CASE REPORT

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The Importance of Preoperative Evaluation in a Patient Considered to Have Advanced Endometrial Cancer: A Rare Case Report

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ABSTRACT Gastric-type mucinous endocervical adenocarcinomas of the cervix uterus are a newly classified mucinous subtype. They are much more aggressive than other endocervical adenocarcinomas and show an unusual metastatic pattern. They tend to present at more advanced stages and have worse survival rates. Therefore, the differential diagnosis of gastric-type adenocarcinoma is very important. Because the risk of recurrence is significantly higher and 5-year disease-specific survival is reduced in these patients. Furthermore, it is not associated with human papillomavirus (HPV) infection and p16 immunohistochemistry is typically negative. We present our patient who was operated on with the suspicion of endometrial carcinoma extending to the parametrium, whose smear and HPV results were negative, but whose final pathology result was reported as gastric-type mucinous cervical adenocarcinoma.

Keywords: Cervical adenocarcinoma; gastric type cervical carcinoma; non-human papillomavirus cervical carcinoma

Endocervical adenocarcinoma accounts for approximately 20-25% of cervical cancers.[1-5] Its incidence has been increasing in recent years. Gastric type is a subtype of mucinous adenocarcinoma and shows distinct morphologic features and an aggressive clinical course.[6,7] Most mucinous adenocarcinomas are considered to be associated with human papillomavirus (HPV), but studies have shown that gastric type mucinous endocervical adenocarcinomas of the uterine cervix [gastric-type adenocarcinoma (GAC)] are mostly not associated with HPV infection.[8,9] The 5-year disease-free survival rate of patients (38%) is significantly lower than that of patients with other adenocarcinomas (74%).[7]

CASE REPORT

A 66-year-old patient presented to us with an abdominal mass. The tumour marker values of the patient were as follows: cancer antigen (CA) 125: 685, CA 19-9: 3002 carcinoembryonic antigen (CEA): 8.36. Colonoscopy and gastroscopy evaluation were performed. Gastroscopy revealed no pathology except hiatal hernia. Colonoscopy was normal. Pap smear was negative for malignancy and negative for HPV. No serious pathology was observed in the cervix. Preoperative imaging (Figure 1) showed that the uterine volume increased with age and the contours were irregular. Heterogeneous pathological lesion areas approximately 7.5 cm in length and 3 cm in thickness covering the uterine body and partially the cervix were observed. Contrast enhancement was present in the parametrial fatty planes on the right and a mass forming lesion approximately 5x3 cm in size was observed in the right adnexal region.

The right ovary is not clearly distinguishable from the defined mass. No pathological intrapelvic

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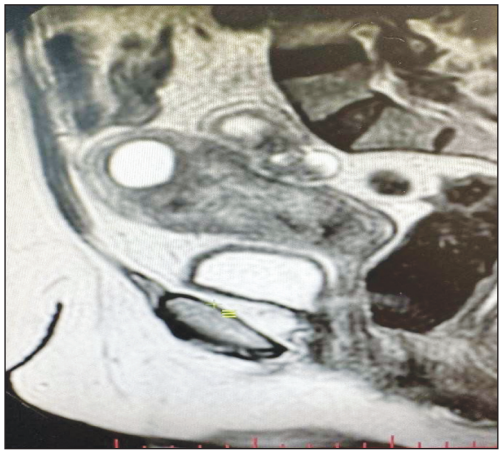

FIGURE 1: MRI image of the patient.

lymph node was seen. A large mass lesion involving the uterine body and cervix, infiltrating the adnexal tissue and invading the right parametrium (endometrial CA invading the parametrium) was observed. There was a small amount of ascites in the abdomen and nodular soft tissue implants in the omentum consistent with peritoneal carcinomatosis. Positron emission tomography/computed tomography imaging showed no pathological F-18 fluorodeoxyglucose uptake lesions except uterus. The patient was referred to the gynaecological oncology council for evaluation of ureter-rectum invasion and appendix tumour. It was considered as a tumour of primary adnexal origin by the council. Histopathological evaluation of the endometrium was recommended. The mass was observed to touch the right ureter. Appendix tumour could not be excluded. No invasion was observed in the rectum. Appendectomy and frozen section laparotomy were planned.

