

Teaching Case

Complete response of pleural effusions caused by extramedullary hematopoiesis to low-dose, single fraction palliative radiation therapy: Case report and literature review

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Introduction

Pulmonary extramedullary hematopoiesis, either in the lung parenchyma or the pleura, is an unusual sequela of marrow-depleting disorders that can precipitate symptomatic compromise of the respiratory system. In case reports of patients with pulmonary extramedullary hematopoiesis, low-dose external beam radiation therapy that targets the lungs has been shown to palliate respiratory symptoms and control pulmonary extramedullary hematopoiesis-associated pleural effusions with mixed results.¹⁻¹¹ Here, we present a case of symptomatic bilateral pulmonary extramedullary hematopoiesis-associated pleural effusions that were effectively managed with low-dose radiation therapy. The patient provided written consent to report the details of her case, including the use of images.

Case

A 62-year-old woman with myelofibrosis was evaluated in the Department of Radiation Oncology in March of 2017 for dyspnea secondary to refractory

pleural effusions in the setting of pulmonary extramedullary hematopoiesis. She had received 4 prior courses of radiation therapy for extramedullary hematopoiesis over the previous 13 years at another institution. Limited available records showed that the patient had received 15 Gy in 21 fractions to T6-T11 in 2005, 25 Gy in 10 fractions to the pelvis in 2009, 25 Gy in 10 fractions for brain involvement in 2010, and 30 Gy in 12 fractions to T7-9 in 2014, resulting in relief of symptoms on each occasion.

The patient had been on maintenance therapy with hydroxyurea for several years. Five months prior to consultation with radiation oncology, she began to experience dyspnea and was found to have bilateral pleural effusions. Sequential thoracenteses resulted in improvement of symptoms. Cytology was negative for malignant cells. Four months prior to consultation, an indwelling catheter was placed in the right pleural space, and the patient reported removing between 150 and 600 mL of pleural fluid 3 times per week.

During consultation with radiation oncology, the patient reported moderate dyspnea and was no longer was experiencing symptomatic improvement with removal of pleural fluid. Her oxygen saturation on room air was 91%. Pulmonary function testing showed proportionally reduced lung volumes, including a total lung capacity 61% of predicted and a corrected diffusing capacity for carbon monoxide 48% of predicted, suggesting pulmonary parenchymal involvement in addition to her known pleural involvement.

Conflicts of interest: No conflicts of interest to disclose.

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Figure 1 Chest computed tomography scan demonstrating left-sided pleural effusion, right-sided pleural catheter with small residual pleural effusion, and diffuse pleural thickening consistent with extramedullary hematopoiesis.

A chest computed tomography scan demonstrated a left-sided pleural effusion, a right-sided pleural catheter with residual pleural effusion, and diffuse pleural thickening consistent with pleural extramedullary hematopoiesis (Fig 1). A technetium-99m sulfur bone marrow scan demonstrated diffuse uptake in the liver and lungs consistent with hepatic and pulmonary extramedullary hematopoiesis (Fig 2). Magnetic resonance imaging of the thoracic and cervical spine demonstrated epidural and paraspinous soft tissue thickening from C5 to T6 consistent with extramedullary

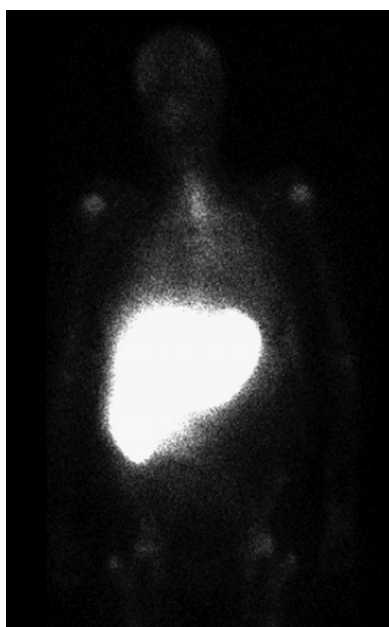


Figure 2 Technetium-99m sulfur bone marrow scan in antero-posterior orientation demonstrates diffuse moderate uptake in both lungs, marked uptake in the liver, and diffuse bone marrow expansion.

hematopoiesis. There was associated severe spinal canal narrowing with mild T2 hyperintense signal in the spinal cord, consistent with compression myelopathy. The patient had no signs or symptoms indicative of cord compression at the time of consultation.

