Case Report

Adaptive Radiotherapy for an Uncommon Chloroma

Soufya Majdoul Laurianne Colson-Durand Nu Hanh To
Yazid Belkacemi

Department of Radiation Oncology and Henri Mondor Breast Center, INSERM U955 E07,
and University of Paris-Est Créteil (UPEC), Créteil, France

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Abstract

Granulocytic sarcomas, also referred to as chloromas or myeloid sarcomas, are extramedullary neoplasms that are composed of immature myeloid cells. This uncommon disease is known to be radiosensitive. However, the total dose and dose per fraction are not standardized. In addition, during the course of radiation therapy, significant reduction of the tumor is usually obtained. Thus, target volume reduction may require an intermediate radiotherapy plan evaluation for an adaptive treatment. A second plan at mid-dose is highly recommended.

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Introduction

Granulocytic sarcomas (GS), also referred to as chloromas or myeloid sarcomas, are extramedullary neoplasms that are composed of immature myeloid cells. The term ‘chloroma’ refers to the green color that is imparted to the tissues as a result of the high concentration of myeloperoxidase found within the tumor cells [1]. Additionally, this rare clinical entity is

usually associated with a blood disease, including acute myeloid leukemia (AML). In terms of management strategy, combined treatment based on systemic and local therapy, including surgery or mainly radiotherapy (RT), is indicated in the large majority of cases. In the treatment sequence, RT can play a central role because of the high radiosensitivity of the tumor using a minimal dose [2, 3]. While several chloroma tumor sites have been reported in the literature, to our knowledge, none have been treated with adaptive RT (ART) [2]. The aim of the ART approach is to identify an early response and the need for replanning treatment for patients receiving RT against such a radiosensitive tumor. ART is effective in addressing the impact of this change on the planned dose distribution and, at some particular sites, can allow the sparing of organs at risk as well as reduce RT volumes to potentially prevent secondary malignancies in long survivors.

Here, we report the first case of ART administered to a patient with chloroma of soft tissues after allogeneic stem cell transplantation.

Case Report

We report a 60-year-old white man with a history of AML in the first complete remission after allogeneic stem cell transplantation. Four years later, he developed a mass of soft tissues in the lower third of the posterior compartment of his left thigh, gradually increasing, as well as stiffness of the left knee.

Diagnosis

Clinical examination found a 10-cm mass in the left popliteal mass with bending limitation. No abnormality was seen in the complete blood count parameters. MRI showed a bulky mass syndrome of $12 \times 7 \times 4$ cm in the lower part of the posterior ledge of the left thigh in contact with the posterior cortex of the lower metaphysis femur. This appeared in hypodensity in T1 and in heterogeneous hyperdensity in T2 on the MRI. At diagnosis, the positron emission tomography-CT (PET-CT) revealed metabolic tumor syndrome in the popliteal muscle, with a standardized uptake value (SUV_{max}) of 11.8 (fig. 1). As part of the workup, bone marrow analyses revealed normal cellular marrow with no excess of immature cells, but with some atypia and signs of dysmyelopoiesis.

Biopsy of the mass found a subcutaneous location of myeloblastic acute leukemia with transdifferentiation to plasmacytoid dendritic phenotype blasts. Immunohistochemical study showed expression of CD34+, CD33+, and 50% of CD117. The proliferation index was evaluated at 60%.

Treatment

The participants of the multidisciplinary board meeting recommended combined chemotherapy [using Azacitidine (Vidaza)] and RT to the tumor bed. Radiation CT scan simulation was performed in the treatment position using personalized means for immobilization. 3D conformal RT planning target volume (PTV) was defined as the gross tumor volume plus 1 cm of margin surrounding the tumor. This resulted in a total PTV of 560 cm³. The prescribed dose to the PTV was 30.6 Gy given in 17 fractions, i.e. 5 fractions a week delivered using 6 MV lateral photon beams. Due to the well-known radiosensitivity of this type of tumor, a limited dose of 1.8 Gy per fraction was chosen.

Results

ART was planned after administration of two-thirds of the prescribed dose, namely 19.8 Gy, using the second CT scan simulations with the same conditions. After this dose, the PTV decreased to a residual volume of 157 cm³ (fig. 2). Thus, ART allowed delivering the rest of the dose (as a boost) of 10.8 Gy to only 28% of the initial PTV with significant sparing of healthy tissue of the knee joint and the cartilage.

