Stage 1B cervical cancer in a pregnant woman at 25 weeks of gestation

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Summary

Cervical cancer associated with pregnancy is rare (0.05%), although it is the most frequently diagnosed malignancy in pregnant women. We present the case of a 28-year-old woman at 25 weeks of gestation diagnosed with Stage 1B cervical cancer. Treatment was delayed until fetal maturity, and an elective cesarean section was performed at 33 weeks' gestation, followed by a total hysterectomy preserving the ovaries, and a pelvic lymphadenectomy. A review of the literature on the treatment of cervical cancer during pregnancy relevant to the case described is also presented.

Key words: Cervical cancer; Pregnancy; Hysterectomy; Delay in treatment.

Introduction

Cervical cancer is the malignancy most frequently diagnosed in pregnant women [1-4]. Nevertheless, cervical cancer associated with pregnancy is rare, diagnosed in only 0.05% of pregnant women [5]. Because of this low frequency, it is difficult to establish a clear set of guidelines for treatment, a circumstance further complicated by the pregnancy and the woman's preference for continuing it or terminating it. Until recently, the usual recommendation was to abort the pregnancy if diagnosis occurred before 20 weeks of gestation, and to delay treatment until fetal maturity if the diagnosis occurred during the second half of the third trimester. The main problem lies in the management of cervical cancer diagnosed between the end of the second trimester and the beginning of the third. There are published studies showing no negative effect of pregnancy on the progression of the disease during this period [6-9]. Consequently, delaying treatment in these women is acceptable as long as the woman is willing to accept the risk, and it can be demonstrated that the prognosis and risk of relapse for cervical cancer is not significantly high. Another element to take into consideration is that the stage at which the disease is diagnosed may alter its management, especially in advanced cases in which delaying treatment may have a significant impact on the prognosis.

We present the case of a pregnant woman in whom Stage 1B cervical cancer was diagnosed at 25 weeks gestation, and a discussion of the management of this case in light of the recent literature.

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Case Report

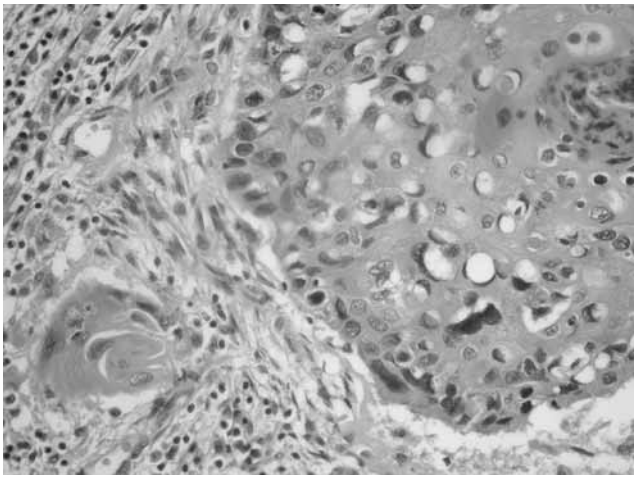
A 28-year-old woman at 25 weeks of gestation was referred to our hospital presenting with cervicovaginal cytology results indicating a diagnosis of squamous cell carcinoma. She had no family history of cancer. Her gynecological history included a conization performed in her country of origin (Ecuador) in 1999, normal cytology results until 2003, and irregular menstrual cycles prior to pregnancy. She had had three prior pregnancies, two of which ended in a normal delivery and one in a spontaneous abortion that did not require curettage. The pregnancy in question was followed starting at 20 weeks, when the above-mentioned cytology was performed because no cytology results were available for the previous three years.

On examination the external genitalia were normal. Through a vaginal speculum a white lesion 1.5 cm in diameter was observed on the anterior cervical labium, while the vagina was normal. In a colposcopy performed with prior application of acetic acid, the above-mentioned lesion was observed, and the colposcopic image showed a variegated exophytic leukoplasia. The cytology was repeated, a cervical smear taken for HPV testing, and a colposcopically directed biopsy was performed. On vaginal examination the cervix was found to be closed, of normal length, and mobile. Rectal examination ruled out the presence of parametrial involvement.

