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Case Report

Villoglandular Papillary Adenocarcinoma of the Uterine Cervix in a Pregnant Woman: A Case Report and Review of Literature

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DEDE, M., DEVECİ, G., DEVECİ, M.S., YENEN, M.C., GOKTOLGA, U., DILEK, S. and GUNHAN, O. *Villoglandular Papillary Adenocarcinoma of the Uterine Cervix in a Pregnant Woman: A Case Report and Review of Literature*. Tohoku J. Exp. Med., 2004, **202** (4), 305-310 —— Villoglandular papillary adenocarcinoma (VPA) of cervix is rare but a well recognized variant of cervical adenocarcinoma with favorable prognosis occurring in younger age group. A 28-year-old white woman, gravida 3, para 2 was admitted for abnormal vaginal bleeding, when she was pregnant at 8th weeks of gestation. Physical examination revealed about 2.5 cm polipoid lesion of the cervix protruding into vagina. Histopathological findings were consistent with cervical VPA. After termination of pregnancy, radical hysterectomy type III was performed. The patient underwent second, third and fourth laparotomies because of recurrent pelvic masses. At the end of five years follow-up period, she died because of the complication of recurrent tumor. VPA is not an innocent tumor, and can be complicated by recurrence and metastasis. More radical surgical and medical attempts should be planned. ——— uterine cervix; adenocarcinoma; villoglandular type

Villoglandular papillary adenocarcinoma of cervix was described as a distinct entity (Young and Scully 1989). It occurs generally in young women with an average age of 35 years. The etiology has not been well established. An association between oral contraceptive use and human papilloma virus (HPV) infection is being suggested. The prognosis has been reported as extremely good compared with other variants of cervical adenocarcinoma. We have reported the first case associated with pregnancy in a 28 year-old patient whose prognosis was not good.

CASE REPORT

A 28 year-old white woman, gravida 3, para 2 was admitted with abnormal vaginal bleeding

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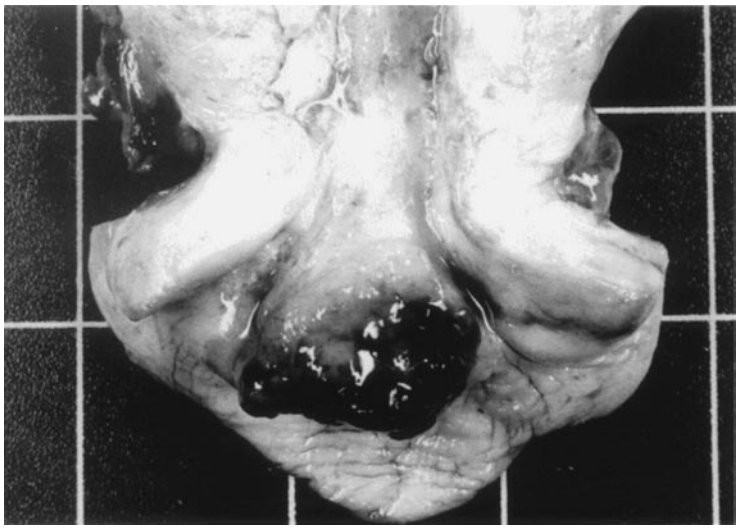

Fig. 1. Post operative macroscopic appearance of cervical polypoid mass.

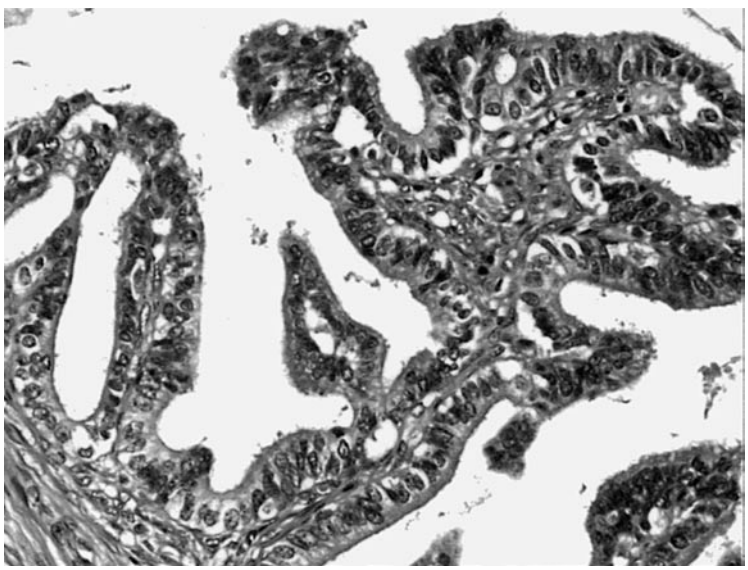

Fig. 2. Typical histological patterns for villoglandular papillary adenocarcinoma of cervix; large cystic glandular and finger-like structures with stroma resembling those of the normal cervix (Hematoxilin Eosin, ×200).

