Uterine serous papillary carcinoma Clinical and immunopathological study of 9 cases

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Summary

From January 1993 to December 1998, nine patients with serous papillary endometrial carcinoma (SPEC) were diagnosed and treated at the 2nd Department of Obstetrics and Gynecology, Areteion University Hospital. The incidence of SPEC in our Clinic was 6.77%. The mean age of patients was 65.5 years (range 54-82 years). All patients underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy and epiploectomy. Abdominal and para-aortic lymph node sampling was performed in all cases and peritoneal washings were examined cytologically. Histological sections of the specimens, stained with haematoxylin-eosin, were retrieved from the Laboratory of Pathology and re-evaluated by two pathologists. All cases conformed to the diagnostic criteria for SPEC. Immunohistochemical studies were performed in paraffin blocks retrieved from the files, by a streptavidin-viotin method for the detection of vimentin (ENZO monoclonal ab), secretory component (DAKO polyclonal ab), CEA (DAKO monoclonal ab), EMA (DAKO monoclonal ab). The hormonal receptor status, assessed by appropriate positive and negative controls, was studied as well. The presence of mucin and glycogen was studied by histochemical reaction, PAS, PAS diastase and mucicarmine.

Serous papillary carcinoma is an unusual but distinct type of endometrical adenocarcinoma, a non-hormonal dependent tumor, with aggressive biologic behavior. Its recognition is mandatory for a correct therapeutic approach.

Key words: Uterus; Adenocarcinoma; Serous carcinoma; Papillary carcinoma; Immunohistochemistry.

Introduction

Serous papillary carcinoma of the endometrium (tubal type carcinoma, high grade papillary carcinoma, serous adenocarcinoma) is a special and unusual variant of uterine cancer, recently classed in the WHO/ISGP classification of endometrial tumors [1].

Serous papillary endometrial carcinoma (SPEC) comprises 1-7% of all uterine cancers and represents a highly aggressive form of endometrial adenocarcinoma [2-5]. On the microscopic level SPEC presents similar morphology to ovarian serous papillary carcinoma, although ultrastructurally this cancer shares characteristics with both ovarian and endometrial adenocarcinomas [6, 7].

In view of the implications of the diagnosis of SPEC for prognosis and therapy this neoplasm must be distinguished from a variety of benign and malignant papillary proliferations of the endometrium, such as villoglandular or clear cell adenocarcinoma as well as secondary neoplastic lesions such as tubal or ovarian cancer [8].

The aim of this study was to present the clinical and pathological characteristics of nine cases of SPEC with special emphasis on certain immunohistochemical characteristics which permit a correct diagnosis.

Materials and Methods

From January 1993 to December 1998, 133 women with endometrial cancer were evaluated and treated at the 2nd Clinic of Obstetrics and Gynecology at Areteion University Hospital. Nine cases were diagnosed as PSEC. The hospital records were reviewed for clinical information such as previous medical history, symptoms, diabetes, hypertension, weight, hormonal treatment and various laboratory examinations such as pap smear test, diagnostic curettage, CA125 levels, computed tomography and U/S studies executed at the time of the patients admission to the hospital. All patients underwent total abnormal hysterectomy, bilateral salpingo-oophorectomy and epiploectomy. In one case sigmoidectomy was performed as well because of colon involvement by the neoplasm. Abdominal and para-aortic lymph node sampling was done in all cases and peritoneal washings were examined cytologically.

Histological sections of all the specimens, stained with hematoxylin-eosin, were retrieved from the files of the Pathology Laboratory and re-evaluated by two pathologists (A.P. and A.K.P.). The histological grade and extent of the disease were evaluated based on the depth of invasion, lymphovascular invasion, involvement of isthmus-cervix, adnexal involvement, and lymph node status, as well as the status of the free-of-disease endometrium. All cases conformed to the diagnostic criteria for SPEC, because the disease was located predominantly to the uterine cavity and the ovarian involvement if existent was superficial in the cortex or confined to the lymphatics of the ovarian hilus. Nuclear grading and depth of invasion were assessed in all cases according to the revised FIGO system for endometrial carcinoma (1988) [9].

