Table of Contents

Original Articles

Cytomorphologic Spectrum of Hurthle Cell Lesions of Thyroid: A Study of 54 Cases .................................................................06
K.R. Anila, Nileena Nayak, Preethi Sara George, K. Jayasree

Rosai–Dorfman Disease – Five Years Retrospective Analysis from Tertiary Cancer Center ..............................................................11
K. Aradhana, B. Thejaswini, Shamsundar, R. Nanda, Usha Amritham, G.V. Giri

Lung cancer epidemiology among the Bahraini population, 1998–2011 ......................................................................................18
Najat Mohamed Abulfateh, Randah R. Hamadeh, Majida Fikree

Epidemiology of Colorectal Cancer in Iraq, 2002–2014 ....................................................................................................................23
Safauldeen Abdulrahman Al Dahhan, Faris H. Al Lami

Profile of High Grade Gliomas – A Single Center Experience ........................................................................................................27
Basharat Mujtaba Jan, Arif Hussain Sarmast, Abdul Rashid Bhat, Altaf Rehman Kirmani

Assessment of Sunitinib Alternative Prescription Schedules in Metastatic Kidney Cancer: A Study of 10 Cases ..........................33
Habib Diallo, Hasnae Alaoui Mhamdi, Salma Elouarzazi, Mohamed Fadi, Rhizlane Belbaraka

Human Papilloma Virus (HPV) in Sinonasal Papillomas and Squamous Cell Carcinomas: A PCR–based Study of 60 cases ..........37
Ambreen Beigh, Ruby Reshi, Sheikh Junaid, Mehnaz Sultan Khuroo, Summyia Farook

Cancer Statistics in Giresun Province, Turkey: a 12–Years Retrospective Review ........................................................................43
Ayşe Gül Çebi, Egemen Akgün, Tuncer Öztürk, Esin Avcı

Review Article

Risk Factors of Cancer in the United Arab Emirates ........................................................................................................................49
Hira Abdul Razzak, Alya Harbi, Wael Shelpai, Ahmad Qawas

Case Reports

Lymphoid Proliferation in Eyelid: A Primary follicular lymphoma case ..................................................................................................58
Deivy Cruzado–Sánchez, Walter Andree Tellez, Solon Serpa–Frias, Grisnery Maquera

Transanal Minimally Invasive Surgery (TAMIS), First in Kuwait: A Case Report ........................................................................61

Tumor Recurrence at Donor Site of Pectoralis Major Myocutaneous Flap with Tumor–free Primary Oral Carcinoma ..................64
Rakesh Kain, Suvashiis Dash

Vaginal Metastasis of Renal Clear–cell Cancer .................................................................................................................................67
Rehailia–Blanchard Amel, Morel Adeline, Rancoule Chiloé, He MingYuan, Magné Nicolas, Falkowski Sabrina

T cell Large Granular Lymphocytic Leukemia with Pulmonary Hypertension ................................................................................72
Sidra Khalid, Hamed Daw, Miriam Jacob, Megan Nakashima

Fatal Outcome of Recurrent Infantile Pelvic Desmoid Tumor Treated with Tamoxifene ..................................................................75
Lamiae Amaadour, Zineb Benbrahim, Othmane Zouiten, Nezar Bourdi, Youssef Lamrani Alaoui, Asmae El Mazzi, Nawal Hammam, Nawfel Mellas

Conference Highlights/Scientific Contributions

• News Notes .........................................................................................................................................................................................79
• Advertisements ................................................................................................................................................................................83
• Scientific events in the GCC and the Arab World for 2018 ........................................................................................................84
Corresponding Author: Dr. Rehailia-Blanchard
Amel Radiation Oncology Department, Institute de Cancérologie Lucien Neuwirth, 108 Bis, avenue Albert Raimond, 42270 Saint Priest en Jarez, France
Tél: +33 477 91 71 06, Fax: +33 477 91 71 97, Email: amel.rehailia-blanchard@icloire.fr

Case Report and Literature Review

Vaginal metastasis of renal clear-cell cancer

Rehailia-Blanchard Amel1, Morel Adeline2, Rancoule Chloé1, He MingYuan1, Magné Nicolas.1, Falkowski Sabrina3

1Dept. of Radiotherapy, Lucien Neuwirth Cancer Institute, Saint Priest en Jarez, France
2Dept. of Oncology, Curie Institute, Rene Huguenin Hospital, Saint Cloud, France
3Department of Oncology, CHU Limoges

Abstract

Background: Vaginal metastases originating from renal cancer remain a rare event, with less than 100 cases reported in the literature. The spreading mechanism is still under scrutiny. The tumoral bleeding often is a symptom revealing vaginal metastases.