when she was pregnant at 8 weeks of gestation on July 1997. Gynecological examination revealed about 2.5 cm polipoid lesion originating from anterior and posterior portion of the cervix protruding into vagina. Pap smear and cervical punch biopsies were performed. Cytologically, the smear showed circular groups of cells with peripheral nuclei and cytoplasm directed towards the center forming rosettes with generally uniform cells but few showing marked atypia. In the microscopy of cervical biopsy, a neoplastic lesion was noted. The tumor was composed of finger-like or branching papillae supported by fibrovascular core, containing stromal cells and covered by stratified columnar cells. Both preoperatively histopathological and cytological findings were consistent with cervical villoglandular papillary adenocarcinoma. The patient was described as Stage Ib1. In

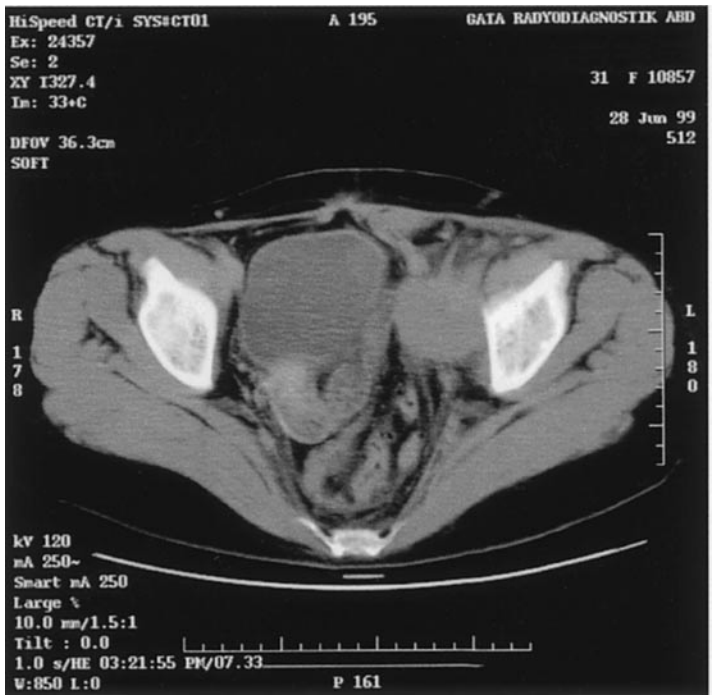

Fig. 3. CT scan indicates a solid mass with heterogenic contrast media showing spicular extensions in left obturator region.

the neoplastic epithelial cells, immunoperoxidase staining for HPV types 16 and 18 was negative. After termination of the pregnancy, radical hysterectomy type III was performed with a midline incision. Grossly, the hysterectomy specimen revealed an exophytic, polypoid mass, measuring 2.5×2×2 cm in diameters and occupying the posterior portion of the cervix by protruding into the vagina (Fig. 1). Histologically, cervical tumor was composed of large cystic glandular and papillary structures surrounding by stroma resembling those of the normal cervix (Fig. 2). The papillae supported by fibrovascular cores covered by stratified columnar endocervical type epithelial cells. The nuclei of the cells were oval with indistinct nucleoli. Mild to moderate cytological atypia was present with some variation in nuclear size and shape. Three to four mitotic figures per 10 high power-fields were present in the epithelial cells. Inflammatory cells were present within fibrous cores of the papillae and in the cervical wall surrounding the tumor. No invasion focus of atypical small gland in the wall of cervix was noticed. Vascular and lymphatic channel invasion was not identified. The endometrium was disease-free.

