Stage I ovarian carcinoma: different clinical pathologic patterns

Liane Deligdisch, M.D.,[a] *Frédérique Pénault-Llorca, M.D., Ph.D.,*[b] *Peter Schlosshauer, MD.,*[a] *Albert Altchek, M.D.,*[c] *Michele Peiretti, M.D.,*[d] *and Farr Nezhat, M.D.*[c]

[a] The Mount Sinai School of Medicine, Department of Pathology, New York, New York; [b] Centre de Lutte Contre le Cancer de la Région Auvergne, Department of Pathology, Clermont-Ferrand, France; [c] The Mount Sinai School of Medicine, Department of Obstetrics, Gynecology and Reproductive Science, New York, New York; and [d] University of Cagliari, Department of Obstetrics and Gynecology, Cagliari, Italy

Objective: To analyze clinicopathologic patterns of early ovarian carcinoma.
Design: Retrospective chart and histopathology review.
Setting: Mount Sinai School of Medicine, New York and the Centre Jean Perrin, Clermont Ferrand, France.
Patient(s): Seventy-six consecutive cases of Fédération Internationale de Gynécologie et d'Obstétrique stage I ovarian carcinoma.
Intervention(s): Surgical staging.
Main Outcome Measure(s): Symptomatology, pathology, and histology analysis.
Result(s): Twenty-two cases (29%) were serous papillary carcinomas and 54 were nonserous carcinomas (71%) (40 endometrioid, 10 clear cell, and 4 mixed endometrioid and clear cell carcinomas). Ninety-eight percent of ovarian endometriosis, 95% of endometrial carcinomas, and 83% of endometrial polyps and hyperplasias were associated with nonserous carcinomas. Most patients with serous papillary carcinoma presented with asymptomatic pelvic masses; patients with nonserous carcinomas presented with pelvic pain or abnormal vaginal bleeding with or without pelvic mass.
Conclusion(s): Over two thirds of stage I ovarian carcinomas were nonserous, and were diagnosed because of associated symptoms: pelvic pain with endometriosis and/or adnexal masses, or vaginal bleeding from endometrial pathology. Serous papillary carcinomas were often asymptomatic and diagnosed during follow-up evaluations in breast cancer patients. Stage I ovarian carcinoma has different clinical and pathologic patterns than advanced ovarian carcinoma. The risk of ovarian and endometrial malignancy should be taken into consideration during evaluation of patients with endometriosis and breast cancer histories. (Fertil Steril® 2007;88:906–10. ©2007 by American Society for Reproductive Medicine.)

Key Words: Stage I ovarian carcinoma, endometriosis, endometrial neoplasia

Ovarian neoplasms of epithelial origin represent the most common group of malignant ovarian tumors, among which serous carcinomas are the most prevalent. Often there is a delay in diagnosis such that the majority of cases are diagnosed in Fédération Internationale de Gynécologie et d'Obstétrique (FIGO) stages III and IV. Only approximately 24% of all ovarian carcinomas are diagnosed in FIGO stage I (1). This study of FIGO stage I ovarian carcinoma aims to correlate histopathologic patterns with the associated symptomatic pathology likely to have an impact on early diagnosis.

MATERIALS AND METHODS

The study included 76 consecutive patients diagnosed from 1998 to 2004 with FIGO stage I ovarian carcinoma (OC) at the Mount Sinai School of Medicine in New York (57 cases) and the Centre Jean Perrin in Clermont-Ferrand, France (19 cases). All patients underwent surgical staging and cytoreduction, including peritoneal washings. Histologic slides were reviewed by three pathologists who have expertise in gynecologic pathology (L.D., F.P-L., and P.S.). Clinical charts were reviewed, including each patient's initial evaluation and reasons for presentation.

