Case report

Radiotherapy for isolated granulocytic sarcoma: Case report and review of literature

Jose Antonio Domínguez Rullán a,b,*, Eva Fernández Lizarbe b, Belén Capuz c, Miguel Piris d, Sonsoles Sancho García b

a Hospital Ramón y Cajal, Madrid, Spain
b Radiation Oncology, Hospital Ramón y Cajal, Spain
c Radiophysics, Hospital Ramón y Cajal, Spain
d Hematology, Hospital Ramón y Cajal, Spain

Introduction

Granulocytic sarcoma, also known as myeloid sarcoma or chloroma, is an infrequent extramedullary tumour of immature myeloid cells. Chloromas can appear in the absence of marrow involvement but usually develop in association with acute myeloid leukemia (AML) and other hematological malignancies like myelodysplastic syndrome (MDS) or during the accelerate phase of chronic myeloid leukemia (CML) [1]. The most common sites of presentation include skin, lymph nodes, bone, soft tissue and peristium, although it has been described in other atypical locations (eyes, CNS, testes...). The incidence of 2.5–9.1% in AML is low and can occur concomitantly during initial presentation or at the time of relapse [2].

Treatment strategies include systemic therapy while radiotherapy and surgery have been used to improve local control. Information about the best treatment approach is not clear and due to its poor prognosis, optimization of multimodality management is essential. Low-dose radiation therapy could have a role in cases with inadequate response to chemotherapy, at recurrence or progression, isolated chloromas or in the palliative setting when symptom relief is required. We conducted a review of literature to assess the role of radiotherapy for this rare leukemia manifestation.

Case report

We report the case of a 71 year-old male who develops an asymptomatic slow growing 1.5 cm skin nodule in the chest. Extirpation biopsy was conducted and histopathology examination showed infiltration of immature large cells. Immunohistochemical staining identified neoplastic cells positive for CD34, CD117 and myeloperoxidase (MPO) and negative for CD123 suggesting the diagnosis of chloroma. Subsequent bone marrow biopsy revealed low evidence of myeloid blasts (1%) and CT scan was normal. With diagnosis of isolated myeloid sarcoma the patient continued follow-up without further treatment.

The patient remained disease-free for 9 months, when a small skin nodule appeared in the left forearm and extirpation biopsy showed relapse of chloroma without marrow involvement and negative PET/CT scan. Observation was decided and 3 months later the patient developed local recurrence (without evidence of blasts in BM) and was referred to our clinic for consideration of radiotherapy plus systemic chemotherapy. At this time, the patient refused chemotherapy and radiotherapy to 30–36 Gy was proposed (Fig. 1).

Radiotherapy (RT) was provided using 6 MV linear accelerator photons and the RT field included the gross tumour volume and the skin scar with a 20 mm margin. The prescribed dose of 36 Gy (dose-per-fraction of 2 Gy) was decided taking into account that RT was going to be administered as a single modality treatment and the radiation site, but additional 4 Gy where required to achieve a complete response. Treatment was completed between September 14 and October 9, 2015 (40 Gy total dose). RT was well tolerated and the only side effect seen during follow-up was mild dry desquamation within the treatment field.

At one-month follow-up the patient remained disease-free but in next evaluation the patient developed local relapse (Fig. 2) and physical examination showed left axillary and supraclavicular masses. The liver and spleen were not palpable beneath the ribs. The CT scan revealed pathological cervical-supraclavicular left lymph nodes and a left axillary mass of 45 × 70 mm (Fig. 3). Bone marrow tests and immunophenotyping at this time showed progression to LMA, with evidence of 20% of myeloid blasts with a prominent monocytic component (Fig. 4).

An idarubicin and cytarabine regimen (12 mg/m² idarubicin on days 1–3 and 200 mg/m² cytarabine on days 1–5) was administered in December 2015 after which complete bone marrow response was obtained and the pathological lymph nodes, left axillary mass and skin nodule decreased in size.