A course of palliative radiation therapy was recommended; 100 cGy in 1 fraction was prescribed to the lungs and areas of epidural and paraspinous involvement (Fig 3). During and immediately after the delivery of radiation, the patient did well with no adverse effects. Her hydroxyurea was held prior to treatment and then was restarted after verification that her blood counts were at baseline. Three weeks after treatment, the patient reported that her breathing was better and fluid drainage from her pleural catheter had decreased from 250 to 150 mL per session. Five weeks after treatment, the patient reported that her dyspnea had resolved, her oxygen saturation on room air had improved from 91% to 96%, and she had no further drainage from the catheter. Subsequently, her pleural catheter was removed 8 weeks after radiation therapy.

Discussion

Single low-dose radiation therapy led to successful palliation of symptoms and resolution of bilateral pleural effusions within 2 months of treatment. Although the patient in this case initially experienced an improvement with pleural catheter placement alone, her parenchymal disease remained untreated prior to her lung-directed radiation therapy, which may have been why her symptoms had returned and progressed. Previously, the patient's extramedullary disease had been palliated with radiation therapy at another institution at much higher doses than what likely was necessary because doses as low as 50 cGy can induce apoptosis of bone marrow stem cells.¹² In contrast to other forms of management, low-dose radiation therapy is an attractive option because it is non-toxic, convenient, noninvasive, and provides palliation by directly reducing extramedullary hematopoiesis.

Extramedullary hematopoiesis may be managed with exceptionally low doses of radiation therapy. In the setting of pulmonary extramedullary hematopoiesis, various dose and fractionation schedules have been employed (Table 1).¹⁻¹¹ Of the 12 cases identified in the literature, outcomes included complete resolution of effusion in 7 cases, partial resolution in 2 cases, and no change in 3 cases. Among these cases, there was no discernible relationship between dose-fractionation and patient outcome. Several cases from the literature were managed with doses up to 20 times higher than the dose used in this case. Given the complete response to low-dose radiation therapy in this case and multiple cases in the literature, we typically employ 100 cGy in a single fraction as an initial therapy, reserving higher doses for patients who are refractory to this introductory regimen.

Table 1 Summary of cases from the literature of pulmonary extramedullary hematopoiesis that were managed with radiation therapy

Source	Age	Sex	Diagnosis	Effusion type	Treated side	Dose (cGy)	Fractions (No.)	Outcome
Smith et al. ¹	46	Female	Thalassemia intermedia	Hemothorax	Left	1500	Not specified	Complete resolution
Kupferschmid et al. ²	73	Female	Myelofibrosis	Hemothorax	Right	140	10	Complete resolution
Bartlett et al. ³	61	Female	Myelofibrosis	Hemothorax	Left	150	10	Complete resolution
Oren et al. ⁴	33	Female	Myelofibrosis	Exudate	Right	1400	10	Partial response; complete resolution with 6-mercaptopurine
Ibabao et al. ⁵	40	Male	Thalassemia major	Exudate	Bilateral	900	Not specified	No change after 14 days; complete resolution with talc pleurodesis
Weinschenker et al. ⁶	76	Female	Myelofibrosis	Exudate	Bilateral	200	4	Partial response; patient died of sepsis secondary to perineal infection more than 5 months after radiation therapy
Koch et al. ⁷	66	Female	Myelofibrosis	None	Bilateral	100	1	Complete resolution
Koch et al. ⁷	61	Female	Myelofibrosis	Not specified	Left	150	10	Complete resolution
Nadrous et al. ⁸	71	Male	Myelofibrosis	Exudate	Bilateral; left	100; 150	Not specified	Complete resolution
Aessopos et al. ⁹	53	Male	Thalassemia intermedia	Exudate	Right	1000	7	No change; patient treated with repeat thoracentesis and died of pneumonia and cardiac failure several weeks after radiation therapy
Pornsuriyasak et al. ¹⁰	38	Male	Beta thalassemia	Hemothorax	Bilateral	2000	10	Complete resolution
Monga and Silverman ¹¹	53	Male	Myelofibrosis	None	Right	1400	7	No change; patient developed bloody pleural effusion and died 1 week after radiation therapy