She was followed up per three months for two years and per six months for one year. A mass of 5 cm in diameter was revealed on the left adnexial site 30 months after surgery and bilateral salpingo-oopherectomy was performed at second laparotomy. Post-operative histopathological diagnosis was ovarian endometrial cyst. Twelve months after second surgery a pelvic mass was noted on physical examination. Bilateral renal enlargement and bowel obstruction were identified on computerized tomography (CT) and third laparotomy was planned (Fig. 3). Descending colon and left ureter were obliterated by a huge pelvic mass in left hypochondriac region. Total resection of the mass, partial colon resection, urethral releasing and also lymphadenectomy were performed. Microscopic examination of the mass was identical to previous cervical adenocarcinoma, and there were metastasis in three nodes. External radiotherapy was given and about 6 months later, another pelvic mass recurrence of

six cm in diameter was observed on CT examination. Fourth laparotomy was performed and frozen pelvis was observed. Histopathological diagnosis of incisional biopsy was VPA. After last operation 6-cure chemotherapy (paclitaxel 175 mg/m^2 + carboplatin AUC 5) was planned. But the patient died because of tumoral complications on the fifth year of first diagnosis of the disease.

Discussion

Villoglandular papillary adenocarcinoma (VPA) of the cervix is a well-differentiated form of cervical adenocarcinoma that occurs predominantly in young women. In contrast to other types of cervical adenocarcinoma, villoglandular type shows an excellent prognosis (Hopson et al. 1990; Jones et al. 1993). Over 45 cases of VPA of the cervix reported in the literature (Gilks and Clement 1992; Jones et al. 1993; Costa et al. 1995; Hurteau et al. 1995; Skopelitou and Hadjiyannakis 1996; Stanley-Christian et al. 1997; Borgo et al. 1998; Lu et al. 1998; Zhou et al. 1998; Chang et al. 1999; Lakhtakia et al. 2000; Yamazawa et al. 2000). After the description of the first 13 patients by Young and Scully (1989), 24 cases were reported by Jones et al. (1993) and 7 by Kaku et al. (1997), and 4 by Costa et al. (1995), and 3 by Hopson et al. (1990). This is the second pregnant patient with VPA after the description by Hurteau et al. (1995).

The mean age of the patients ranges from 33-37 years. Grossly, all tumors present as friable papillary or polipoid masses, protruding from the cervical canal and ranging diameter from 0.5-7 cm. Microscopically, the tumors are composed of finger like papillary projections comprised of cells with mild-moderate atypia with moderate mitotic activity. Treatment modalities range from cone biopsies to simple and radical hysterectomy with or without pelvic lymph node dissection and pre-postoperative radiation therapy (Reed et al. 1993; Datta 1997; Bouman et al. 1999).

The actual incidence of VPA subtype is unknown. Undoubtedly, examples of this tumor type have been nonspecifically included in the well-differentiated category in previous reports, while in other reviews it may have been included along with serous and clear subtypes of papillary adenocarcinoma.

The etiology of VPA of the cervix has not been well established (Liao and Manetta 1993). An association between oral contraceptive use and VPA was suggested by Jones et al. (2000). Although there are reports of an association between oral contraceptive use and cervical adenocarcinoma, a specific association is not found between the patients with reproductive function and cervical adenocarcinoma. Our patient had no history of use of oral contraceptive drug. An association with HPV was suggested, but immunoperoxidase staining for HPV were negative in the presented case.

Generally, the management of cervical cancer during pregnancy depends on gestational age, clinical stage and woman's desire about the maintaining of the pregnancy. In the case of VPA in a pregnant patient reported by Hurteau et al. (1995), the tumor was noted at 20 weeks gestational age, and the patient had 32 weeks of gestational age when she underwent a Cesarean radical hysterectomy. The patient was alive and well after a follow-up period of 14 months. In contrast, cervical classic adenocarcinomas have an overall five-year survival rate of around 50% (Young and Scully 1990; Alfsen et al. 2000). However, five-year survival rates are reported between 60% and 83% for VPA patients with stage 1 disease. From this point, if a pregnancy in the future is desired for a VPA patient with stage 1 disease, removal of the tumor by excision or cone biopsy with close follow up may be advocated without further treatment.

In conclusion, VPA of the cervix is rare but a well recognized variant of adenocarcinoma of cervix that occurs in young women, also along with pregnancy. In view of fact that VPA can show recurrence and metastasis, we do not agree with other authors in issue of the innocence of this clinical entity in young patients to remain conservative in their management. We strongly agree

with Bouman et al. (1999) for the definition of "Beware of a wolf in sheep's clothing" for VPA.

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