Lymphovascular involvement was proven by the presence of complete endothelial covering of the suspicious spaces and by immunostaining for factor 8. Immunohistochemical studies were performed in paraffin blocks retrieved from the files, by a streptavidin-viotin method for the detection of vimentin (ENZO monoclonal ab), secretory component (DAKO polyclonal ab), CEA (DAKO monoclonal ab), EMA (DAKO monoclonal ab).

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The hormonal receptor status, assessed by appropriate positive and negative controls, was studied as well. The presence of mucin and glucogen was studied by histochemical methods, PAS, PAS diastase and mucicarmine.

Results

The incidence of SPEC in our Clinic was 6.77%. Mean age of patients was 65.5 years (range 54-82 yrs). All patients were postmenopausal, six were obese, two presented hypertasis. No one was under HRT or estrogen therapy and all had children. Three patients reported repeated metrorrhagias. All patients were investigated by computer tomography and ultrasonography. The results of these studies were consistent with ovarian cancer (in 6/9 cases) while the diagnosis of endometrial cancer was considered in 3/9 cases. In the three cases with the main symptom of metrorrhagia, a diagnostic curettage was performed which showed poorly-differentiated endometrial carcinoma. In 6/9 cases, the Ca 125 levels were elevated and in 3/9 cases they were within the normal range.

During exploratory laparotomy, in 7/9 cases an extensive uterine carcinoma was observed that infiltrated the adnexa and the omentum, as well as the serosa of the sigmoid colon in one case. No evidence of lymph node metastases was found and a sampling of para-aortic and pelvic lymph nodes was done which proved negative for metastatic disease. Clinical staging showed that 2/9 cases were Stage I, 4/9 cases were Stage III and 3/9 cases were Stage IV. Six patients received adjuvant chemotherapy and three patients received chemo- and radiotherapy. A follow-up of at least three years was available. Six patients died within three years after surgery with disseminated disease, and one patient died from unrelated causes. No correlation between survival and clinical stage of the disease was found. Re-evaluation of histological sections confirmed the diagnosis of SPEC (Figure 1). A focal clear cell change was observed although no glycogen was demonstrated (Figure 2). In 4/9 cases, there was an element of endometrioid differentiation of the carcinoma present in more that 10% of the tumor mass examined, and these tumors were designated as mixed-type adenocarcinomas.

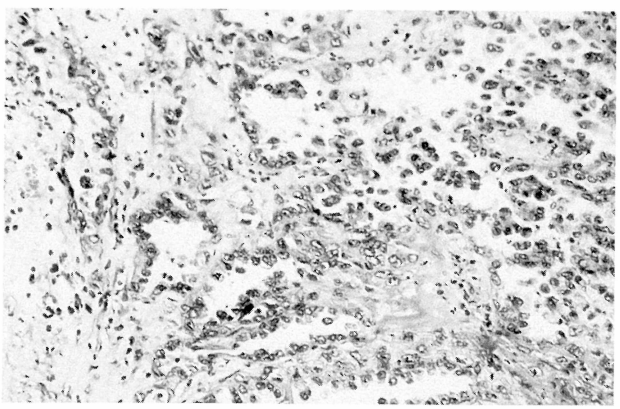

Figure 1. — Histological section of a serous papillary endometrial adenocarcinoma (HE x 100).

