

Two Cases of Vanishing Endometrial Carcinoma

¹Yakup Kumtepe, ²Pasa Ulug, ¹Ilhan Delibas and ²Elif Demirci
¹Department of Obstetrics and Gynecology, ²Department of Pathology,
Faculty of Medicine, Ataturk University, 25240 Erzurum, Turkey
³Nenehatun Maternity Hospital, 25700 Erzurum, Turkey

Abstract: In gynecological cancer, diagnosis is made by biopsy before radical surgery except for ovarian cancers. Endometrial biopsy is a gold standard for endometrial cancer. In some cancers such as prostate and colon as well endometrial cancer final tissue may not confirm presence of cancer although, initial biopsy is positive for malignancy prior to radical surgery. This is called vanishing cancer. In this report, the researchers presented two cases which had been diagnosed endometrioid type endometrial carcinoma on endometrial biopsy sampling. However, in hysterectomy specimen there was no residual cancer. These types of cases exist in low prevalence which may be subjected to medicolegal issue should be known by the clinician, pathologist and patient.

Key words: Vanishing cancers, endometrial cancer, endometrial biopsy, tissue, pathologist, Turkey

INTRODUCTION

Endometrial carcinoma is the most common gynecologic malignancy (Altekruse *et al.*, 2007). It is usually presented with postmenopausal bleeding which allows its relatively early diagnosis being possible. The surgical removal and staging of endometrial carcinoma are often made after a tumor positive endometrial sampling taken either by dilatation curettage (D and C) or pipelle aspiration technique as well as hysteroscopy. Rarely, no residual carcinoma is found in subsequent hysterectomy specimen although, no preoperative radiotherapy, chemotherapy or progestin treatment is administered (Stovall *et al.*, 1989, 1991; Eifel *et al.*, 1983; Christopherson *et al.*, 1982). In studies evaluating different sampling methods of the endometrium, the prevalence of absence of carcinoma in hysterectomy specimens after positive histological diagnosis ranges from 0.5-2.5% (Stovall *et al.*, 1989, 1991). In majority of these cases, previous biopsy sites especially the ones which are obtained by hysteroscopy can be identified by demonstration of inflammation and associated epithelial regeneration in the hysterectomy specimen hence, dismissing the doubt of the pathologist about whether the previous endometrial biopsy and hysterectomy specimen belong to the same patient (Colgan *et al.*, 1999). In this report the researchers presented two cases which had been diagnosed to have endometrioid type endometrial

carcinoma on endometrial samplings however, histological examination of subsequent hysterectomy specimens had revealed no residual cancer.

CASE 1

A 46 years old postmenopausal woman presented with excessive vaginal bleeding after 1 year cessation of menses. Her Body-Mass-Index (BMI) was 18. She was receiving no hormone replacement therapy. Ultrasonography revealed 30 mm endometrial thickness and normal ovaries. On D and C 1 g of tissue was collected. Histological examination revealed a fair amount of moderately differentiated endometrioid adenocarcinoma. No endometrial or endocervical polyps were detected. The tumor showed moderate mitotic activity (8 mitoses per 10 high power fields), some apoptotic activity and a moderate acute lymphoplasmacytic inflammatory response (Fig. 1). About 2 weeks later she underwent surgery including peritoneal washing, Total Abdominal Hysterectomy with Bilateral Salpingoopherectomy (TAH-BSO), omentectomy and bilateral pelvic and paraaortic lymphadenectomy. Preoperative progestin therapy was not applied. There was no remarkable gross pathology within the cervical canal and 20 mm thick endometrium. In histopathological examination, there was no malignancy in any of the specimens removed during the surgery. Entire endometrium and neighboring myometrium of the

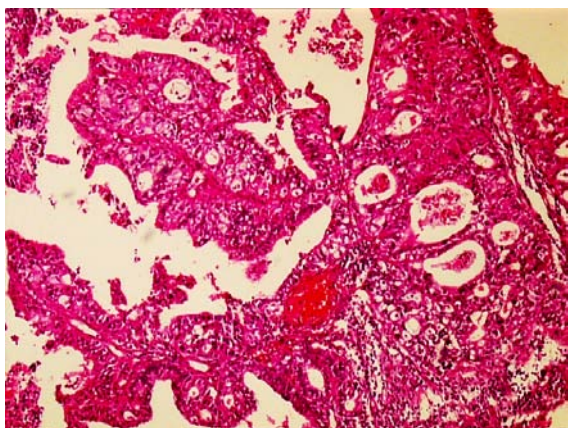


Fig. 1: Uterine curetting of the case 1: Endometrioid adenocarcinoma comprised of atypical pleomorphic cells with large hyperchromatic nuclei and moderately increased mitotic activity that formed cribriform pattern and microglandular structure in some areas (H and E, x200)

