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A rare occurrence of urinary bladder carcinoma in pregnancy

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Abstract
The incidence of malignant tumors in pregnancy is reported as 2.35 cases every 10000 pregnancies. Of these, urological malignancy are particularly uncommon. Our patient was diagnosed with bladder carcinoma in pregnancy at 8 weeks of gestation. The tumor was resected in the early second trimester and intravesical Bacille Calmette-Guerin (BCG) was administered after the histopathological confirmation of the diagnosis. Regular follow ups were conducted for pregnancy and evaluation of bladder pathology. Patient had an uneventful full term vaginal delivery and postpartum course. With limited evidence in literature, there are no established guidelines to manage this rare malignancy in pregnancy. Here we describe the dilemmas and challenges faced for optimization of the wellbeing of both the mother and the baby. The close collaboration between the oncosurgeon, urologist and obstetrician and the involvement of the patient and her family resulted in a successful outcome.

Keywords: Urological malignancy, bladder carcinoma in pregnancy, intravesical BCG

Introduction
The World Health Organization has reported that almost 830 women die daily as a complication during antenatal period and childbirth [1]. Some pregnancies are at increased risk of complications due to the preexisting health conditions and some pregnancies become high risk as they progress due to the threat to the health or life of the mother along with the fetus. We report one such rare and challenging case of management of a patient diagnosed with a rare urological malignancy in first trimester of pregnancy.

Case History
A 26-year-old primigravida visited us at outpatient clinic at 11.5 weeks gestation for second opinion as she was advised termination of pregnancy for a recently diagnosed bladder tumor. She gave a history of painless hematuria a month prior to conception when she was treated for a urinary tract infection. She had a repeat episode of hematuria at 8 weeks gestation when an ultrasound had reported a 4.0 x 3.4 x 2.2 cms mass within the bladder. There were no associated symptoms of burning micturition, fever, flank pain, nausea, and vomiting or weight loss. She had no history of tobacco addiction or occupational and chemical exposure. There was no family history of any malignancy. Before making a recommendation, the patient underwent routine investigations that included a hemogram, renal function tests and coagulation studies which were within normal limits. Her urine examination showed hematuria (100-120 RBCs/hpf) with no malignant cells seen on cytology.
A repeat ultrasound confirmed the polypoid mass in posterior wall of bladder with vascularity. Dual marker revealed a normal NT scan with screen negative for trisomy 21, 13 and 18.
In a joint consultation with urology and oncology colleagues, the patient was explained about the high suspicion of bladder carcinoma and need for urgent management. She was presented with the following options making her understand the associated risks with each.

1. Continuing the pregnancy with simultaneous management of bladder mass
2. Continuing the pregnancy and treating the bladder condition in the postpartum period
3. Termination of the pregnancy followed by immediate management of the bladder mass

Patient was determined to continue pregnancy and she chose the first option accepting the need for immediate surgical management followed by immunotherapy for her condition and the risks of miscarriage, preterm birth and hemorrhage associated with her pregnancy.

At 13 weeks gestation, she underwent a cystoscopy under general anesthesia and the solid vascular tumor was resected from left posterior wall of bladder. Histopathology diagnosed a high grade papillary urothelial carcinoma, WHO Grade III, with non-invasion of the lamina propria and a TNM staging Stage Ta (high grade). This was followed by the instillation of intravesical Bacille Calmette-Guerin (BCG) immunotherapy once every week for six weeks as per the standard guidelines.

Intravesical BCG is used as a biological response modulator and is Category C drug for which an additional consent for administration was taken after discussing its use with patient and family members. Post immunotherapy, antenatal Magnetic Resonance Imaging was undertaken in lieu of cystoscopy. MRI revealed no residual abnormal wall thickening or mass in the posterior wall or elsewhere in the bladder. Monthly urine cytology and ultrasound assessment of the bladder were performed for evaluation of her condition.

The antenatal course was uneventful in the second and third trimesters. Anomaly scan, fetal 2D Echo, growth scan and near term sonography were all normal. Patient went in spontaneous labor at 38.6 weeks and delivered 3.3 kgs baby vaginally with no intrapartum and postpartum complications. She had regular visits post-delivery and a year later there was recurrence of the tumor. The mass was resected again followed by six sessions of intravesical BCG therapy. Presently she has a complete remission since more than a year but still continues to have routine follow ups every three months.

