Bladder cancer in the second trimester of pregnancy: tough decisions. A case report with review of the literature

Mohamed Amine Lakmichi, Reda Zehraoui, Zakaria Dahami, Said Mohamed Moudouni, Amal Bassir, Abderaouf Soumani and Ismail Sarf

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Abstract: We report a rare case of a patient presenting with a nonmuscle invasive papillomatosis transitional cell carcinoma of the bladder in the second trimester of pregnancy. We describe the management dilemmas encountered and the challenging treatment option selected to optimize outcome for the patient and infant. Close collaboration between urologists, obstetricians and medical colleagues is needed for optimal, safe and effective management of bladder tumours during pregnancy.

Keywords: orthotopic neobladder, pregnancy, radical cystectomy, transitional cell carcinoma

Introduction

Malignant tumours are rare in pregnancy and the overall incidence is around 2.35/10,000. The most common tumour in pregnancy is a malignant melanoma, followed by cancer of the cervix and breast [Mitra *et al.* 2003]. A literature review failed to find any evidence that pregnancy has deleterious effects on the incidence or clinical course of malignancy compared with that in nonpregnant women of reproductive age, except in the case of malignant melanoma [Mitra *et al.* 2003]. Urological tumours are very uncommon in pregnancy but they represent particular problems in diagnosis and management. The authors report a new case of bladder cancer in the second trimester of pregnancy.

Case history

A 28-year-old nonsmoking nulligravid woman presented to the emergency department with the complaint of painless gross haematuria for 2 days. During urological consultation, the patient reported no prior episodes of gross haematuria but a significant history of chronic nocturia and urinary frequency. She denied any history of urinary tract infections, nephrolithiasis or other genitourinary complaints. She had no history of tobacco use and no occupational or chemical exposure. She did not have dysuria, fevers, chills, nausea, vomiting, flank pain or weight loss.

On physical examination she voided wine-coloured urine with small clots. The remainder of the physical examination was otherwise unremarkable. Recent routine blood tests, including haemoglobin, haematocrit and coagulation studies, were within normal limits. Her urinalysis revealed microscopic haematuria and was otherwise unremarkable.

An ultrasound scan revealed multiple space-occupying lesions within the bladder, suggestive of bladder tumours. The kidneys were normal in appearance. A cystoscopy confirmed multiple papillary tumours, approximately 10–12 mm in size, of the posterior and lateral walls of the bladder. The trigone and the bladder neck were not involved, bilateral orifices had clear efflux of urine and there were no other noted mucosal lesions.

Complete transurethral resection (TUR) of the tumours was performed under general anaesthesia and sent to pathology. Histological examination demonstrated a grade 2 transitional cell carcinoma (TCC) with no muscle invasion (stage pTa). A second TUR was considered since multiple tumours were present. Four weeks later, a second look cystoscopy was performed demonstrating early recurrent bladder tumours located in the vault of the bladder, approximately less than 10 mm in size. The tumours were resected *en bloc*. Then, resection of the former resected sites was

Correspondence to:

Mohamed Amine Lakmichi, PhD
Assistant Professor,
Urology Surgeon,
Urology Department,
University Hospital
Center Mohammed the
VIth, Faculty of Medicine
and Pharmacy, Cadi
Ayyad University, No. 2,
Avenue Menara, Bab Jdid,
Marrakesh, Morocco
amintakmichi@yahoo.com

Reda Zehraoui
Zakaria Dahami, PhD
Said Mohamed Moudouni, PhD
Urology Department,
University Hospital Center
Mohammed the VIth,
Faculty of Medicine and
Pharmacy, Cadi Ayyad
University, Marrakesh,
Morocco

Amal Bassir, PhD
Abderaouf Soumani, PhD
Obstetrics and Gynecology
Department, University
Hospital Center
Mohammed the VIth,
Faculty of Medicine and
Pharmacy, Cadi Ayyad
University, Marrakesh,
Morocco

Ismail Sarf, PhD
Head of the Urology
Department University
Hospital Center
Mohammed the VIth,
Faculty of Medicine and
Pharmacy, Cadi Ayyad
University, Marrakesh,
Morocco

performed. The final pathology revealed a grade 2 TCC with no muscle invasion (stage pTa). No tumours were found in anterior sites of the resection and no carcinoma *in situ* was noted on the edges of the resection areas in both pathology exams.

Intravesical bacille Calmette-Guérin (BCG) immunotherapy was administered in a maintenance schedule after patient consent was obtained. She developed further recurrences after the first six BCG bladder instillations. Then, contact was lost with the patient, despite multiple calls.

Eight months later, the patient presented at 24 weeks' gestation with gross haematuria. Renal ultrasound scan showed moderate right hydronephrosis and a dense irregular bladder mass with a monochorionic monoamniotic pregnancy. Abdomen and pelvic MRI scan was performed and demonstrated a large bladder tumour occupying the anterior, lateral and posterior walls (Figures 1 and 2). Pelvic lymph nodes did not appear to be involved. The upper urinary tract was unremarkable except for moderate right hydronephrosis. Cystoscopy showed a large papillary mass occupying the whole bladder mucosa, but no involvement of the bladder neck and urethra was noted. Following discussion with the patient, her family, urologists and the obstetrician, it was decided to leave further management until after delivery because treatment would involve a radical cystectomy. Apart from occasional haematuria there were no antenatal problems. Oral iron therapy was given.