However, in January 2016 the tumour progressed in the left forearm nodule and second-line FLAG-IDA regimen (30 mg/m² fludarabine and 2 g/m² cytarabine on days 1–4, 10 mg/m² idarubicin on days 1–3 and 300 µg/m2 G-CSF on days 1–5), was initiated with...
skin progression with confluent erythematous papules involving the left arm and bone marrow relapse with 9% of myeloid blasts. Third-line FLUGA regimen (40 mg/m² oral fludarabine and 75 mg/m² sc cytarabine on days 1–4) was initiated in April 4, 2016. Two weeks later the patient presented in the emergency room with rectal bleeding. An urgent blood test showed a haemoglobin level of 9.8 g/l, platelet level of 8000/µL, prolongation of the prothrombin time (PT 43.3), fibrinogen level of 75.5 mg/dl, D-Dimer > 3500 0 µg/L so disseminated intravascular coagulopathy was diagnosed. Treatment included transfusion of platelets, fresh frozen plasma and fibrinogen with clinical and hematological improvement. CT-scan during admission showed cervical-supraclavicular, mediastinal and lung progression. The patient developed rapid neurologic decline and died on April 22, 2016.

Discussion

Granulocytic sarcoma in the absence of marrow involvement is a rare entity and timing to systemic and local therapy represents a treatment dilemma. The experience in treatment of chloromas is limited and only few retrospective series and clinical case reports release some information about clinical management.

Local therapy (surgical resection and radiotherapy) cannot avoid or delay the transformation to AML, and progression usually occurs within 10–12 months after the diagnosis. This suggests that isolated chloroma should be considered as a systemic disease and initial treatment should include chemotherapy with or without transplantation. A retrospective study showed that 25% of patients initially treated without systemic therapy didn’t progress to hematological diseases during follow-up (3.5–16 years) [3]; but most series demonstrate that 88–100% of patients progressed to AML with exclusive local therapy [4].
Consolidation radiotherapy should be considered if not important toxicities are expected due its location. In some series addition of radiotherapy has been related with a prolonged failure free survival and chloroma incomplete response to systemic therapy has been associated with early bone marrow relapse [5,6]. Benefit of radiation therapy in overall survival has not been demonstrated [7,8].

Excellent response rate and local control of chloroma is achieved with low-dose radiotherapy. Different fractionation schedules have been used and most studies support prescription dose of 20–40 Gy (2 Gy per fraction) [9,10]. Chloromas are radiosensitive and the complete response rate was 43% (10–19.99 Gy), 86% (20–29.99 Gy) and 89% (>30 Gy) [9]. In Memorial Sloan-Kettering Cancer Center series, with median dose of 20 Gy there was only one local failure in 33 treatments to a sub-site that only received 6 Gy [8]. A recent series including 36 radiation courses for leukemia cutis observed that complete response rate and local control were comparable in low-dose (<26 Gy) and high-dose regimens although longer median duration of local control was seen in the >26 Gy cohort [11]. Doses of at least 20 Gy are recommended and some authors suggest 24 Gy in 12 fractions as a safe and optimal regimen [8,12]. AML patients showed better long-term outcomes compared with other types of leukemia [11].

Target volume should include the visible gross tumour or prechemotherapy extent of disease with 15–25 mm margins. Electrons are utilized for superficial myeloid sarcomas; especially after chemotherapy; and photons for deeper lesions.

Extramedullary disease has been related with unfavorable prognosis and allogeneic hematopoietic stem cell transplantation (allo-HSCT) could be used after chemotherapy. A retrospective review analysed a cohort of 99 patients (30 with isolated myeloid sarcoma), 52% of patients underwent allo-HSCT in first remission and at 5 years overall-survival was 48%, with no significant differences in outcomes when comparing isolated and leukemic granulocytic sarcoma. The role of (allo-HSCT) has not been completely established but could be considered as an effective and optimal therapy in first remission. [13,14].

Conclusions

Granulocytic sarcoma is frequently associated with worst prognosis and radiotherapy has not shown in the literature a survival benefit. In the presence of bone marrow involvement, radiation is an option for palliation or consolidation when complete response is not achieved after chemotherapy.

In the recurrence setting, radiation should be considered as consolidation after chemotherapy re-induction, especially in those patients who relapse after allogeneic transplantation.

In cases of isolated chloromas radiation therapy could improve progression free survival, principally in those with poor or incomplete response to systemic therapy. We suggest adding low-dose radiotherapy has a good toxicity profile and might add benefit in local control.

Prospective randomized studies of combined multimodality treatment are needed to better define the role of radiotherapy in chloroma both in the absence or with marrow involvement and at the time of relapse.

Disclosure

The following authors have nothing to disclose:

Jose Antonio Domínguez Rullán.
Eva Fernández Lizarrabe.
Miguel Piris.
Belén Capuz.
Sonsoles Sancho García.

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