Primary high grade papillary serous carcinoma of cervix: report of a case

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ABSTRACT

Introduction: Papillary Serous Cervical Carcinoma (PSCC) is a very rare type of primary adenocarcinoma of the cervix. Herein, we report such a case of PSCC and describe its presentation and treatment. **REPORT OF CASE**: Our patient was a 65-year-old woman presented with vaginal spotting 14 years after menopause. Vaginal examination was not remarkable; however, transvaginal ultrasound showed cervical irregularity. A Pap smear was done for her that revealed atypical cells. The patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy. Pathologic examination and Immunohistochemical study disclosed PSCC. Metastatic evaluations including abdomen and pelvic MRI and chest CT scan were negative. Therefore, pathologic stage was IB1. Due to inadequate lymph node dissection, the patient received adjuvant external beam radiotherapy (45 Gy in 25 fractions). Subsequently, adjuvant endocavitary brachytherapy (3 fractions of 4 Gy) was delivered; however, she refused to receive any adjuvant chemotherapy. After 12 months she is well and is doing her regular daily life. **Conclusion**: PSCC is a rare case and although Radiotherapy is usually done for patients, its treatment is not well known.

Keywords: cervix Uteri, adenocarcinoma, chemotherapy, radiotherapy, papillary, neoplasm

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INTRODUCTION

While the most common pathologic type of cancer in the cervix is squamous cell carcinoma (SCC) Adenocarcinoma amounts to less than 20% of cases. A very rare type of adenocarcinoma of the cervix is primary papillary serous cervix carcinoma (PSCC). This type of tumor was introduced in the late years of 20th century and is not a common malignancy in the cervix. Due to rarity of this type of tumor, the presence of Primary lesion in ovary and endometrium and Metastasis from other primary cancers must be ruled out (1). Till 2018, 113 cases of PSCC were reported and we and Herein we report and share our experience in a case of PSCC and presentations and treatment (2). Our case received radiotherapy and has a good survival.

CASE REPORT

The Patient is a 65-year-old woman (G3P3L3) visited a gynecology clinic after having experienced vaginal spotting for 2 months. This spotting occurred 14 years after the patient's menopause. She had no other complaints such as pain, dyspareunia. Her menstrual cycles were regular with no problem till menopause. She had no history of diabetes mellitus, heart disease and other chronic disease. She also had no family history of any cancers and was not smoker. She had used OCP for 6 years, between, 31-37 years old. In general and vaginal phys-

ical examination nothing was found. HPV test was not done for her and the results of a Pap smear showed atypical cells. Transvaginal ultrasonography also revealed atrophic uterus with irregular anterior and posterior lines and 2mm endometrial thickness and fluid in the endometrial cavity. Right and left ovaries showed 20x11mm and 45x20mm thin wall cysts, respectively. Serum tumor markers, including CA 125, HE4 and CEA were found within the reference range. The patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy. On gross examination of the uterus, an oval shape white mass measuring 1.2x0.7x0.7 cm was seen in the middle part of the endocervical canal. Right and left ovaries showed cystic lesion with internal and external smooth surfaces. Microscopic examination of the endocervical mass revealed papillary structures that were lined by highly atypical cells with large nuclei and prominent nucleoli, and papillary high grade serous carcinoma was diagnosed (fig1). Immunohistochemical staining was positive for WT1, P16 and negative for ER and Vimentin (Fig2). The tumor invaded the endocervical wall (the depth of invasion was 0.7 cm). All surgical margins were free of tumor and the tumor was 1cm far from the deep margin (the lateral wall of the endocervix). Ovarian cysts were found benign serous cystadenoma. Endometrium was atrophic and the tumor was limited to the cervix. All 7 dissected nodes were free of tumor.

Metastatic evaluations including Abdomen and Pelvic MRI and Chest CT scan were normal and repeated annually. The patient had no other systemic diseases or cancer. Due to inadequate lymph node dissection, the patient received external beam radiotherapy (up to 45 Gy in 25 fractions). Then she was offered 4 Gy brachytherapy for 3 fractions. However, she refused to undergo chemotherapy. After 24 months she is well and is doing well. Before preparing this report, written consent, was prepared and patient was informed about it.

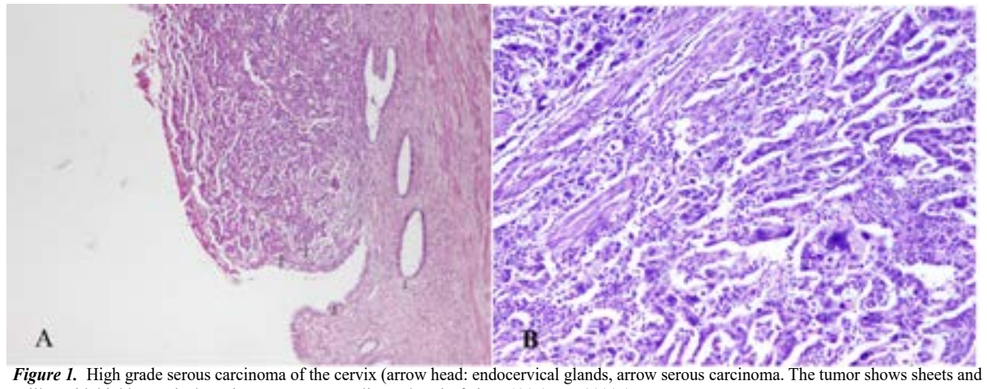

Figure 1. High grade serous carcinoma of the cervix (arrow head: endocervical glands, arrow serous carcinoma. The tumor shows sheets and papillae with highly atypical carcinoma. Haematoxylin and eosin stain, ×40(A) & x 200(B).

