Bilateral multifocal renal oncocytoma in pregnancy

Schalk W. Wentzel,
Lodewikus P. Vermeulen
Department of Urology, Universitas Academic Hospital and Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa

Abstract

Renal oncocytomas are the most common benign solid renal tumor, accounting for 3-7% of renal neoplasms. Oncocytomas are multifocal in 2-12% and bilateral in 4-14% of cases. Multifocal bilateral oncocytomas represent only 1.4% of renal cases. We present an extraordinary case of a patient with multifocal bilateral renal oncocytomas during pregnancy. An electronic literature search revealed fewer than 30 reports of on cases of bilateral multifocal renal oncocytomas, none of them occurring in pregnancy. The management of this patient differed from the recommended guidelines for renal masses suspected to be malignant because elective caesarean section and nephrectomy in the second trimester was refused.

Introduction

Oncocytomas have been reported in multiple organs, including the kidney, thyroid, parathyroid, salivary and adrenal glands. Oncocytoma is the most common benign solid renal tumor, accounting for 3-7% of all renal neoplasms and it usually occurs unilaterally. Oncocytomas are multifocal in 2-12% and bilateral in 4-14% of cases, while multifocal bilateral oncocytomas represent only 1.4% of renal cases.

An electronic literature search yielded fewer than 30 reports of cases of bilateral multifocal renal oncocytomas, none of them occurring in pregnancy. However, several cases of renal cell carcinoma (RCC) in pregnancy have been reported. Co-existence of RCC and oncocytomas in the same lesion or elsewhere in the kidney occurs in 7-32% of cases. A possible association between cystic kidneys and oncocytomas has also been suggested in the literature.

We present an extraordinary case of a patient with multifocal bilateral renal oncocytomas during pregnancy.

Case Report

A 33-year-old female (gravida 2, para 1, gestation 24 weeks) presented to the Department of Obstetrics and Gynecology, Universitas Academic Hospital in Bloemfontein, South Africa, with gestational hypertension, chronic renal failure and hypochromic normocytic anemia. She was referred to the Department of Urology. Abdominal ultrasound revealed bilateral multifocal renal tumors. The patient had no history of previous medical problems and no family history of renal disorders. She was a non-smoker and had had an uneventful first pregnancy.

On physical examination, the patient’s blood pressure was 145/105 mmHg and she was clinically anemic. Obstetric signs for gestation (24 weeks at the time of referral) were normal. Proteinuria was detected by means of urine dipstick test and confirmed by 24-h urine analysis. Urine microscopy and culture were negative. Abnormal hematologic and biochemical laboratory results are shown in Table 1. Findings of liver function tests and clotting profiles were within normal limits.

Abdominal magnetic resonance imaging (MRI) revealed three tumors (diameter range 1.3-4 cm) in the right kidney, and one tumor (diameter 5 cm) in the left kidney (Figure 1). Color Doppler ultrasound was negative for tumor thrombus in the renal veins and inferior vena cava. Ultrasound-guided fine-needle aspiration cytology of the renal masses was non-diagnostic.

With a provisional diagnosis of bilateral renal cell carcinoma, the patient’s team of physicians advised caesarean section at 28 weeks gestation with simultaneous right radical and left partial nephrectomy. Right partial nephrectomy was not possible due to a central hilar tumor. After counseling and discussion of all risks involved, including those to the fetus, the patient’s parents refused surgery. The option of elective caesarean section at 34 weeks gestation followed by renal surgery four weeks later was accepted by the patient, who indicated that she was willing to risk metastatic disease in the event of the tumors being malignant. A healthy baby boy was delivered by caesarean section.

Four weeks later, a right radical nephrectomy and left partial nephrectomy were performed. All the lesions had histological features compatible with oncocytoma. Immunohistochemical stains were negative for CD10 and vimentin, but strongly positive for CK7. Ultrastructural evaluation demonstrated cells densely packed with mitochondria. Although CK7 positivity would favor chromophobe renal cell carcinoma, the histological and ultrastructural features were consistent with oncocytoma (Figures 2-4). The normal renal parenchyma had features typical of chronic interstitial nephritis.

The patient was examined for signs of Birt-Hogg-Dubé syndrome, but there were no abnormal dermatological features and computed tomography of the chest showed no pulmonary cysts. The patient had an uneventful recovery and her serum creatinine stabilized at 490 μmol/L (normal range 60-100 μmol/L). Although dialysis was not required, she was referred to the Division of Nephrology for further evaluation of the interstitial nephritis.