Case: The present work reports patient case having vaginal metastasis of renal clear-cell cancer. The vaginal metastasis was treated by a 3-D conformational radiotherapy. Our experience is discussed with respect to an updated literature review concerning the medical management of vaginal metastasis related to kidney cancer.

Conclusion: In our case, a 15 Gy hypofractionated-radiotherapy is efficient to control bleeding on the vaginal metastases of the kidney cancer. To add up a 15 Gy hypofractionated-radiotherapy in 5 fractions is an option if bleeding is still present. The tolerance of the treatment is excellent and no side effects have been described.

Keywords: Vaginal metastases, Renal cell carcinoma, bleeding, radiotherapy

Introduction

Kidney cancer represents nearly 3% of all adult cancers(1). Approximately 30% of patients have a metastatic disease at the time of diagnosis. The most common metastatic sites were lung (50–60%); bone (30–40%); liver (28%); lymph nodes (15–30%); adrenal glands (10–15%) and brain (10–13%) (1). Among the unusual sites of metastasis, the vagina is a rare localization; only a little number of cases has been reported in the literature.

The tumoral bleeding is a symptom present in 6 to 10% of patients (2). Such hemorrhagic events may i) decrease quality of life, ii) require hospitalization, and iii) in extreme cases lead to death. The hemostatic radiotherapy has appeared relevant as a therapeutic strategy in palliative supportive care, being an indication in case of tumoral bleeding (2).

The present work reports on a 76-year-old Caucasian woman having a metastatic renal clear-cell cancer, with a vaginal invasion histologically confirmed. The vaginal metastasis was treated by a 3-D conformational radiotherapy. Our treatment is discussed with respect to an updated literature review concerning the medical management of vaginal metastasis related to kidney cancer.

Case description

The case of a 76-year-old woman was reported at the time of diagnosis. She has been followed at the University hospital of Limoges (France) since 2008 for a left kidney tumor discovered incidentally. A left nephrectomy allowed the histological diagnosis of clear-cell renal carcinoma grade 3 according to Furhman. This tumor was strictly intra renal and with a macroscopic invasion of renal vein; it was ranked pT3B in healthy margins. In October 2010 there was a local recurrence in the lodge of nephrectomy associated with lung metastases. According to the Motzer classification, the patient was ranked as belonging to the good prognosis group (normal rates of calcemia, LDH and hemoglobin and 100–Karnofsky index). In the absence of any contraindication regarding the use of angiogenesis inhibitors, the patient started a daily treatment of 37.5 mg Sunitinib, 4 weeks over a 6-week period. Due to hypertension and several episodes of epistaxis grade 3, the Sunitinib dose was eventually decreased to 12.5 mg.
At this dosage, the drug was tolerated. At 3 months, the CT (computed tomography) scan showed a progression in the lodge of nephrectomy. Sunitinib was therefore replaced with Sorafenib. From October 2010 to April 2011 the treatment had been continued with good tolerance.

In April 2011, the patient has metrorrhagia. A large lesion of the lower third of the anterior vagina wall was clinically observed. A complementary MRI (Magnetic Resonance Imaging) showed a probable malignancy origin of the lesion. The vaginal biopsy confirmed the diagnosis of metastatic clear-cell renal carcinoma. Regarding this clinical progression, Sorafenib was stopped and an Everolimus had been introduced. Regarding the recurrent bleeding, a complementary haemostatic and palliative surgical resection, no healthy margins, was performed in August 2011. In the meantime, the Everolimus treatment was continued without side effects and without iconographic progressive disease. In September 2012, a clinical progression of the lesion was observed, which was associated with a recurrent bleeding. The clinical examination showed a large lesion at the entrance of the vagina (Figure 1). An indurated lesion of the anterior vagina wall was palpated, which was responsible for a significant bleeding.

The biological tests allowed ascertaining an anemia grade 2. Before considering a haemostatic treatment, a pelvic MRI was performed (Figure 2).

The pelvic MRI showed a perineal mass, localized from the lower third of the vagina to the vulva, which was responsible for compressing the external urethral meatus and pushing the clitoris.

The importance of tumor size and her extension in depth did not allow brachytherapy. A 3–D haemostatic conformational radiotherapy was therefore performed. An external 15 Gy radiotherapy was achieved in 5 fractions via a linear accelerator rapidarc®, with an 18 MeV energy. During radiation sessions, Everolimus and all other drugs were stopped. The patient is currently treated with 25mg Sunitinib 2 weeks over a 3–week period. The follow-up one month after the end of that radiotherapy treatment has evidenced a 40% decrease of the vaginal metastasis, with a concomitant bleeding stop. The biological tests evidenced anemia grade 1.