The patient was admitted to the labour ward during the 33rd week of pregnancy and later had a caesarean section due to failure to progress in labour. No particular technical difficulties were encountered during the caesarean section from the large bladder tumour. The patient's postnatal period was uneventful.

After further discussion with the patient and her family about treatment options, the patient decided to undergo anterior pelvectomy with orthotopic neobladder. She did not require any additional hospitalizations or need transfusions while waiting for surgery. Four weeks after delivery and under general anaesthesia, she had an open anterior pelvectomy with conservation of the ovaries and pelvic lymph node dissection through the same caesarean section incision.

Figure 1. (T1) Magnetic resonance imaging of the abdomen and pelvis (coronal section): bulky bladder tumour.

Figure 2. (T2) Magnetic resonance imaging of the abdomen and pelvis (coronal section). Note the 24th week's pregnancy.

Urinary diversion was a Camey Neobladder II. The postoperative course was uneventful.

Breast feeding was avoided for 1 week after surgery and milk expressed during that time was discarded. Final histopathology of the removed tissue showed the papillary TCC of the bladder, grade 2, stage pTa with free margins. The bladder neck was tumour free as were the low ureters and lymph nodes.

After surgery, the patient was followed up every month during the first 6 months, then every 3 months until 18 months (the last follow up before this publication). The follow up consisted of a clinical examination and blood tests. However, an

abdominopelvic CT scan was performed every 6 months. The whole follow up was uneventful. No pelvic recurrence was shown on the CT scan and the kidneys were functioning normally. The infant is thriving at 18 months of age.

Discussion

Bladder cancer is rare in pregnancy, with one review identifying only 27 cases of nonbilharzial bladder carcinoma in pregnant women [Spahn *et al.* 2005], 74% presenting with TCC. Five patients had muscle-invasive tumours. However, in the general population, more than 90% of bladder cancers are TCCs and more than 70% of all newly diagnosed bladder cancers are superficial. Around 80–90% of patients with bladder cancer present with painless haematuria. In these women, delayed presentation is common because urinary symptoms in pregnancy are often ignored and haematuria mistaken for vaginal bleeding. Thus, examination is often performed to exclude placenta praevia, abruptio placentae or retained products following abortion or miscarriage [Mitra *et al.* 2003]. When recognized as haematuria, complete evaluation should be conducted and bladder cancer considered in the differential diagnosis. Although cystitis is the most common cause of haematuria in pregnancy [Choate *et al.* 1964], full investigation is needed if it does not respond to the appropriate medication. Catheterization of the bladder may be necessary if the source of the bleeding remains in doubt. Although bladder cancer is rare in pregnancy, frank haematuria should be treated with a high index of suspicion. Bladder ultrasonography could be useful, but in one study only half of the tumours were identified by ultrasonography in 27 pregnant women with bladder cancer [Spahn *et al.* 2005]. Flexible cystoscopy under local anaesthesia is considered the most useful test in evaluating haematuria in pregnancy. TUR of the bladder tumour under regional or general anaesthesia can be performed at any time during pregnancy [Shrotri and Ross, 2008]. In pregnant women, bladder cancer staging should be performed using MRI rather than CT scan to avoid fetal X-ray exposure.

Treatment of a low-grade TCC of the bladder which occurs during pregnancy can usually be deferred until after delivery. Most cases of TCC during pregnancy are superficial and can be treated endoscopically. Although superficial

bladder carcinoma is transurethrally resected alone, outcome and prognosis are good [Spahn *et al.* 2005]. There are no reported cases in the literature about the instillation of mitomycin C for bladder cancer during any stage of pregnancy. One pregnant patient has been given intravesical BCG for bladder carcinoma *in situ* [Wax *et al.* 2002]. In the case of high-grade muscle invasive bladder cancer, delaying treatment until the infant is delivered at term would necessitate a high risk of disease progression and poor prognosis for the mother.

Fortunately, in our case, because the progress of low-grade nonmuscle invasive bladder cancer is slow radical cystectomy could be carried out after an early delivery. Our patient was completely aware of all the medical risks and after long discussions she decided to maintain her pregnancy until delivery of a viable premature baby was possible. After delivery, a compromise was reached on discussion with the patient, her family, the urology team and the obstetrician and radical surgery performed.

Limited experience has resulted in a paucity of information on the optimum management of pregnant women with cancer. However, reports of single cases, or small series, highlight the difficult decisions needed and the potential conflict between the management of the tumour and the avoidance of harm to the fetus, as illustrated in our case. Compromise may be necessary and decisions need to be taken based on limited knowledge, which often presents conflicting viewpoints and recommendations [Brendan *et al.* 2007]. To our knowledge and throughout the literature, none of the pregnant women with bladder cancer had anterior pelvicotomy and orthotopic bladder replacement shortly after delivery.

Finally, close collaboration between urologists, obstetricians and medical colleagues is needed for optimal, safe and effective management of bladder tumours during pregnancy.

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