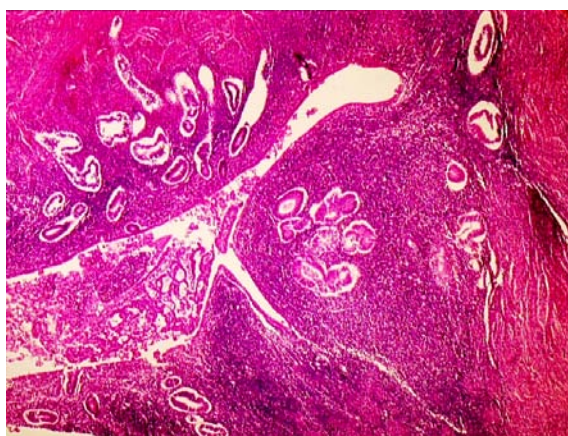


Fig. 2: The endometrium in the hysterectomy specimen revealed neither malignancy nor a definite biopsy site (H and E, x100)

hysterectomy specimen was examined and the only pathology detected was some foci of adenomyosis. The endometrial sampling slides were reviewed to exclude possible misdiagnosis and confirmed the presence of carcinoma. After 6 months surgery, she was well with no evidence of disease and did not receive any adjuvant therapy.

CASE 2

A 48 years old premenopausal woman presented with abnormal vaginal bleeding. Her BMI was 20. Endometrial biopsy was performed by use of the D and C technique and displayed hyperplasia with complex atypia and well differentiated endometrioid-type endometrial carcinoma. No polyp was identified. She received no preoperative progestin therapy. She underwent surgery 16 days after the biopsy including peritoneal washing, TAH-BSO, omentectomy and bilateral pelvic and paraaortic lymphadenectomy. Thorough histopathological examination of the hysterectomy specimen revealed no residual tumor but foci of adenomyosis. Other specimens removed during the surgery were also negative for malignancy. Previous slides of endometrial biopsy were reviewed and confirmed the diagnosis of endometrial carcinoma. After 4 months surgery she was well with no evidence of disease and was not on any adjuvant therapy (Fig. 2).

In both of the hysterectomy specimens, there were no overt findings pertaining to a post-biopsy reparative process such as necrosis, vascular thrombi or giant cell reaction.

DISCUSSION

Goldstein *et al.* (1995) reported the vanishing cancer phenomenon in 1995 in 13 tumor negative prostatectomy specimens despite previous tumor positive prostate biopsies (Goldstein *et al.*, 1995). Since, then number of vanishing prostatic cancer case reports are increasing in number and its prevalence is reported as 0.6% (Bostwick and Bostwick, 2004). In 2007, Dube *et al.* (2007) described 3 cases which had positive biopsy examinations for endometrial cancer but no residual tumor detected in hysterectomy specimens and suggested the recognition of vanishing cancer phenomenon for endometrium first time after its wide acceptance for the prostate (Dube *et al.*, 2007). Their pathological examination failed to detect previous biopsy sites in hysterectomy specimens. They performed DNA profiling to confirm the shared identity of endometrial biopsy and hysterectomy specimen and to dissipate the suspicion of switched specimen or tissue contamination.

The diagnosis of vanishing endometrial carcinoma was suggested to be based on 3 criteria (Dube *et al.*, 2007). First, the diagnosis of carcinoma must be proven by a review of the biopsy. Attention must be given to the probability of switched specimen inconsistency between gross examination and pathology slides and laboratory contamination. Second, the entire endometrium of the hysterectomy specimen should be examined and there should be no evidence of malignancy or biopsy site stigmata. Third since, preoperative radiotherapy and high-dose progestins can eradicate endometrial carcinoma there should be no history of those treatments (Renaud and Plante, 2001). DNA profiling was not

suggested as a criterion but it can be used in cases of suspected tissue contamination or switching of endometrial biopsy and in cases of medicolegal inspection.

The vanishing endometrial carcinoma phenomenon could be attributed to the removal of the tumor by the instrument used for sampling of the endometrium which is proposed as curative biopsy theory although, a study revealed that <50% of the endometrium was sampled in 60% of patients who underwent curettage procedures (Kommu, 2004; Stock and Kanbour, 1975). Endometrial carcinoma developed on a polyp can be removed more easily by curettage but in the cases there was no evidence of endometrial polyps in any of the specimens. Low-volume malignant tissue may have been totally removed during the D and C procedure. The phenomenon can also be explained by induction of inflammatory or cytotoxic immune responses following biopsy procedure which ends with termination of the malignant foci. In highly mitotic tumors, brisk cellular turnover may also lead to self-termination of malignancy (Kommu, 2004). There was no high mitotic activity demonstrated in any of the cases. Interestingly in both of the cases there were adenomyotic foci in hysterectomy specimens. In a recent study, it was found that the expression of RANTES (regulated on activation, normal T cell expressed and secreted), a chemotactic factor for T cells which can induce the proliferation and activation of killer cells known as CHAK (Chemokine-Activated Killer) was significantly higher in the endometriotic tissue and ectopic endometrium than that of the normal endometrium without endometriosis (Wang *et al.*, 2010). Since, adenomyosis is a type of ectopic endometrium similar to endometriosis, it may be possible to hypothesize that increased RANTES and activated CHAK cells within the endometrium of adenomyotic uterus combined with the effect of endometrial biopsy procedure which also induces an inflammatory reaction may trigger exaggerated inflammatory and cytotoxic immune responses resulting in eradication of malignant cells. However, to elucidate whether immune response plays a role in the vanishing cancer phenomenon further studies are needed which focus on the effects of endometrial biopsy on histological and biochemical milieu in the endometrium of adenomyotic uteri.

