“Shrinking Lung” Radiation Technique in Hodgkin’s Disease

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Case report

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Abstract

We present a case of Classical Hodgkin lymphoma, nodular sclerosis subtype, Stage IIB EX presenting with a large left lung mass, mediastinal lymph nodes, night sweats, 19% weight loss, erythrocyte sedimentation rate (ESR) of 110 ml/hr and a suboptimal response to 6 cycles of ABVD (Adriamycin, Bleomycin, Vinblastine and Dacarbazine) chemotherapy. The patient then underwent radiation to the left lung followed by radiation to residual disease using what we describe as a “shrinking lung” radiation technique. A PET-CT done 8 months after radiation treatment was completed demonstrated a complete response. This case highlights the use of a traditional radiation technique in treatment of chemotherapy refractory Hodgkin’s lymphoma to achieve a complete remission.

Introduction

We present a case of Classical Hodgkin lymphoma, nodular sclerosis subtype, AJCC 7th edition Stage IIB EX (extranodal and bulky) presenting with a large left lung mass, mediastinal lymph nodes, night sweats, 19% weight loss, erythrocyte sedimentation rate (ESR) of 110 ml/hr and a suboptimal response to 6 cycles of ABVD (Adriamycin, Bleomycin, Vinblastine and Dacarbazine) chemotherapy. Figures 1 and 2 show the PET-CT scans before and after 6 cycles of chemotherapy. The patient then underwent radiation to the left lung to 18 Gy followed by radiation to residual disease using what we describe as a “shrinking lung” radiation technique to a total dose of 36 Gy. Figure 3 shows post radiation PET-CT 8 months after radiation treatment demonstrating a complete response. This case highlights the use of a traditional radiation technique in treatment of chemotherapy refractory Hodgkin’s lymphoma to achieve a complete remission.

Case Report

This 27-year old female patient presented in February 2015 with worsening dyspnea on exertion that began several months prior to presentation. This was associated with other symptoms that included a 20-pound weight loss over several months, intense pruritus, decreased appetite, pleuritic chest pain and cough that prompted a visit to the emergency room where subsequent imaging revealed a large intrathoracic mass causing collapse of the left upper lobe. She had no other relevant past medical history, a surgical history only relevant for recent lung biopsy, and no allergies but she did report previous tobacco use.

A biopsy of this mass on 2/20/15 was performed that revealed Nodular Sclerosing Classical Hodgkin’s Lymphoma. Baseline labs on 3/11/15 included an ESR 110 ml/hr, both human immunodeficiency virus (HIV) p24 antigen as well as HIV-1/2 antibodies were negative, uric acid 5.7 mg/dL (normal). A complete blood count (CBC) with differential on 3/11/15 revealed mild leukocytosis with white blood cell (WBC) count 18.6×10^9 cells per liter, anemia with hemoglobin level 9.2 g/dL, and mild thrombocytosis with platelet count 583×10^9 per liter. A baseline transthoracic echo on 3/18/15 revealed normal right and left

ventricular function but moderate to severe tricuspid regurgitation. Pulmonary function tests on 3/18/15 revealed mild restriction with mild impairment in gas exchange.

Baseline PET-CT on 3/10/15 revealed a hypermetabolic mass in left upper lung that measured $11.6 \times 8.4 \times 12.8$ cm with maximum standardized uptake value (SUV) near 9, with narrowing of distal left mainstem bronchus and left lower lobe bronchus, subcarinal lymph nodes measuring $2.6 \times 1.7 \times 2.8$ cm and subcentimeter inferior left neck lymph node. The patient was treated with 6 cycles of ABVD between 3/11/15 and 8/19/15. A follow up PET-CT after 4 cycles of ABVD on 7/8/15 revealed a significant improvement in active lymphoma with mass now measuring $3.4 \times 2.3 \times 8.2$ cm, with maximum SUV 6.4. Another follow up PET-CT after 6 cycles of ABVD on 9/2/15 revealed a slight increase in hypermetabolic activity of the left upper lobe mass of unchanged size but maximum SUV increased to 7.8 compared to 6.4 previously. A PET-CT done subsequently on 10/7/15 revealed redemonstration of an fluoro-deoxy-glucose (FDG)-avid lesion in the left upper lobe similar in extent but now with an air-filled cavity with maximum SUV of 6.4.

Due to persistence of a bulky residual hypermetabolic left lung mass, the patient was referred to Radiation Oncology for treatment of her persistent classical Hodgkin's Lymphoma. The patient was treated initially from 9/24/15 to 10/5/15 with AP/PA technique using a field-in-field technique with control points for dose homogeneity to 1200 cGy in 8 fractions with 150 cGy fraction size to whole left lung (Fig. 4). This was followed by radiation treatment from 10/20/15 to 10/23/15 with 4 fractions using AP/PA technique with control points to a smaller lung field in 150 cGy fraction size to 600 cGy (Fig. 5). A "shrinking field" radiation technique was then utilized with intensity-modulated radiation (IMRT) to treat the residual mass between 10/26/15 and 11/5/15 to another 1800 cGy to a total dose of 3600 cGy (Fig. 6). A composite dose accumulation revealed left lung mean dose of 31.38 Gy (maximum 36.93 Gy and minimum 18.34 Gy). The volume receiving at least 20 Gy (V20) for the left lung for the AP/PA treatment was 92.65%. The composite dose accumulation for the planning target volume for 18 Gy (PTV18Gy) revealed a mean dose of 35.99 Gy (maximum 37.05 Gy and minimum 32.1 Gy).