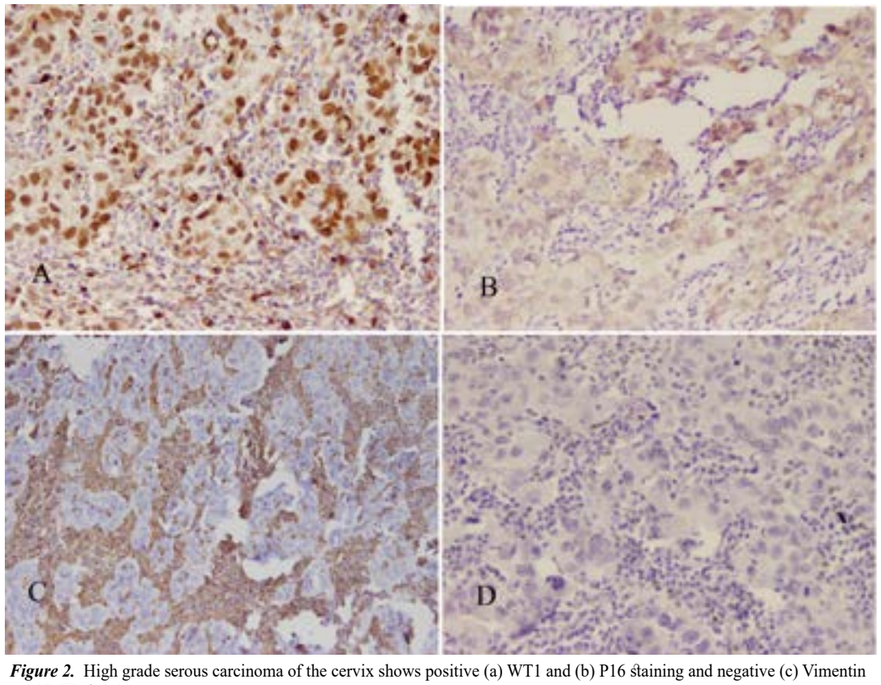

Figure 2. High grade serous carcinoma of the cervix shows positive (a) WT1 and (b) P16 staining and negative (c) Vimentin and (d) ER staining.

DISCUSSION

Papillary carcinoma is commonly seen in the ovaries and fallopian tubes. Only 5% of endometrium adenocarcinoma are papillary and is rarely seen in the cervix (3). The incidence of PSCC is not known. Rose et al. in a retrospective study reported that 463 patients with cervical cancer, 86 cases had adenocarcinoma of which 2 cases had PSCC (3). Jonska-Gmyrek claimed in a review that 113 cases of PSCC had been reported (2). Two peaks of incidence are recognized. First peak is before 40 years and the other peak after 54 years. (1) Our patient is 65-year-old.

Presentation of this type of rare tumor is non-specific and with a number of initial signs such vaginal discharge or bleeding or some patients may be asymptomatic (1, 3-7). Ueda et al. reported one case with PSCC who had been presented with a metastatic mass (8). Our patient presented with vaginal spotting as in most other reports.

Stage of a tumor is important in choosing treatment and in determining prognosis. The largest series of patients with PSCC is presented in a report by Zhou. In that report, the majority of 17 cases the disease was found to be localized. Fourteen patients had stage I disease and 3 patients had stage II-III (9). In the majority of other reported cases, the disease was localized and only 2 cases had metastasis at presentation. Lungs and lymph nodes (LN) were the metastatic sites in the patients (1, 8). Power et al. reported 2 cases with locally advanced PSCC that were inoperable at presentation (7). Kaplan reported a case of PSCC were the disease was first localized but developed peritoneal carcinomatosis after 2 years (5). Our case as in majority of reports was localized to the cervix and had stage IB1.

Most reports showed no increase in levels of CA-125 in non-metastatic patients (3, 5). Whereas, in metastatic cases, this marker had increased. In 3 reports on found that serum level of CA-125 increased to 343, 242 and 2480 (1, 7, 8). Watrowski et al. reported a non-metastatic PSCC case who had high levels of CA-125 recorded as 159 (4). Zhou reported 4 cases with high levels of CA-125 were all the patients had an unsuccessful outcome (9). In a report from uterus papillary serous carcinoma, high levels of CA-125 was associated with stage and recurrence (4). Our patient as expected had normal level of CA-125.