Discussion

The overall incidence of malignant tumors in pregnancy is one to two cases every 1000 pregnancies [2]. The most common cancers associated with pregnancy are gynecological, breast, hematological and dermatological [3]. Urological tumors are extremely uncommon in pregnancy of which bladder tumors are rare [4].

The most common risk factors are cigarette smoking, which increases the risk of developing bladder carcinoma by four to seven times, followed by the occupational hazard of exposure to aromatic amines used in various chemical industries. Chronic bladder infection, long standing indwelling catheter, bladder calculi or genitourinary tuberculosis can be the predisposing factors. Pelvic irradiation as a treatment for other pelvic malignancies can be the iatrogenic cause leading to bladder carcinoma years later. A genetic predisposition may exist in young patient with no other risk factors.

The most common presenting symptom of bladder carcinoma is painless hematuria. Its incidence in a patient with gross hematuria is 20% and with microscopic hematuria is 2%. Bladder irritation symptoms of urinary frequency and urgency can occur in patients with bladder carcinoma in situ. Obstructive symptoms like decreased force of stream, intermittent stream and incomplete voiding are seen if the tumor is situated near the urethra or the bladder neck [5]. Thus, we can see that our patient had this uncommon tumor with painless gross hematuria of one episode and presence of microscopic hematuria without any predisposing conditions.

In 2005, Spahn reported three cases of bladder carcinoma during pregnancy and presented a literature review of 27 cases underlining the rarity of the condition [6]. In this series 81% patients presented with hematuria initially mistaken as vaginal bleeding in 22%. Ultrasound could identify the lesion in just half the number of patients suggesting that any doubtful bleeding episode in pregnancy should be assessed with utmost care.

Our patient was evaluated at the first episode in pregnancy which led to the early diagnosis. The objectives to treat the superficial, nonmuscle-invasive bladder cancer are to eradicate the existing pathology, prevent the recurrence and progression of the disease.

Transurethral resection of the bladder tumor is the preferred initial step followed by intravesical instillations of various chemotherapeutic agents including BCG, mitomycin, doxorubicin or thiotepa. Of these BCG is the preferred drug over others since its introduction in 1976. The exact mechanism of action is unknown but accepted theory is that BCG stimulates an immunological response in the form of local inflammatory reaction which subsequently leads to shedding of the tumor cells thereby reducing the rate of disease progression [7]. The systematic review and meta-analysis of intravesical therapy for the treatment of nonmuscle invasive bladder cancer published in 2017 concluded BCG to be the only agent associated with decreased recurrence as well as decreased progression risk of the disease [8]. Due to the rarity of this event in pregnancy, there is lack of sufficient literature with each case having to be individualized to assess benefits and risks. A review article on the treatment of different cancers in pregnant women suggests that pregnancy termination will not alter the prognosis of the patient or the biological behavior of the tumor [9]. An analysis of obstetric and neonatal outcomes in 215 patients with malignancies in pregnancies had 56.7% patients initiating targeted treatment during pregnancy with no increase in the incidence of congenital malformations.

There was increased prevalence of preterm labor with 51.2% neonates needing intensive care mainly due to prematurity [10]. Hence, it is our duty to comply the choice of the women after counselling her with the targeted therapies and possible associated favourable and unfavorable outcomes.

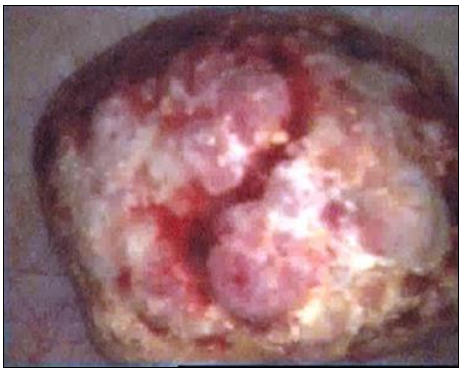

Fig 1: Cystoscopic appearance of bladder tumor

Conclusion

Management of bladder malignancy in pregnancy is complicated as there is no recommended strategy due to rarity of such cases. In addition to the risk of the primary disease there exists risks of treatment for the pregnant woman and her fetus. It is hence important to individualize management in each case with the involvement of the patient and respect for her decision. In the situations of dire consequences, maternal wellbeing should be accorded utmost priority. Such patients need a multidisciplinary approach, access to maternal and neonatal intensive care units with high quality super specialty care to give them the best possible outcomes.

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