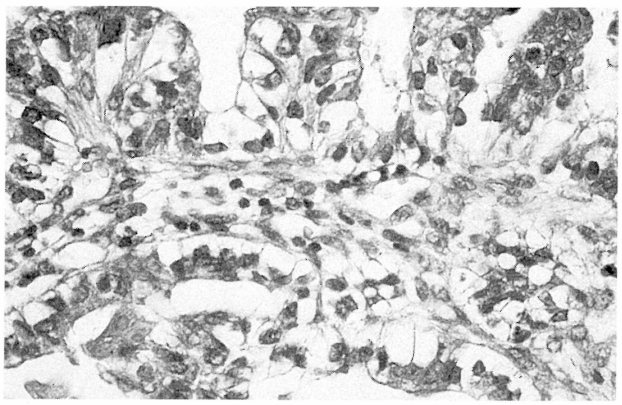

Figure 2. — Histological section of a serous papillary adenocarcinoma with focal clear cell morphology (HE x 250).

Seven tumors were nuclear grade III and two were nuclear grade II. In 6/9 cases, extensive infiltration of the myometrial wall greater than 1/2 of the thickness was observed. All cases presented a positive immunostain reaction to vimentin EMA and low molecular weight cytokeratins. A negative reaction for a secretary component, estrogen and progesterone receptors was observed. In 3/9 cases a positive immunostain reaction was observed in spaces infiltrated by neoplastic cells which proved to be vascular spaces.

Discussion

Endometrial cancer represents a heterogeneous group of neoplasms which is comprised of many distinct morphological variants. The most common variant is endometrioid cancer which represents the main hormonedependent adenocarcinoma of the uterus. Many other morphological types are encountered such as mucinous, endocervical, adenosquamous and clear cell, as well as serous papillary adenocarcinoma which represents a non hormone-dependent tumor [1]. This morphological variety is explained in view of the mullerian derivation of these tumors and the ability of the mullerian epithelium to differentiate in many epithelial types. There are case reports that describe the various characteristics of SPEC [6, 9, 10]. Special emphasis as to its aggressive biology and bad prognosis was reported in the series of Hendrickson *et al.* [2] established by the follow-up of 26 cases. Its striking similarity to ovarian papillary carcinoma even to the point of containing psammoma bodies, was emphasized together with strict criteria for the differential diagnosis among these cancers which permit the recognition of primary vs. secondary involvement of the uterus [11-16].

On the microscopic level, a distinct morphology with complex papillary folds, fine or broad, and a central core in the fibrovascular connective tissue can be observed. Small epithelial papillae and tufts are observed as well as a focal papilloglandular pattern with a slit-like lumina. Psammoma bodies are encountered in 30% of the cases.

In our cases no psammoma bodies were found. Cytologically these tumors are comprised of small or medium sized cells with round or pleomorphic nuclei with marked mitotic activity. In about 40% of these cases there is a deep myometrial invasion and extensive lymphatic infiltration, and this was observed in all of our cases.

The differential diagnosis must be made from non-neoplastic processes such as papillary syncytial metaplasia of the endometrium, characterized by blunt cellular histology and superficial growth as well as from various neoplastic processes such as villoglandular endometrioid adenocarcinoma and clear cell adenocarcinoma. In the villoglandular form of endometrioid cancer papillary formations are orderly and delicate with a smooth surface and columnar cells, pseudostratified with a low degree of nuclear atypia.

Clear cell adenocarcinoma of the endometrium is characterized by the presence of prominent clear cells with hobnailed morphology, containing epithelial mucin and glucogen. These cells may present a tubulocystic pattern with hyalinized cores but the cytologic morphology is usually characteristic and aids the correct diagnosis.

Immunohistochemistry is not especially helpful in the diagnosis, presenting immunostain patterns similar to other endometrial adenocarcinoma. A primary ovarian carcinoma must be excluded by careful examination of the ovaries. A characteristic of SPEC is its propensity for deep myometrial penetration (40% of the cases) and lymphatic extension (50-78% of the cases) without any uterine enlargement. In 35-50% of all cases during surgical exploration, the disease is found to be more extensive than the clinical examination showing involvement of the peritoneum, omentum, the diaphragm and other viscera.

In conclusion, serous papillary carcinoma is an unusual but distinct type of endometrial adenocarcinoma with aggressive biologic behavior. It is a non-hormonal-dependent tumor and its recognition is mandatory for a correct therapeutic approach.

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