Another common feature of the patients was their very low body mass index (18 and 20, respectively). It is well known that high BMI is a major modifiable risk factor for endometrial cancer and generally expected patient phenotype is overweight or obese postmenopausal woman. In previous vanishing endometrial cancer case reports, there was no information available about BMI of

patients. The researchers believe that attention must be given to BMI in future cases to elucidate whether low/normal BMI and vanishing cancer phenomenon show any association. The recognition of the entity of vanishing cancer of endometrium has 2 clinical implications. First, it can help to dismiss the suspicion of clinicians and patients about a laboratory or pathologist error. Second although, the diagnosis of vanishing cancer of endometrium of endometrioid type is classified as FIGO stage 1a and deserves no adjuvant therapy, clear cell or serous histological types of the same stage may be considered for neoadjuvant radiotherapy or chemotherapy (Santin *et al.*, 2004).

CONCLUSION

In this study, as more sensitive diagnostic tools such as uterine imaging techniques become more available, the frequency of low-volume disease increases. Further studies for introducing widely acceptable sequential protocols for the diagnosis of vanishing cancer of endometrium are necessary. The recognition of this phenomenon will present clinical and medicolegal advantages to both gynecologic pathologists and gynecologic oncologists.

REFERENCES

- Altekruse, S.F., C.L. Kosary, M. Krapcho, N. Neyman and R. Aminou *et al.*, 2007. Seer cancer statistics review, 1975-2007. National Cancer Institute. Bethesda, MD, USA.
- Bostwick, D.G. and K.C. Bostwick, 2004. Vanishing prostate cancer in radical prostatectomy specimens: Incidence and long-term follow-up in 38 cases. *BJU Int.*, 94: 57-58.
- Christopherson, W.M., R.C. Alberhasky and P.J. Connelly, 1982. Carcinoma of the endometrium. II. Papillary adenocarcinoma: A clinical pathological study, 46 cases. *Am. J. Clin. Pathol.*, 77: 534-540.
- Colgan, T.J., R. Shah and N. Leyland, 1999. Post-hysteroscopic ablation reaction: A histopathologic study of the effects of electrosurgical ablation. *Int. J. Gynecol. Pathol.*, 18: 325-331.
- Dube, V., D. Macdonald, D.J. Allingham-Hawkins, S. Kamel-Reid and T.J. Colgan, 2007. Vanishing endometrial carcinoma. *Int. J. Gynecol. Pathol.*, 26: 271-277.
- Eifel, P.J., J. Ross, M. Hendrickson, R.C. Cox, R. Kempson and A. Martinez, 1983. Adenocarcinoma of the endometrium analysis of 256 cases with disease limited to the uterine corpus: Treatment comparisons. *Cancer*, 52: 1026-1031.

- Goldstein, N.S., L.R. Begin, W.W. Grody, J.M. Novak, J. Qian and D.G. Bostwick, 1995. Minimal or no cancer in radical prostatectomy specimens. Report of 13 cases of the vanishing cancer phenomenon. *Am. J. Surg. Pathol.*, 19: 1002-1019.
- Kommu, S., 2004. A model to explain the vanishing prostate: The curative biopsy theory. *Br. J. Urol. Int.*, 94: 939-940.
- Renaud, M.C. and M. Plante, 2001. Medical treatment of endometrial carcinoma for the premenopausal woman wanting to preserve her ability to have children. *J. Obstet. Gynaecol. Can.*, 23: 213-219.
- Santin, A.D., S. Bellone, T.J. O'Brien, S. Pecorelli, M.J. Cannon and J.J. Roman, 2004. Current treatment options for endometrial cancer. *Expert Rev. Anticancer Ther.*, 4: 679-689.
- Stock, R.J. and A. Kanbour, 1975. Prehysterectomy curettage. *Obstet. Gynecol.*, 45: 537-541.
- Stovall, T.G., G.J. Photopulos, W.M. Poston, F.W. Ling and L.G. Sandle, 1991. Pipelle endometrial sampling in patients with known endometrial carcinoma. *Obstet Gynecol.*, 77: 954-956.
- Stovall, T.G., S.K. Solomon and F.W. Ling, 1989. Endometrial sampling prior to hysterectomy. *Obstet. Gynecol.*, 73: 405-409.
- Wang, X.Q., J. Yu, X.Z. Luo, Y.L. Shi, Y. Wang, L. Wang and D.J. Li, 2010. The high level of RANTES in the ectopic milieu recruits macrophages and induces their tolerance in progression of endometriosis. *J. Mol. Endocrinol.*, 45: 291-299.