Discussion

The vagina usually becomes a tumoral site by contiguity. Clear–cell adenocarcinoma of vagina remains rare and represents around 9% of primary vaginal tumors (3). In the uterus, the exposure to diethylstilbestrol (DES) is related to clear–cell adenocarcinoma of the cervix and
<table>
<thead>
<tr>
<th>Author</th>
<th>Age at diagnosis</th>
<th>Kidney</th>
<th>Vagina localization</th>
<th>Time to metastasis</th>
<th>Symptoms associated</th>
<th>Prognostic/Survival</th>
<th>Treatment of the vagina metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allard (3)</td>
<td>58</td>
<td>Left Kidney</td>
<td>Mid portion of the left sidewall</td>
<td>Synchronous metastasis</td>
<td>Bleeding</td>
<td>No data</td>
<td>surgery</td>
</tr>
<tr>
<td>Tarrazà (4)</td>
<td>77</td>
<td>Left Kidney</td>
<td>Apex of the vagina</td>
<td>Synchronous metastasis</td>
<td>Bleeding</td>
<td>No data</td>
<td>No data</td>
</tr>
<tr>
<td>Tarrazà (4)</td>
<td>65</td>
<td>Left Kidney</td>
<td>Anterior vagina wall</td>
<td>Synchronous metastasis</td>
<td>Bleeding</td>
<td>No data</td>
<td>No data</td>
</tr>
<tr>
<td>Tarrazà (4)</td>
<td>69</td>
<td>Left Kidney</td>
<td>Left sidewall</td>
<td>Synchronous metastasis</td>
<td>Bleeding</td>
<td>No data</td>
<td>No data</td>
</tr>
<tr>
<td>Tarrazà (4)</td>
<td>82</td>
<td>Right Kidney</td>
<td>Apex of the vagina</td>
<td>Synchronous metastasis</td>
<td>Bleeding</td>
<td>No data</td>
<td>No data</td>
</tr>
<tr>
<td>Bozacì (5)</td>
<td>19</td>
<td>No data</td>
<td>Posterior vagina wall</td>
<td>1 year</td>
<td>Bleeding</td>
<td>No data</td>
<td>Surgery completed by radiotherapy</td>
</tr>
<tr>
<td>San Miguel (6)</td>
<td>53</td>
<td>Right kidney, Invaded the renal sinus, Significant collateral circulation</td>
<td>Anterior vagina wall And the right vaginal cul de sac</td>
<td>Synchronous metastasis</td>
<td>Bleeding</td>
<td>No data</td>
<td>Hemostatic radiotherapy</td>
</tr>
<tr>
<td>Milathianakis (7)</td>
<td>67</td>
<td>Left kidney</td>
<td>Anterior vagina wall</td>
<td>2 years</td>
<td>Bleeding</td>
<td>No data</td>
<td>Chemotherapy and immunotherapy</td>
</tr>
<tr>
<td>Lialos (8)</td>
<td>69</td>
<td>Left kidney</td>
<td>Anterior vagina wall</td>
<td>Synchronous metastasis</td>
<td>Bleeding</td>
<td>Alive 24 months after the diagnosis</td>
<td>Hemostatic radiotherapy (30 Gy in 10 fractions)</td>
</tr>
<tr>
<td>Martinez Ruiz (9)</td>
<td>44</td>
<td>Right kidney with presence of thrombus in the renal vein without vena cava</td>
<td>Anterior vagina wall</td>
<td>No data</td>
<td>Bleeding</td>
<td>No data</td>
<td>Embolization and immunotherapy</td>
</tr>
<tr>
<td>Mendese (10)</td>
<td>53</td>
<td>Left kidney</td>
<td>Anterior vagina wall</td>
<td>Synchronous metastasis</td>
<td>No data</td>
<td>No data</td>
<td>Surgery</td>
</tr>
<tr>
<td>Present case</td>
<td>76</td>
<td>Left Kidney</td>
<td>lower third of the anterior vagina wall</td>
<td>3 years</td>
<td>Bleeding</td>
<td>Alive</td>
<td>Hemostatic radiotherapy and tyrosine kinase inhibitor</td>
</tr>
</tbody>
</table>

Table 1: Reports of renal cell carcinoma with vaginal metastases since 2004. See (4) and (5) that reported 68 cases for the 1983–1994 period and 22 cases for the 1994–2005 period, respectively.