The first evaluation after RT showed complete clinical response without skin toxicity. The patient, who had significant functional deterioration of the knee at diagnosis, recovered normal knee function and mobility at 2 months after RT. In terms of imaging response, the PET-CT showed a significant metabolic response of the left popliteal mass at 2 months, and the SUV_{max} was 2.4 versus 11.8 (–80%) prior to RT (fig. 3).

Discussion

Chloromas are rare and considered an extramedullary clinical mass of immature myeloid cells. This entity was described for the first time by Burns [4] in 1811. In 1853, it was dubbed as chloroma by King [5] because of the greenish color taken by the tumor when exposed to air, due to the presence of myeloperoxidase in its cells [6]. Since 2008, GS has been included in the classification of the World Health Organization as one of the major subgroups of cancer in acute leukemia. While chloromas are known to most often develop in the context of AML, they can be diagnosed in chronic myeloid leukemia or myelodysplasia [7–9]. Given its low incidence, the therapeutic management of GS is still not consensual. The current management strategies are based on a combination of systemic and local therapies, with a crucial role for RT [2].

GS cases are generally referred for RT in the event of extramedullary progression, marrow relapse, or for rapid symptom relief. RT results in excellent local disease control and palliation of symptoms without significant toxicity. The recommended RT dose against chloromas is also not consensual, with at least 20 Gy in 10 fractions being most common [2, 6, 7].

To the best of our knowledge, we report the first case of a soft tissue recurrence of a chloroma in a 60-year-old patient previously transplanted for AML. Due to the functional impact of the tumor, RT was urgently decided on and delivered in 2 courses, with adaptive volume to the response. This concept for radiosensitive tumors can allow significant reduction of the dose delivered to healthy tissues and reduce potential functional toxicity (such as stiffness of the knee in our case) or late effects and secondary cancers in long survivors.

Conclusion

The rationale for considering systematic ART and a low dose per fraction for GS is evident in the context of the high radiosensitivity of the tumor and the potentially rapid local response. ART can allow for a reduction of the irradiated volumes, compared to treatments using conventional RT, in many locations, with improvement of the therapeutic ratio. Thus, we recommend systematic imaging evaluation of the tumor response during RT for treatment replanning and dosimetry adaptation to the early response of chloromas.

Statement of Ethics

The patient has signed an informed consent. The case report publication has been approved by the local Ethics Board.

Disclosure Statement

The authors declare no conflicts of interest.

References

- 1 Schultz J, Shay H, Gruenstein M: The chemistry of experimental chloroma. 1. Porphyrins and peroxidases. *Cancer Res* 1954;14:157–162.
- 2 Yossi S, De Talhouet S: Radiotherapy of chloroma or granulocytic sarcoma: a literature review. *Cancer Radiother* 2016;20:60–65.
- 3 Bakst R, Wolden S, Yahalom J: Radiation therapy for chloroma (granulocytic sarcoma). *Int J Radiat Oncol Biol Phys* 2012;82:1816–1822.
- 4 Burns A: Observation of Surgical Anatomy, Head and Neck. Edinburgh, Thomas Royce and Co, 1811, pp 364–366.
- 5 King A: A case of chloroma. *Monthly J Med* 1853;17:97.
- 6 Neiman RS, Barcos M: Granulocytic sarcoma: a clinicopathologic study of 61 biopsied cases. *Cancer* 1981;48:1426–1437.
- 7 Paydas S, Zorludemir S, Ergin M: Granulocytic sarcoma: 32 cases and review of the literature. *Leuk Lymphoma* 2006;47:2527–2541.
- 8 Byrd JC, Edenfield WJ, Shields DJ, Dawson NA: Extramedullary myeloid cell tumors in acute nonlymphocytic leukemia: a clinical review. *J Clin Oncol* 1995;13:1800–1816.

Fig. 1. Imaging at diagnosis before RT. **a** Tumor volume in MRI. **b** Tumor volume in PET-CT imaging.

Fig. 2. Dosimetry evaluation of the tumor coverage (95% isodose). **a** At the beginning of RT. **b** At 20 Gy.

Fig. 3. Tumor control at 2 months after RT. **a** MRI results. **b** PET-CT results.