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Original article

Pelvic radiotherapy in the setting of rheumatoid arthritis: Refining the paradigm



Radiothérapie pelvienne chez les patientes atteintes de polyarthrite rhumatoïde

T. Felefly^{a,b}, R. Mazon^{a,b,1}, A. Huertas^{a,b}, C.H. Canova^{a,b}, P. Maroun^{a,b}, M. Kordahi^c, P. Morice^{b,d}, É. Deutsch^{a,b}, C. Haie-Méder^{a,b}, C. Chargari^{a,b,e,f,*}

^a Service de curiethérapie, département de radiothérapie, Gustave-Roussy, 114, rue Édouard-Vaillant, 94805 Villejuif, France

^b Université Paris-Saclay, 114, rue Édouard-Vaillant, 94805 Villejuif, France

^c Université Paris Descartes, 12, rue de l'École-de-Médecine, 75006 Paris, France

^d Département de chirurgie, Gustave-Roussy, 114, rue Édouard-Vaillant, 94805 Villejuif, France

^e Institut de recherche biomédicale des armées, BP 73, 91223 Brétigny-sur-Orge cedex, France

^f École du Val-de-Grâce, 1, place Alphonse-Laveran, 75230 Paris cedex 05, France

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ABSTRACT

Purpose. – Conflicting results concerning the toxicity of radiotherapy in the setting of rheumatoid arthritis were reported in literature. This work describes the toxicity profiles of patients with rheumatoid arthritis undergoing pelvic radiotherapy for gynecologic malignancies at our institution.

Patients and methods. – Charts of patients with rheumatoid arthritis who underwent pelvic radiotherapy for cervical or endometrial cancer in a curative intent at the Gustave-Roussy Cancer Campus between 1990 and 2015 were reviewed for treatment-related toxicities. Acute and late effects were graded as per the Common Terminology Criteria for Adverse Events version 4.0 scoring system.

Results. – Eight patients with cervical cancer and three with endometrial cancer were identified. Median follow-up was 56 months. Median external beam radiotherapy dose was 45 Gy. All patients received a brachytherapy boost using either pulse- or low-dose rate technique. Concomitant chemotherapy was used in seven cases. Median time from rheumatoid arthritis diagnosis to external beam radiation therapy was 5 years. No severe acute gastrointestinal or genitourinary toxicity was reported. One patient had grade 3 dermatitis. Any late toxicity occurred in 7 / 11 patients, and one patient experienced severe late toxicities. One patient with overt systemic rheumatoid arthritis symptoms at the time of external beam radiation therapy experienced late grade 3 ureteral stenosis, enterocolitis and lumbar myelitis.

Conclusion. – Pelvic radiotherapy, in the setting of rheumatoid arthritis, appears to be feasible, with potentially slight increase in low grade late events compared to other anatomic sites. Patients with overt systemic rheumatoid arthritis manifestation at the time of radiotherapy might be at risk of potential severe toxicities.

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R É S U M É

Objectif de l'étude. – La toxicité reliée à la radiothérapie chez les patients atteints d'une polyarthrite rhumatoïde est débattue dans la littérature. Cette étude décrit la toxicité de la radiothérapie pelvienne chez les patientes traitées dans notre institution pour des tumeurs gynécologiques.

Patients et méthodes. – La toxicité à court et à long termes chez les patientes souffrant de polyarthrite rhumatoïde et prises en charge à visée curative à l'institut Gustave-Roussy pour un cancer du col utérin ou de l'endomètre entre 1990 et 2015 a été rétrospectivement revue. L'intensité de la toxicité a été rapportée selon la Common Terminology Criteria for Adverse Events, version 4.0 (CTCAE version 4.0).

Mots clés :

Pelvis

Radiothérapie

Polyarthrite rhumatoïde

Cancers gynécologiques

Toxicité

* Corresponding author at: Service de curiethérapie, département de radiothérapie, Gustave-Roussy, 114, rue Édouard-Vaillant, 94805 Villejuif, France.

E-mail address: cyrus.chargari@gustaveroussy.fr (C. Chargari).

¹ Deceased author.

Résultats. – Huit patientes atteintes d'un cancer du col et trois d'un cancer de l'endomètre ont été identifiées. Le suivi médian était de 56 mois. La dose médiane de radiothérapie externe était 45 Gy. Toutes les patientes ont reçu une curiethérapie de bas débit de dose ou de débit pulsé. Sept patientes ont reçu une chimiothérapie concomitante. Le temps médian écoulé entre le diagnostic de la polyarthrite rhumatoïde et la radiothérapie était de 5 ans. Aucune patiente n'a souffert d'une toxicité immédiate digestive ou urinaire sévère. Une patiente a été atteinte d'une radiodermite de grade 3. Sept des patientes ont souffert d'une toxicité tardive et chez 9 % elle était sévère. Une patiente qui a souffert d'une manifestation systémique de la polyarthrite rhumatoïde au moment de la radiothérapie a été atteinte d'une sténose urétérale, une entérite et une myélite lombaire de grade 3.