Because of rarity, the optimal treatment is currently not well known. The patient observed for these studies has all had surgery before chemotherapy and radiotherapy (RT) (1, 5). Rose et al. reported a case of PSCC that was limited to the cervix that responded well to radiotherapy and was well for 32 months and she had received no adjuvant treatment (3). Kaplan et al. administered chemotherapy and RT on a patient who was seen to respond well for 24 months. The patient received carboplatin-paclitaxel and 45 Gy to pelvic and 3×5Gy brachytherapy to vaginal cuff (5). In uterus papillary serous carcinoma, carboplatin and paclitaxel has been reported to be more effective (4). We offered adjuvant external radiotherapy and vaginal brachytherapy to our patient. It seems that radiotherapy may be the effective adjuvant or neoadjuvant treatment for PSCC.

No specific chemotherapy regimen for metastatic patients has been identified (1). Ueda et al. reported a case of PSCC with metastasis and a good response to chemotherapy. They also used carboplatin and paclitaxel (8). Power et al. reported 2 cases that received carboplatin and paclitaxel, only partial response to the treatment was seen. Both of them died 10 and 36 months after diagnosis (7). Zhou reported that patients with metastasis showed no response to chemotherapy (9).

Fortunately there are reports from patients with good prognosis. Watrowski et al. reported a case of 61 years old patient who had developed cervical mass. The pathology result showed PSCC. This patient did not receive adjuvant therapy and after 38 months she is well after her treatment and is currently disease free. This patient had bilateral breast cancer and received tamoxifen. Interestingly the patient had experienced no initial symptoms before she was diagnosed with cervical cancer. The lesion was discovered in a routine follow-up examination (4).

PSCC is not always behaving well. Kaplan reported a case of PSCC in a 39 years-old patient with a family history of papillary carcinoma of ovary. These close family members included the patients mother and twin sister. The patient had undergone prophylactic surgery (bilateral salpingo-oophorectomy) but developed PSCC. She had no complaint and the non-bleeding mass in the cervix was found during evaluations for abnormal vaginal bleeding and the pathology results showed PSCC. The patient received concurrent chemotherapy, radiotherapy and brachytherapy but after 24 months she developed peritoneal carcinomatosis. The patient's mother and sister both died of cancer and review of the documents showed that both of them had died from papillary serous carcinoma of ovary (5). In the other reports we found no case with family history of PSCC.

Paraneoplastic syndromes are reported in these patients. In Power's report, 2 cases with PSCC and associated paraneoplastic syndrome. These patients were 59 and 64 years and developed dysarthria and cerebellar ataxia from which they both died (7). Ueda et al. reported a case of PSCC in which the patient had metastasis of the neck at presentation. She also had mediastinal and para-aortic nodes. The only primary source of cancer was found in the cervix. She received chemotherapy and after 6 cycles of carboplatin and paclitaxel showed near complete response. (8)

Prognostic factors are not fully determined. Togami reported 12 cases with PSCC out of which 3 patients with T2 disease lived for 5 years. These patients developed extra-pelvic metastasis to LNs and peritoneum. Seven patients from 8 who were alive at the time of report had T1N0 disease. The other patient had T1N1 tumor (10). Zhou et al. reported 17 patients with PSCC among which 14 had stage I disease and 3 patients had stage II-III. In their report, 7 patients out of 17 patients developed a recurrence and 6 of them died at time of report. All of 3 patients with stage II-III and 3 patients with stage Ib died from PSCC. Most of the patients who died had LN metastasis and later developed peritoneal metastasis. Liver, lung and skin were other metastatic sites (9). The evidences indicate that patients with stage II and above have a poor outcome.

In a report from japan, only 0.4% of patients with cervical cancer had PSCC. Kitade et al. reported 5 cases of PSCC with interesting points. From them, 2 cases had developed 2nd primary breast cancer. Prognosis in their study was excellent and survival of them was 26-210 months. Four cases were disease free (56-210) months. From 4 cases with long time disease free, although 2 cases had pelvic and Para aortic lymph node metastasis that received chemotherapy and radiotherapy. All of them were well and 1 case who had peritoneal metastasis was receiving bevacizumab (11). We hope our patient would have live long with similar prognosis to cases of this study. Our patient is well but some authors believe PSCC to be an aggressive tumor (7, 8). The longest case of survival was found in a report by Zhou. They reported 8 cases of stage I PSCC with a mean disease free survival of 76 (6-132) months. All of the patients were well at the time of report was undertaken (9).

CONCLUSION

PSCC is an extremely rare disease and in most reports in stage II and above has a poor prognosis. Associated risk factors are not well known. Current adjuvant or neoadjuvant Treatment is in accordance with the cervix SCC.

CONFLICT OF INTERESTS

None declareds

ABBREVIATIONS

PSCC; Papillary Serous Cervical Carcinoma, SCC; squamous cell carcinoma, LN; lymph nodes, RT; radiotherapy.

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