Notes:
2. The second reference (Clinically significant bleeding in incurable cancer patients: effectiveness of hemostatic radiotherapy) is a general review about hemostatic radiotherapy.
vagina among young women. The required treatment is usually, when possible, surgery.

The vaginal metastases close to adenocarcinoma sites are, in 65% of cases, originated from cervix, endometrium, ovarian or colon cancers (3). Vaginal metastases originated from renal cancer are not without precedent but remain a rare event, with less than 100 cases reported in the literature (4,5). Table 1 reports new cases that have been identified after the last review (6).

A comprehensive analysis of all reported data concerning vaginal metastases of renal clear-cell cancer (Table 1) (3–10) highlighted clinical and therapeutic similarities. The clear-cell renal carcinoma metastases preferentially occur in the geriatric and menopaused populations.

The bleeding often reveals vaginal metastases. In this case, a symptomatic-treatment is proposed, namely hemostatic radiotherapy, embolization, or palliative surgery; joint treatments being possible as well.

The spreading mechanism is still under scrutiny. In most of cases, vaginal metastasis originated from left-sided renal tumors; the right-sided renal origin is a particularly rare event. This is well rationalized by angiography highlighting retrograde flow from the left renal vein to the left ovarian vein, which is followed by the ovarian filling and vaginal plexus (11). In those rare cases of right-sided renal origin, a retrograde flow from the inferior vena cava to the right ovarian artery appears as an alternative hypothetical spreading mechanism (11).

Our clinical case supported hematogenous spreading by retrograde flow from the left renal vein. The corresponding histology highlighted macroscopic renal vein invasion. This explanation emphasizes how crucial the renal pedicle clamping is, when performing the primary surgery.

To date vaginal metastasis does not appear correlated to poor survival prognosis. It must be stressed that when undifferentiated carcinoma or adenocarcinoma is detected in the vagina, the renal carcinoma relapse is possible. It was shown that such relapses can occur when nephrectomy has long been performed (up to 23 years after the primary surgery) (11,12). The rarity of this metastatic site does not justify a vaginal cytology in the follow-up of patient with renal clear cell carcinoma.

Hyofractionated radiotherapy is efficient to control bleeding on the vaginal metastases of the uterine cancer. To date, this technique is a valid therapeutic option (13,14). However, uterine cancer is considered as a radiosensitive cancer. Such data do not permit to predict the quality of response to radiotherapy for metastases of renal cancer and what kind of schedule is the most appropriated.

The radiosensitivity of tumor cells is measured in vitro by survival curves. The cell survival curve highlights a conventional splitting within the 1.8–2 Gy range. Kidney cancer is commonly accepted to be radioreistant because the survival fraction at 2 Gy is high in vitro. In case of radioreistance, it is thus possible to increase the dose per fraction, obtaining a better therapeutic response. For the patient case reported here, we chose a 15 Gy hyofractionated-radiotherapy in 5 fractions. An evaluation of the patient was planned a month after the end of the treatment. If the response to the treatment was assumed insufficient (important bleeding, anemia grade 2 and more) a new 10 fraction—irradiation up to 30 Gy was possible. The tolerance of the treatment was excellent and no side effects have been described. Lialos and al. (6) also treated the patient with a 30 Gy hyofractionated—radiotherapy in 10 fractions with a satisfactory efficacy.

In conclusion, 3-D haemostatic conformational radiotherapy has appeared an efficient therapeutic option for the treatment of hemorrhagic vaginal metastasis of renal cancer. Although the literature is modest and our experience with this case is limited, 15 Gy in 5 fractions or 30 Gy in 10 fractions has been an adapted treatment in this indication.

References
7. Métastases vaginales d’un carcinome à cellules rénales
   Urofrance (Internet). (cité 18 avr 2017). Disponible sur:

   MA, Skoufi G, Messinis IE. Vaginal metastasis from renal

   Vaginal metastasis of a clear renal cell carcinoma. Arch

10. Mendese GW, Ayvazian PJ, Li C. Renal cell carcinoma
    presenting as a perineal mass: case report and review of

11. Mulcahy JJ, Furlow WL. Vaginal metastasis from renal
    cell carcinoma: radiographic evidence of possible route of

12. Pruthi RS, Richman M, Derksen JE, Maygarden S. Stage T1
    renal cell carcinoma relapsing in the vagina 10 years after

    pelvic irradiation for palliation and life prolongation in
    patients with cancer of the cervix and corpus uteri. Gynecol

    radiotherapy in carcinoma of the uterine cervix. Int J
    Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet. sept