Conclusion. – La radiothérapie pelvienne, dans un contexte de polyarthrite rhumatoïde, semble faisable, avec peut-être une augmentation légère de la toxicité tardive de bas grade par comparaison à l'irradiation d'autres localisations. Les patients souffrant de manifestations systémiques au moment de la radiothérapie pourraient être à risque accru de toxicité sévère.

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1. Introduction

The possibility to deliver radiotherapy in patients with connective tissue disease has been debated for a long time and remains a challenging issue for radiation oncologists. More particularly, rheumatoid arthritis, one of the most common connective tissue diseases, has been the subject of controversy in literature. Some reports showed increased radiation-induced toxicity for patients with rheumatoid arthritis while other studies did not report any significant difference compared to normal population undergoing therapeutic irradiation [1]. More generally, studies focusing on pelvic irradiation have suggested a higher risk of severe toxicity in patients with connective tissue disease [2]. Due to the scarce number of patients with connective tissue disease treated with ionizing radiation at curative doses, most reports included multiple connective tissue disease subtypes, with multiple irradiated anatomic sites. In this short report, we examined the outcome of patients with rheumatoid arthritis undergoing pelvic radiotherapy for gynecological malignancies at our institution, with special focus on safety concerns.

2. Materials and methods

2.1. Inclusion and exclusion criteria

The Gustave-Roussy Cancer Campus patient database was searched for patients diagnosed with rheumatoid arthritis and treated in the Radiation Oncology department between 1990 and 2015. Patients with histologically proven cervical or uterine endometrial malignancies and receiving an external beam radiation therapy as part of their curative intent treatment were included in this retrospective analysis. Patients who received vaginal vault brachytherapy only, who had primarily a metastatic disease, whose either primary treatment or follow-up was done in other institutions, who consulted Gustave-Roussy for a second opinion and those who were diagnosed with rheumatoid arthritis after treatment completion were excluded.

2.2. Data collection and statistical analysis

Charts were reviewed for age, histology, tumor characteristics, rheumatoid arthritis history and treatment, treatment details including radiotherapy technique, chemotherapy and surgery. Acute adverse events were defined as any toxicity occurring during and within 3 months after completion of radiotherapy. Later

events were considered as late toxicities. Toxicity scoring was done according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

3. Results

3.1. Patients and treatment

Eighty-seven patients with gynecologic malignancies treated with radiotherapy and diagnosed with rheumatoid arthritis were found. A total of 11 patients fulfilled the inclusion criteria. Median follow-up was 56 months. Patients and treatment characteristics are summarized in Table 1. Median age at diagnosis was 58 years (range: 36–80 years). Eight patients received a primary intent radiotherapy for radical treatment of cervical cancer. Two of them had undergone a coelioscopic para-aortic lymph node dissection as part of the primary staging. Three patients were referred for postoperative radiotherapy as adjuvant treatment of a uterine endometrial carcinoma after undergoing upfront total abdominal hysterectomy with bilateral salpingo-oophorectomy.

All 11 patients received a pelvic irradiation and, among them, three patients received an extended field irradiation including the pelvis and para-aortic lymph nodes area. A bidimensional conventional radiotherapy technique with orthogonal beams was used in three patients. Five patients received a three dimensional conformal technique and three patients were treated using an intensity-modulated irradiation technique. Median dose delivered by external beam radiation therapy was 45 Gy (ranging from 39.6 Gy to 56 Gy) and three cervical cancer patients received a boost to macroscopically involved pelvic lymph nodes, sequential and at 2 Gy per fraction in two cases and as an integrated boost to a total dose of 55 Gy in fractions of 2.2 Gy in one patient treated with intensity-modulated radiotherapy. Concomitant chemotherapy was delivered in seven patients, weekly cisplatin 40 mg/m² in six patients, and carboplatin/etoposide in one patient. Median number of cycles was 5 (range: 4–6 cycles).

All patients received a brachytherapy boost, using the vaginal mold technique. Patients with cervical cancer received an image-guided adaptive uterovaginal brachytherapy boost aimed at delivering 15 Gy to 90% of the intermediate risk clinical target volume, given with pulse-dose rate technique without exceeding 0.5 Gy per pulse to organs at risk in six out of eight cervical cancer patients and with low-dose rate technique in the two remaining patients. Patients with uterine endometrial cancer received a

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