The cytology results showed high-grade SIL with cells suggestive of squamous cell carcinoma. The result of the microarray-based HPV test was negative, and the biopsy revealed a moderately differentiated squamous cell carcinoma (Figure 1). Since it was difficult to determine how invasive the lesion was, large loop excision of the cervical transformation zone (LLETZ) was indicated. This confirmed the presence of squamous cell carcinoma in the entire specimen, measuring 1.2 x 1 x 0.5 cm, clinically Stage 1B. The results of blood work were normal, and ultrasound imaging showed a single normally developed fetus.

The treatment possibilities were discussed with the patient, and with her approval it was decided to delay treatment until fetal maturity, since the malignancy was detected at an early stage. The patient was scheduled for clinical and obstetric follow-up visits, which included magnetic resonance imaging at 32 weeks of gestation to rule out the possibility of disease progression and parametrial involvement.

Fig. 1



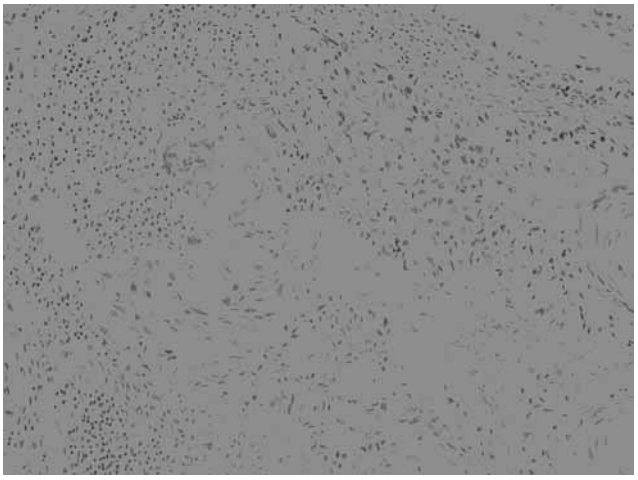


Fig. 2

Figure 1. — Moderately differentiated squamous cell carcinoma with a microinvasive focus.
Figure 2. — Squamous cell carcinoma of the cervix moderately differentiated and focally keratinized to a depth of 4 mm.

At 32 weeks a dose of intramuscular betametasone was administered with a repeat dose 24 hours later to achieve fetal pulmonary maturation. Third-trimester ultrasound showed a normal fetus weighing approximately 2,050 g. At 33 weeks an elective cesarean section was performed by median laparotomy and longitudinal hysterotomy without surgical manipulation of the bladder. The premature female neonate, weighing 2420 g and with Apgar scores of 7, 9 and 10, was admitted to the neonatal unit for mild respiratory distress, and discharged at 13 days. During surgery the parametrial area was evaluated. There was no appearance of involvement, and no apparent pelvic or paraaortic adenopathies were observed. The postpartum period was uneventful except for a urinary tract infection, and the patient was discharged six days following the cesarean section.

At 19 days following the cesarean (11 weeks after the cytological diagnosis) the patient underwent a radical hysterectomy preserving both ovaries, and a bilateral pelvic lymphadenectomy with complete examination of the abdominal cavity. Lysis of minor adhesions was performed without difficulty, and during the procedure the patient received one unit of red blood cells for moderate bleeding. The results of the postoperative hemogram were 10.8 mg/dl hemoglobin and 32.2 hematocrit.

The postoperative period was complicated by several fever spikes and abdominal pain. A hematoma measuring 11.1 x 9.4 cm was diagnosed by CAT scan, and severe anemia required transfusion of two units of two red blood cells prior to another surgical intervention to drain the hematoma, which was located in the vaginal fornix. In addition, a small abscess in the abdominal wall was observed, and cultured positive for Pseudomonas aeruginosa. Intravenous antibiotic treatment was administered without incident during the postoperative period following the second surgery, and the patient was discharged 19 days following the first surgery.

Study of the surgical specimen showed squamous cell carcinoma of the cervix to a depth of 4 mm, moderately differentiated and focally keratinized (Figure 2), with marked lymphocytic infiltration in the transformation zone. The 15 pelvic lymph nodes removed were negative. The tumor board of our hospital concluded that the diagnosis of Stage 1B moderately differentiated cervical cancer did not warrant further treatment. In subsequent follow-up visits, both the patient's cytology results and physical examinations were normal. Her last follow-up visit was a year following the intervention.

