abdominal discomfort completely improved and cytopenias rised to secure levels.

Introduction

The spleen is an abdominal hematopoietic organ, usually not palpable, involved in different functions such as blood pathogen elimination, aged blood-cell destruction and extramedullary hematopoiesis. Splenomegaly refers to a pathological enlargement of the spleen, and is generally defined as craneocaudal growth of spleen more than 11 cm. Splenomegaly is the leading clinical sign of various lymphoid and myeloid malignancies, but also can occur as a secondary manifestation of a broad spectrum of benign non-neoplasic diseases. Splenomegaly can be developed in malignant myeloproliferative and lymphoproliferative diseases like myelofibrosis, prolymphocytic leukemia, hairy cell leukemia, non-Hodgkin's lymphoma or chronic lymphocytic leukemia, but also due to benign conditions like liver cirrhosis, amyloidosis or Gaucher's disease.

Splenomegaly physiopathology includes four mechanisms. First, reticuloendothelial and lymphoid-system hyperplasia, typically present in autoimmune diseases such as autoimmune hemolytic anemia. Spleen in this illness accumulates large number of

* Corresponding author.

http://dx.doi.org/10.1016/j.tipsro.2017.08.002

defective red blood cells, which results in an enlarged hyperfunctioning spleen (splenomegaly). Second, extramedullary hematopoiesis in myeloproliferatives syndromes, including anemia and leukoerythroblastic reaction. Third, portal hypertension and passive congestion in cirrhotic patients. Last, infiltration of proteins (amyloidosis and Gaucher disease) or tumor cells [1]. The symptoms of an enlarged spleen can include pain cause by Gerota capsule distension, a sense of fullness, discomfort in the left upper quadrant, early satiety and diarrhea due to organ compression and cytopenias due to hypersplenism [5,6]. In some patients the spleen becomes so enlarged that its lower pole protrudes into the pelvis or crosses the midline into the lower right or upper right abdominal quadrants. In these patients with a massively enlarged spleen symptoms could be ischemia and pain due to splenic infarction.

Treatment of symptomatic splenomegaly depends on its etiology: chemotherapy in haematologic tumors [6,7], transjugular intrahepatic portosystemic shunt (TIPS) used for reducing portal venous pressure [8,9], radiofrequency [10,11], splenic embolization [12,13], splenectomy [14,15] or radiotherapy. Effectiveness of splenic irradiation for palliation of splenomegaly symptoms is well known since beginning of the 20th century, both in malignant and non-malignant disorders. Underlying mechanism of splenic irradiation seems to be related to a reduction of tumor burden in the spleen as well as to splenic reticuloendothelial system suppression.

In this paper, we present 5 patients who received splenic low-dose irradiation for malignant and non-malignant conditions. The indications, setting, results and toxicity profile are discussed.

Material and methods

We have retrospectively analyzed the outcomes of 5 patients with splenomegaly referred to our department to consider splenic irradiation for symptomatic splenomegaly between January 2008 and December 2016.

There were 4 females and 1 male, with a median age of 73 years (range 61–86 years). Primary diseases were malignant neoplasms [(acute myeloid leukemia ($n = 1$), non Hogdkin lymphoma ($n = 2$) and prolymphocytic B cell lymphoma ($n = 1$)]. One patient had splenomegaly due to vascular ectasia with liver cirrhosis. Symptoms and signs of splenomegaly included pain or abdominal discomfort in 20%, cytopenia in 40% and both in 40%. At first medical appointment patients and physicians evaluated pain presence (present/absent). If present, pain was referred as mild, moderate or severe. No specific pain-tools were used, because the pain had visceral characteristics and its evaluation in numeric scales was difficult to asses. Median size of the spleen determined by craneocaudal length was 26 cm (range 15.2–34.9 cm).

All patients and treatment parameters are summarized in Table 1. Patients needed radiotherapy for symptomatic control.

Radiation is delivered after three dimensional computer tomography based treatment planning (CT-plan). All patients were planned with non contrast-enhanced computerized tomography (CT scan) because no enhancement of any lesion was mandatory and the whole organ was delimited. CT-plan images are acquired in supine position, every 3 mm CT slice thickness and sent to a Pinnacle® planning system. CT plan images to define treatment volume (spleen) in all slices, surrounded by 1 cm safety margin (to compensate internal organs movements and uncertainties of technique) to create the planning target volume (PTV). We contour bowel, stomach, kidneys and liver as organs at risk to avoid adverse effects. A total dose of 10 Gy in 0.5 Gy fractions was prescribed, and treat two or three fractions per week. In some cases we were able to interrupt treatment before achieving the total prescribed dose due to good response at even lower doses.

In our center, it is used a volume-adaptative technique for splenic irradiation. This technique allows to avoid radiation to surrounding organs such as liver, bowel, stomach or kidneys. During the delivery of the treatment, every two fractions we perform a CT conebeam, obtained by the linac right before treatment. This CT conebeam is registered with CT-plan and has two purposes: first, it is used for image-guided radiotherapy (IGRT) to assure the administration of treatment in the accurate site; second, to monitor spleen volume changes between fractions. Once we detect a volume reduction in the organ, the spleen is recontoured the spleen, recreating a new and smaller PTV and redesign the treatment for this new scenario. It is possible to proceed so because the spleen is an organ with a capsule and all its content stays inside the capsule. With this reduction in volume we achieve better dose-volume histograms for organs at risk and, therefore, less toxicity. We believe that the use of this advantageous technique contribute to a better tolerance of treatment.

Besides pain, diarrhea and sickness evaluation, blood counts are monitored once per week, and supportive treatment prescribed when necessary.

Results

Median radiation doses were 4.85 Gy (range 2.5–10 Gy). The causes for stopping the treatment before 10 Gy are summarized in the Table 1. Median craneocaudal spleen size reduction was 4.6 cm (0–8 cm). Splenic pain and other abdominal disturbances improved in all patients. Median increase of haemoglobin and platelets levels was 1.6 mg/dl and 27.950 cells respectively in the first week after the end of radiotherapy. On Table 2, we reported pre-treatment leukocyte and thrombocyte counts, nadir values and post-treatment values. In consecutive visits both patients and physicians assessed changes in pain intensity as worse, stable, improve or absent. One patient had to interrupt the treatment due to grade II neutropenia. This patient received treatment with ruxolitinib concomitant to radiation therapy and this drug can

Table 1
Patients characteristics and cause of interruption.

Pathology	Gender	Age	Volume pre-treatment (cm)	Symptoms	Dose (Gy)	Response	Interrupt treatment	Cause of interruption
Acute myeloid leukemia	F	61	25	Pain and anemia	5.5	Yes	Yes	Neutropenia Grade II
Non Hogdkin lymphoma	F	77	29	Pain, thrombopenia and anemia	3	Yes	No	Increase platelets, clinical response and reduce of spleen volume
Liver cirrhosis	F	61	13.2	Thrombopenia	3	Yes	No	Increase platelets
Prolymphocytic B leukemia	F	80	23	Anemia and thrombopenia	2.5	Yes	No	Increase platelets and clinical response
Non Hogdkin lymphoma B	M	86	27.5	Pain and thrombopenia	10	Yes	No	Clinical response and reduce of spleen volume