Endometrial curettage was planned for the patient for histopathological diagnosis. However, due to the development of acute abdomen and ureter involvement, endometrial curettage surgery was not performed. Widely metastatic lesions were observed on the omentum during the exploration during the operation. Implants were observed on the hepatic flexura and splenic flexura in paracolic areas. Adhesions were observed between the uterus and the ovaries. Adhesions were observed between the sigmoid column and the infindibulopelvic ligament on the left side and between the cecuum, appendix and the right infindibulopelvic ligament. No lesion was observed on the liver and spleen surface. It was observed that the metastatic masses on the omentum also involved the intestinal meso. Paracolic areas were released and omentectomy was completed. The masses on the splenic flexura and hepatic flexura were excited. Left ureter is natural, right ureter is dilated. An approximately 2 cm mass was observed in the distal part of the right ureter. It was observed that the mass invased the ureter. The adhesions between the appendix and the uterus on the right side were reduced. Appendectomy was done. Adhesions around the ureter were dissected. Hysterectomy and bilateral salpingooophorectomy were performed. Distal ureter was cut and removed by urologists. A new orifice was opened in the bladder and a ureteroneocystostomy was done.

As a result of pathology, it was reported as gastric type cervical adenocarcinoma, HPV unrelated, Grade 2, stromal invasion silva pattern C, with a maximum diameter of 5 cm, widespread in the entire cervical wall. Surgical margins; No tumor was seen in ectocervical surgical margin (8 mm), tumor was present in radial surgical margin. Lymphovascular invasion: (+) perineural invasion: (+) was detected. Myometrium showed diffuse full-thickness cervical adenocarcinoma infiltration. Tumor was present in the uterine serosa. Cervical adenocarcinoma infiltration was found in both ovaries and tubal wall. There was cervical adenocarcinoma infiltration in the right ureteral wall and surrounding fat-connective tissue. Cervical adenocarcinoma infiltration was detected in the adiposeconnective tissue in the left pelvic peritoneum. Excisional biopsy of the right supra-ureteric tumor showed cervical adenocarcinoma infiltration in adipose-connective tissue. Cervical adenocarcinoma infiltration in adipose-connective tissue was detected in the tumor above the right hepatic flexura. Cervical adenocarcinoma infiltration in adipose-connective tissue was detected in splenic flexura coded excision material. Low grade mucinous appendiceal neoplasia was present in the appendix. There was diffuse cervical adenocarcinoma infiltration in the wall. There were malignant cytologic findings in the body fluid and diffuse cervical adenocarcinoma infiltration in the

omental adipose tissue. Estrogen receptor (ER): (-), progesterone receptor (PR): (-), p16: (-), p53: diffuse (+), pax-8: diffuse (+), MUC-6: multifocal foci (+), SATB2: (-) were detected (Figure 2, Figure 3, Figure 4, Figure 5, Figure 6, Figure 7). It was evaluated as Stage 4 disease. Chemotherapy was then planned for adjuvant treatment. Informed consent was obtained from the patient for a case report.

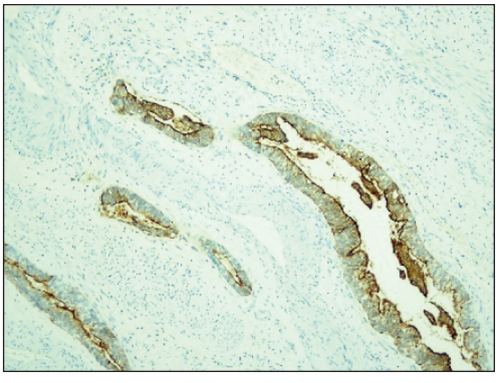

FIGURE 2: Staining with CEA x100.

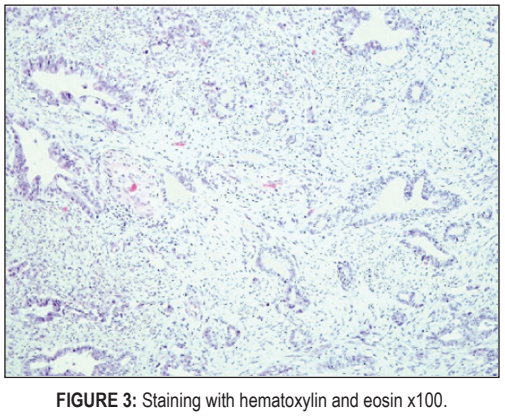

FIGURE 3: Staining with hematoxylin and eosin x100.

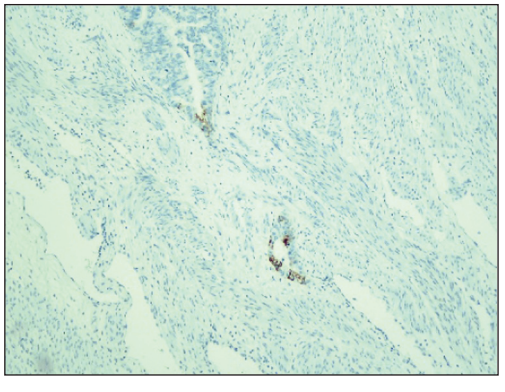

FIGURE 4: Staining with MUC x100.

