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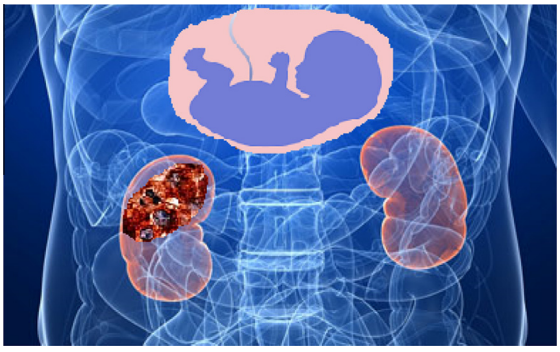
REVIEW

Review on renal cell carcinoma and pregnancy: A challenging situation

Hussein Khaled [a,*], Nasr Al Lahloubi [a], Noha Rashad [b]

[a] Department of Medical Oncology, National Cancer Institute, Cairo University, Egypt
[b] Department of Medical Oncology, Military Armed Hospital Caner Center, Cairo, Egypt

GRAPHICAL ABSTRACT



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ABSTRACT

Renal cell carcinoma is rarely diagnosed during pregnancy. Its management is a real challenge due to the sparse literature and lack of standard guidelines. In this situation, the diagnosis is often delayed as the clinical presentation might resemble other pregnancy-related disorders but it should be one of the diagnostic possibilities in women with recurrent or refractory urinary tract symptoms, renal pain, or mass that could be palpated. Diagnostic approach may include

* Corresponding author. Tel.: +20 122 215 1040; fax: +20 2 5252953.
E-mail address: khussein528@gmail.com (H. Khaled).

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ultrasound examination and sometimes magnetic resonance imaging. If localized, surgery would be the preferred line of treatment. Other treatment modalities, end results of treatment, and review of literature of this rare association will be presented.

Dr. Hussein Khaled is a Professor of medical oncology at the National Cancer Institute of Cairo University. He was the former minister of higher education of Egypt (2012), former vice president of Cairo University for post graduate studies and research (2008–2011), and the former dean of the Egyptian National Cancer Institute (2002–2008). Last year (2015), he won the State Recognition Prize for advanced technological sciences in the medical field. His research activities are focused mainly on bladder cancer (both biological and clinical aspects), breast cancer, and malignant lymphomas, with more than 150 national and international publications (total impact factor of 470, total citations of 1741, and h-index of 22).

Dr. Nasr Allahloubi is a Professor of medical oncology at the National Cancer Institute, Cairo University. He is a member of many international societies: ESMO, ASCO, ASH, EASO, and the Secretory of the Egyptian Universities Promotion Committees (EUPC, Committee number 83). He has many publications and national educational presentations and international poster in SABCS, ASCO, and ESMO. He is leading the scientific meetings of the medical oncology department. He is the MD program instructor and a member for external evaluation committee for the MD examination. He is also a member of the Higher Committee of Medical Specialties; Egyptian Fellowship Board; Medical Oncology; and Ministry of Health.

Dr. Noha Rashad is a medical oncology specialist-Maadi Armed Forces Medical Compound, Oncology Hematology Hospital. She passed the final examinations for MD degree of medical oncology and be a certified member of ESMO (2011).

Introduction

Cancer diagnosis during pregnancy is a rare event. An oncologist can encounter this case in one of two clinical scenarios; either cancer is diagnosed for the first time in a pregnant female or incidental pregnancy occurs during cancer treatment.Treatment of cancer during pregnancy represents a medical dilemma. As pregnant women are usually excluded from clinical trials and due to the rarity of the event, no solid data can support the treatment decision in such setting [1]. Also, the impact of abortion or keeping pregnancy till labor, on prognosis of cancer together with the safety and efficacy of cancer treatment on the maternal and fetal health is not known in many occasions [2].

The landscape of renal cell carcinoma management has changed during the past few years, but surgery remains the main stay modality, and currently there is no role for adjuvant therapy. New targeted agents with proven efficacy in advanced, or metastatic renal cell carcinoma have been developed. However, the effect of these new agents on fetal and maternal outcomes is poorly studied [3].

The aim of this article was to revise the medical literature for data pertinent to this group of patients, aiming to provide answers to questions regarding management of these patients.

Epidemiology and risk factors

Renal cell carcinoma represents about 3% of solid tumors in adults with a slight male predominance [4]. An increase in incidence has been observed during the last two decades, with reports of downward shift of tumor stage and size in many clinical series [4]. Obesity, smoking and hypertension are established risk factors for renal cell carcinoma [5]. High parity among women and other reproductive and hormonal factors has been studied as potential risk factors, but no direct causal effect is evident up till now [4,5]. Since 1980s, steroid receptors were found on normal and cancerous renal cell tissue. Estrogen can induce renal cell carcinoma in laboratory mice. Adipose tissue in obese women is a source of estrogen that may play a role in increasing the risk for RCC [6]. Treatment with progesterone was explored in the past for treatment of metastatic RCC, but abandoned due to unproved efficacy [7]. Accordingly; it was assumed that a possible correlation between hormonal factors and RCC development exists, although the underlying mechanism is not fully understood.

During pregnancy, estrogen and progesterone reach to a high peak. High parity ($\geqslant 5$ pregnancies lasting for more than 4 months) was associated with almost doubling of risk for RCC in comparison with nulliparous women in many reports [8–10]. However, other studies did not show the same association [11,12]. Only one trial showed a strong association for clear cell adenocarcinoma subtype, although the same trial did not show association with live births [13].

A meta-analysis including 14 studies (5 cohort studies, one nested case control, and 8 case control studies) that were published in 2013 concluded that ever parity, i.e. with a history of at least one pregnancy and increased parity numbers are associated with an increased risk of kidney cancer [14].

Oral contraceptives were associated with risk reduction in some series [12], and age of menarche, hysterectomy and age