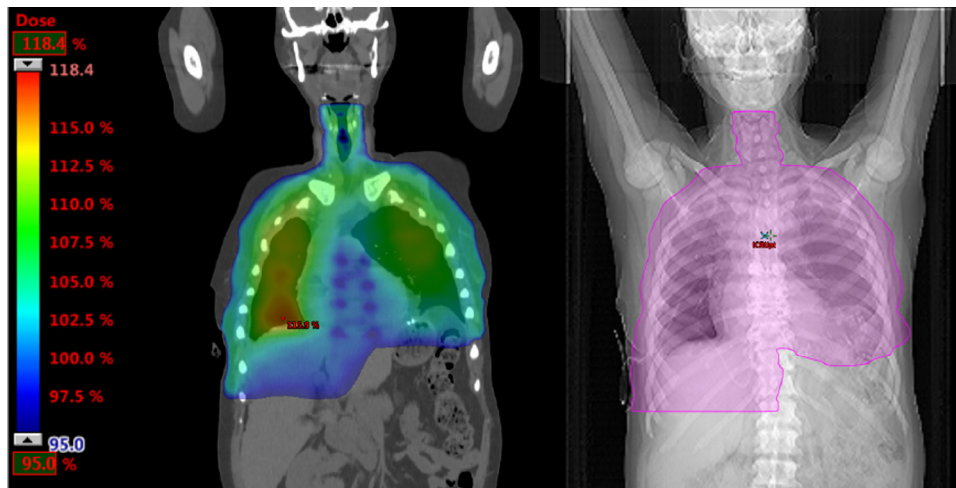


Figure 3 Radiation plan with dose wash on the left and planning tumor volume contoured in purple on the right shows 100 cGy given as a single fraction to the whole lungs and involved spinal segments from C5-T6.

Conclusions

Single-fraction, low-dose radiation therapy is a convenient, nontoxic, and effective treatment for pulmonary extramedullary hematopoiesis with pleural effusion. Hematopoietic tissue is highly radiosensitive, which enables treatment with doses that have no clinically detectable effect on nonhematopoietic tissue. Here, we present a patient with pulmonary extramedullary hematopoiesis refractory to thoracenteses and requiring a chronic pleural catheter who was treated with low-dose radiation therapy. The patient had complete resolution of symptoms and effusions.

References

1. Smith PR, Manjoney DL, Teitcher JB, Choi KN, Braverman AS. Massive hemothorax due to intrathoracic extramedullary hematopoiesis in a patient with thalassemia intermedia. *Chest*. 1988;94:658-660.
2. Kupferschmid JP, Shahian DM, Villanueva AG. Massive hemothorax associated with intrathoracic extramedullary hematopoiesis involving the pleura. *Chest*. 1993;103:974-975.
3. Bartlett RP, Greipp PR, Tefferi A, Cupps RE, Mullan BP, Trastek VF. Extramedullary hematopoiesis manifesting as a symptomatic pleural effusion. *Mayo Clin Proc*. 1995;70:1161-1164.
4. Oren I, Goldman A, Haddad N, Azzam Z, Krivoy N, Alroy G. Ascites and pleural effusion secondary to extramedullary hematopoiesis. *Am J Med Sci*. 1999;318:286-288.
5. Ibbao J, Kassapidis S, Demetis S, et al. Bilateral pleural effusions in a β -thalassemia intermedia patient with posterior mediastinal extramedullary hematopoietic masses. *Hemoglobin*. 1999;23:249-253.
6. Weinschenker P, Kutner JM, Salvajoli JV, et al. Whole-pulmonary low-dose radiation therapy in agnogenic myeloid metaplasia with diffuse lung involvement. *Am J Hematol*. 2002;69:277-280.
7. Koch CA, Li C-Y, Mesa RA, Tefferi A. Nonhepatosplenic extramedullary hematopoiesis: Associated diseases, pathology, clinical course, and treatment. *Mayo Clin Proc*. 2003;78:1223-1233.
8. Nadrous HF, Krowka MJ, McClure RF, Tefferi A, Lim KG. Agnogenic myeloid metaplasia with pleural extramedullary leukemic transformation. *Leuk Lymphoma*. 2004;45:815-818.
9. Aessopos A, Tassiopoulos S, Farmakis D, et al. Extramedullary hematopoiesis-related pleural effusion: The case of β -thalassemia. *Ann Thorac Surg*. 2006;81:2037-2043.
10. Pornsuriyasak P, Suwatanapongched T, Wangsuppasawad N, Ngodngamthaweesuk M, Angchaisuksiri P. Massive hemothorax in a beta-thalassemic patient due to spontaneous rupture of extramedullary hematopoietic masses: Diagnosis and successful treatment. *Respir Care*. 2006;51:272-276.
11. Monga V, Silverman M. Pulmonary extramedullary hematopoiesis involving the pulmonary artery. *Hematol Rep*. 2015;7:5714.
12. Barker CA, Yahalom J. Chapter 18 - Total body irradiation. In: Gunderson LL, Tepper JE, eds. *Clinical Radiation Oncology*. 4th ed. [Internet]. Philadelphia, PA: Elsevier; 2016:341-357, e7.