The patient showed an interval improvement in subsequent PET-CT scans and eventually a PET-CT done on 6/22/16 revealed no active lymphoma (Fig. 3). While on surveillance, a CT of chest, abdomen and pelvis with contrast on 8/8/18 revealed interval development and increase in size of multiple lymph nodes in left axillary, left internal mammary, left mediastinum, retrocrural region and upper left abdomen measuring between 1.1 and 1.7 cm. A PET-CT scan on 8/24/18 did reveal borderline hypermetabolic adenopathy felt to represent an infectious/inflammatory process with SUV values between 3.5 and 5.6. Biopsies performed on 8/16/18 and 9/7/18 included fine needle aspiration and excisional biopsies were all negative for lymphoma as well as Grocott's Methenamine Silver (GMS) stain for fungal organisms. The patient remained clinically in remission for the rest of her life and passed away of unrelated causes in March 2019.

Discussion

In 1832, in an article entitled “Some Morbid Appearances of the Absorbent Glands and Spleen”, Thomas Hodgkin described the disease named after himself^{1,2}. A disease of the hematologic system, Hodgkin’s disease was originally treated with extended field radiation till the 1960’s when chemotherapy became part of the treatment paradigm. In fact it was Gilbert in 1939 who proposed the inclusion of uninvolved areas in the treatment volumes when he described the use of “segmental roentgen therapy”³. This concept was based on the unicentric origin of Hodgkin’s disease and developed the theory of treating both involved nodal areas as well as regions of suspected involvement. In 1950, Peters described improved survival for patients who were treated to both involved nodes as well as to “more commonly involved nodal regions”⁴. Kaplan also held the view of the unicentric origin of Hodgkin’s disease and proposed treatment with definitive intent⁵.

Hodgkin’s disease is presently treated with an array of agents including traditional chemotherapy, immunotherapy, stem cell transplant and radiation therapy. Historically, MOPP (Mechlorethamine, Vincristine, Procarbazine, and Prednisone) chemotherapy was the standard of care for many years⁶. This regimen eventually fell out of favor because of cytotoxicity and effects on fertility. This gradually got supplanted by ABVD (Adriamycin, Bleomycin, Vinblastine and Dacarbazine) chemotherapy^{7,8}. More recently the Bleomycin in ABVD has been supplanted by Brentuximab⁹. Newer agents such as programmed death-1 (PD-1) inhibitors such as Pembrolizumab have also been approved in the setting of relapsed and refractory classical Hodgkin’s disease¹⁰. Meanwhile, patients with refractory disease are often salvaged and then referred for autologous stem cell transplant. With the approval of newer agents including chemotherapy and immunotherapy agents the use of radiation for treatment of residual disease, particularly older techniques may be forgotten or relegated to being a last ditch option. Advances in chemotherapy along with a high success rate have seen a gradual decline in the use of radiation to treat Hodgkin’s disease. The success of salvage radiation therapy following chemotherapy failure has been well documented by Leigh and colleagues who in a retrospective analysis of single institution data documented 26 patients with a complete response (CR) and 2 with a partial response in a cohort treated between 1972 and 1991¹¹. Patients in this group were treated with extended fields such as Mantle, Inverted Y or either just the PA or Pelvis fields alone.

The technique we used was similar to one originally described by Kaplan and Rosenberg¹². Here suggested salvage radiation to a solitary lesion in one lung is done after 6 cycles of MOP chemotherapy followed by ipsilateral whole lung irradiation (1500 cGy over 3–4 weeks) with a boost over involved area to approximately 2000–2500 cGy. This “shrinking lung” technique has also been described by Nautiyal et al. using 3D radiation techniques¹³. Nautiyal et al. described whole lung irradiation (WLI) with use of a 37% transmission lung block on the involved side, (with 150 cGy per fraction) to total dose of 1650 cGy to lung. Alternately, the lung block can be omitted on the involved side for the initial 1500 cGy but fraction size should be reduced to 100–150 cGy. When whole lung irradiation is to be avoided the prechemotherapy volume may be treated to a subclinical dose (18–20 Gy). Residual disease is boosted to a higher therapeutic dose (36 Gy).

Conclusion

To summarize, we present a case of a patient with Hodgkin's disease of the left lung who presented with an inadequate response to frontline chemotherapy and went on to receive whole left lung radiation followed by consolidative radiation to area of residual mass using a "shrinking lung" radiation technique resulting in a sustained remission. This case highlights that older radiation techniques still have a role in the management of Hodgkin's disease even in an era of newer systemic agents.

Abbreviations

ESR -erythrocyte sedimentation rate

ABVD -Adriamycin Bleomycin Vinblastine Dacarbazine

PET-CT -positron emission tomography-computed tomography

Gy -Gray

HIV – human immunodeficiency virus

CBC -complete blood count

WBC -white blood count

ml/hr -milliliters per hour

mg/dl -milligrams per deciliter

SUV – standardized uptake value

FDG -fluorodeoxyglucose

AP/PA -anteroposterior/posteroanterior

IMRT -intensity modulated radiation treatment

V20 -volume receiving at least 20 Gy

PTV -planning target volume

cGy -centigray

GMS - Grocott's Methenamine Silver

MOPP - Mechlorethamine, Vincristine, Procarbazine, and Prednisone

PD-1 -programmed death-1

CR -complete response

MOP - Mechlorethamine, Vincristine, Procarbazine

WLI – whole lung irradiation

Declarations

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Figures

Figure 1

Figure 1

Figure 2

Figure 2

Figure 3

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Figure 4

Figure 4

Figure 5

Figure 5

Figure 6

Figure 6