Discussion

The presence of bilateral renal masses poses a difficult diagnostic and therapeutic challenge. Although renal oncocytomas are generally believed to have no metastatic potential, surgical resection is still indicated. Nephron-sparing surgery in the form of partial nephrectomy or tumor enucleation is recommended.
Cases of renal oncocytoma co-existing with RCC in the ipsilateral or contralateral kidney have been documented. A case of synchronous RCC has also been reported in a patient with bilateral oncocytomas. Renal oncocytoma may be capable of malignant transformation or behavior. Lieber et al. reported that 4 (14.3%) of 28 patients with grade II oncocytoma developed metastases.

The first case of bilateral multifocal renal oncocytomas was reported in 1982 and the term renal oncocytomatosis was used. Although most cases appear to be sporadic, familial renal oncocytomatosis has been described. The syndrome exhibits an increased propensity for bilaterality, multicentricity and onset at an early age. Genetic factors involved in the development of this syndrome have not yet been defined. Multiple and bilateral oncocytomas also occur in Birt-Hogg-Dubé syndrome (BHDS). The BHD1 gene responsible for this syndrome has been mapped to chromosome 17p11.2 and is transmitted in an autosomal dominant pattern. The clinical characteristics of BHDS include cutaneous manifestations and pulmonary cysts or a history of spontaneous pneumothorax. Several different types of renal tumors are also part of the clinical features of BHDS. The skin lesions of BDHS only appear in the third to fourth decade of life. Pulmonary cysts occur in 89% of patients. Our patient presented with only oncocytomatosis. Due to financial constraints, genetic investigations were not performed.

None of the reported cases of oncocytomatosis occurred during pregnancy, although we located approximately 80 cases of renal tumors during pregnancy. The principles of management of renal tumors during pregnancy could be applied in our case, as the true diagnosis was revealed post-operatively and, for all practical purposes, the patient was managed as a case of RCC.

RCC is the most common tumor reported during pregnancy (50%), followed by angiomyolipoma (23%). Diagnosis is usually incidental during pregnancy. Management problems in this situation include: which imaging studies to obtain, the timing of surgery, the operative technique, and fetal care. Ultrasonography is the safest imaging modality for diagnosing a renal mass in pregnancy. For more accurate staging, MRI is advisable, as in pregnancy this is the least harmful.

Radical nephrectomy is recommended for solid renal masses. Optimal management depends on the trimester of pregnancy during which the tumor is discovered. Loughlin recommended surgery in the first or third trimester. If discovered during the second trimester, surgery should be delayed until after 28 weeks of gestation when the fetal lungs have matured. In the third trimester, renal sur-

gery should be performed at delivery. Surgery may be postponed until after delivery if the renal mass is discovered near term. However, delaying surgery can be a potential threat to the patient, allowing cancer cells to spread or tumor invasion to adjacent structures. This is particularly true especially when the tumor is extensive at diagnosis. RCC has an estimated doubling time of 300 days (approx. 10 months).

Potential morbidity is associated with frank hematuria, internal bleeding or thrombosis. Therefore, immediate nephrectomy, irrespective of the stage of pregnancy, has been recom-

Table 1. Patient’s abnormal laboratory findings.

| Investigation                        | Result     | Normal range       |
|--------------------------------------|------------|--------------------|
| Serum urea                           | 9.9 mmol/L | 2.6-7.0 mmol/L     |
| Serum creatinine                     | 269 μmol/L | 60-100 μmol/L      |
| Hemoglobin                           | 9.8 g/dL   | 12.1-16.3 g/dL     |
| Mean corpuscular hemoglobin (MCH)    | 26.4 pg    | 27.3-32 pg         |

| 24-h urinalysis                      |            |                    |
|--------------------------------------|------------|--------------------|
| Protein                              | 0.98 g/24 h| 0.00-0.15 g/24 h   |
| Calcium                              | <1.0 mmol/24 h | 2.5-7.5 mmol/24 h |
| Creatinine clearance                 | 29.6 mL/min| 75-115 mL/min      |

Figure 1. Magnetic resonance imaging: abdomen coronal view, showing bilateral renal tumors.

Figure 2. Macroscopic appearance of the right kidney with multiple tumors.

Figure 3. Overview shows a tumor with a nesting growth pattern, eosinophilic cytoplasm and round nuclei (Haematoxylin and Eosin 10x).

Figure 4. The tumor cells have granular eosinophilic and round nuclei (Haematoxylin and Eosin, high power 100x magnification).
If confronted with a renal tumor during pregnancy, the patient and physicians face difficult ethical issues. The opinions of the parents and the multidisciplinary team must be taken into account when establishing a management plan. The influence of pregnancy hormones on tumor growth must also be considered. Growth of angiomylipomas in pregnancy has been described, although we found no reports concerning the influence of pregnancy hormones on oncocytomas. The association between renal oncocytomas and interstitial nephritis also remains unresolved.

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