Discussion

The incidence of cervical cancer in pregnant women is approximately one case per 1200-10,000 pregnancies [10], although in one study a decline in the number of cases of cervical cancer associated with pregnancy was observed recently [7]. Cervical cancer is diagnosed in the same way during pregnancy as it is in non-pregnant women, on the basis of cytology, colposcopy and biopsy results. It should, however, be remembered that cytology is less reliable during pregnancy because of the changes that take place in the cervix, but it is imperative in cases in which recent cytology results are unavailable or the woman is at risk, as in our case, in which the patient had a history of prior conization but had had no cytologies during the previous three years.

It is noteworthy that although in nearly 100% of women with cervical cancer it is possible to detect human papillomavirus infection [11], in our case the patient tested negative for the virus.

The most frequent form of clinical presentation of cervical cancer is generally vaginal bleeding [12]. In our case, the initial diagnosis was cytological.

Occasionally it is necessary to confirm a diagnosis by conization even if the woman is pregnant [13]. In our case, LLETZ was performed at 26 weeks of gestation. Once a diagnosis was reached and discussed with the patient, it was decided to postpone treatment until fetal maturation, but only after reviewing several published studies supporting this approach to management of Stage 1B cervical cancer [7, 14-16]. In these studies, delay of treatment does not worsen the prognosis, nor is it usually associated with progression of the disease [7, 14-16].

Although the standard approach until recently was to treat immediately in cases under 20 weeks' gestation, the literature reports cases of this type in which treatment was delayed until fetal maturation. In some of these cases neoadjuvant chemotherapy was administered [1, 17] and in others laparoscopy and lymphadenectomy were performed [18] during pregnancy and prior to delay of surgical treatment.

In the majority of cases (74.2%) of cervical cancer in pregnant women, the diagnosis is made in the initial stages of the disease, as in our case.

In 93% of cases, cervical cancer during pregnancy is diagnosed during the first and second trimesters [19]. Another factor affecting treatment is the stage of the disease, since at advanced stages delaying treatment is more likely to worsen the prognosis. In the literature, we found reports of cases of advanced cervical cancer diagnosed during the first trimester and treated with chemotherapy, delaying surgery and/or radiotherapy [20], although the possible long-term consequences of this for both mother and child should be evaluated with care.

Magnetic resonance imaging (MRI) is used in follow-up for pregnant women with cervical cancer in cases of planned delay in treatment to detect progression of the disease [21]. In our case, an MRI was performed prior to cesarean section in order to rule out possible parametrial involvement, which might have been a counterindication for total hysterectomy.

The week chosen for definitive treatment depends on the stage of the disease and fetal maturity. Takushi *et al*. [22] report delaying treatment until 31-41 weeks in pregnant women with disease ranging between Stage 1A1 and 1B2, while in only those women with Stage 1B disease, treatment was delayed until 31-32 weeks. In our case, a cesarean section was performed at 33 weeks, and definitive treatment delayed until 19 days later.

The data from three studies [10, 12, 22] in which treatment was postponed until fetal maturity show that of a total of 26 pregnant women, in 11 cases vaginal delivery was chosen and in 15 cesarean delivery was performed, as in our case. In all cases in which a cesarean section was performed, a hysterectomy was also performed immediately afterward, in the course of the same surgical intervention. In our case, a complete hysterectomy was performed 19 days after the cesarean section, which had the effect of decreasing intraoperative bleeding and facilitating the surgery, since involution of the uterus was more advanced and we found no significant adhesions.

The histological diagnosis confirmed the presence of Stage 1B disease and squamous cell carcinoma, the histologic type most frequently found [12].

In the studies we reviewed [10, 12, 22] on postponing treatment for pregnant women with Stage 1B cervical cancer, the mean delay was between 3.5 and 20.5 weeks (range 2-30 weeks). In our case the delay was 11 weeks. In none of these cases, including ours, was disease progression observed, and all the women are now disease free.

From this literature review, we conclude that it is possible to delay treatment safely in pregnant women with Stage 1B cervical cancer if they are past 20 weeks' gestation. Judging by the results reported in the studies cited above, it even appears to be safe to postpone treatment prior to 20 weeks' gestation.

Management of more advanced cases must be tailored to the circumstances: the week of gestation in which cervical cancer is diagnosed, and the woman's preference.

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