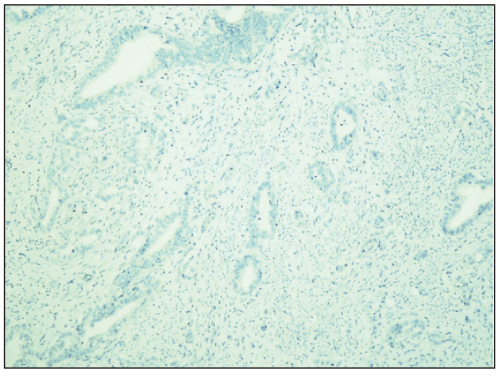

FIGURE 5: Staining with P16 x100.

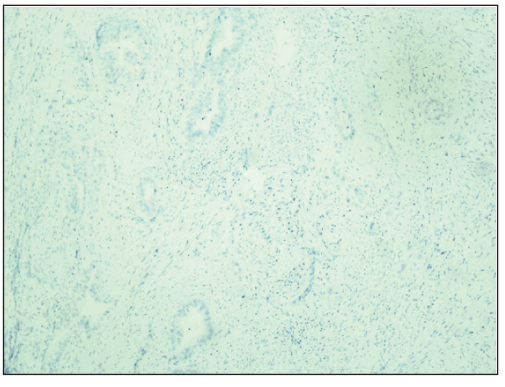

FIGURE 6: Staining with SATB2 X100.

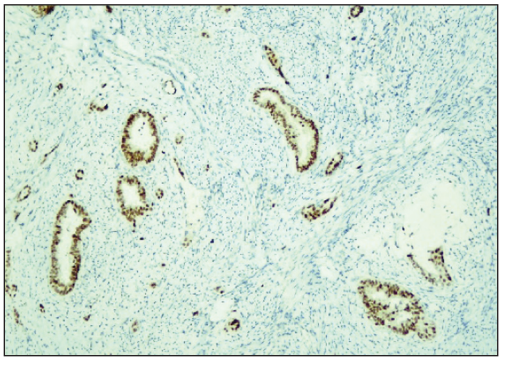

FIGURE 7: Staining with PAX8 X100.

DISCUSSION

GAC is a rare type of mucinous adenocarcinoma and is not associated with HPV. And p16 immunohistochemistry is a crucial marker to differentiate it from other diseases. It is typically negative or focal in GAC.[7] In cervical cancers, both HPV DNA and p16 protein are also usually positive, but almost always negative in GAC.[7,8,10] In some cases, CEA may be an

important marker in the differential diagnosis because CEA is usually negative in clear cell carcinoma but may be increased in GAC.[8] It was thought to be associated with lobular endocervical glandular hyperplasia in pathogenesis. The peripheral changes in the cervical wall may cause the finding of barrel cervix by tightening the tissue. Histologically, apical mitosis and apoptosis are present but inconspicuous. Poorly differentiated glands are lined by cells with variable nuclear changes, including large vesicular nuclei with visible nucleoli. Lymphovascular invasion is common. The gastric markers HIK1083 and MUC6 are frequently positive by immunohistochemistry. These markers may be locally expressed in gastric type adenocarcinoma, in contrast to the diffuse expression seen in lobular endocervical glandular hyperplasia. Paired box (PAX)-8, carbonic anhydrase IX, CEA and cytokeratin 7 are usually positive. PAX2 expression is usually lost. ER and PR are usually negative. In 2018, 322 cervical cancer patients were examined. In this study, it was found that some specific clinical signs such as watery secretion and lower abdominal pain, high serum CA19-9 level and immunohistochemistry are generally helpful in diagnosis.[11] In our case, the CA 19-9 value was found to be 3,002.

Patients with a diagnosis of GAC usually present at an advanced stage and pelvic, abdominal and distant metastases are common. Accurate differential diagnosis of GAC from normal type is very important, as GAC has a worse prognosis and worse clinical outcome. HPV DNA testing and p16 immunohistochemical staining are very important in the differential diagnosis of cervical cancers. When they are negative in cervical cancers, non-HPV-related group, especially GAC, should definitely be considered. The issue of HPV DNA testing alone in cervical cancer screening should be further evaluated.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Sinem Özşahin Kılıç;* ***Design:*** *Sinem Özşahin Kılıç;* ***Control/Supervision:*** *Nilüfer Çetinkaya Kocadal;* ***Data Collection and/or Processing:*** *Hilal Serap Arslan, Sinem Özşahin Kılıç;* ***Analysis and/or Interpretation:*** *Sinem Özşahin Kılıç;* ***Literature Review:*** *Sinem Özşahin Kılıç;* ***Writing the Article:*** *Sinem Özşahin Kılıç;* ***Critical Review:*** *Nilüfer Çetinkaya Kocadal, Sinem Özşahin Kılıç.*

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