Ovarian tumors were classified according to the World Health Organization (WHO) classification (2) and included ovarian serous papillary carcinoma (OSPC), ovarian endometrioid carcinoma (OEC), ovarian clear cell carcinoma (OCCC), and mixed endometrioid and clear cell carcinomas (MC). Tumor stage was assigned according to FIGO criteria (3). For papillary serous and endometrioid carcinomas, tumor grade also was categorized: well (G1), moderately, (G2) or poorly (G3) differentiated depending on the percentage of solid tumor components within the tumor tissue (less than

Received October 21, 2006; revised and accepted December 22, 2006.
Correspondence to: Farr Nezhat, M.D., Department of Obstetrics, Gynecology and Reproductive Science, The Mount Sinai School of Medicine, 1176 5th Avenue, 9th floor, Box 1170, New York, NY 10029 (FAX: 212-987-6386; E-mail: farr.nezhat@mssm.edu).

0015-0282/07/$32.00
doi:10.1016/j.fertnstert.2006.12.035

5%, 5% to 50%, or more than 50% solid tumor, respectively). Clear cell carcinomas were considered high grade (G3). Ovarian tumors of borderline malignancy were excluded from the review. Mucinous tumors were excluded from the review because most displayed features of borderline malignancy, and, in some of the reviewed cases, a coexisting or primary intestinal tumor could not be ruled out. In cases of synchronous endometrial and ovarian tumors, their independence was determined based on accepted criteria, including histologic dissimilarity, no or superficial myometrial invasion, absence of lymphvascular involvement, and no evidence of tumor spread elsewhere (1). Mixed carcinomas were defined as tumors exhibiting two or more different histologic subtypes with each component comprising at least 10% of the total tumor volume.

Additional pathologic findings such as endometriosis, in particular ovarian endometriosis adjacent to the ovarian tumor and endometrial pathology including endometrial carcinoma, endometrial polyps and/or hyperplasia, and associated benign tumors (adenofibroma, fibrothecoma, adenomyomas) were also analyzed.

Histologic findings were correlated with the following clinical data: symptomatic and asymptomatic pelvic masses, vaginal bleeding, gastrointestinal symptoms, ascites, history of breast cancer, BRCA germline mutations (when available), and age of the patients. For statistical analyses, chi-square tests were used. A P-value of $< .5$ was considered statistically significant. This study was approved by the Mount Sinai Institutional review board.

RESULTS

The histopathologic findings are summarized in Table 1. Among a total 76 cases of stage I ovarian carcinoma, 22 (29%) were OSPC and 54 (71%) were nonserous carcinomas (NSC), consisting of 40 OEC, 10 OCCC, and four MC subtypes. Twenty-three carcinomas were well differentiated (G1), 34 moderately differentiated (G2), and 19 poorly differentiated (G3).

Ovarian endometriosis was found in 40 cases, of which 39 were associated with NSC ($P<.0000001$). Sixteen of 17 cases of extraovarian pelvic endometriosis were present in NSC ($P=.038$). Endometrioid type endometrial carcinoma was diagnosed in 19 cases, of which 13 were synchronous tumors; the 18 cases with NSC ($P=.0086$) comprised 17 OEC and 1 OCCC. Most associated endometrial carcinomas were G2; no information was available on the degree of differentiation of four of six cases diagnosed prior to the ovarian carcinoma. Bilateral ovarian tumors (stage IB) were present in 11 OSPC and five NSC ($P=.00027$). Endometrial polyps and/or endometrial hyperplasia were found in 18 cases, of which three were OSPC and 15 NSC. Ovarian adenofibroma was diagnosed in eight patients, seven with NSC.

The clinical data are summarized in Table 2. The average age of the 22 OSPC patients was 61 years. Thirteen were asymptomatic, and pelvic masses were diagnosed on routine examinations; eight patients had a history of previous breast cancer and had been under medical surveillance with transvaginal sonograms. Two patients presented with painful pelvic masses, one with vaginal bleeding, two with increased

TABLE 1

Stage I ovarian carcinoma—pathology.

Pathology	OSPC n (%)	OEC n (%)	OCCC n (%)	MC n (%)	Total n (%)	*P* Value[a]	RR
Total	22 (30)	40 (53)	10 (13)	4 (5)	76 (100)		
Well differentiated (G1)	4 (5)	13 (17)	–	–	17 (22)		
Moderately differentiated (G2)	5 (7)	24 (32)	–	2 (3)	31 (41)	.031	1.97
Poorly differentiated (G3)	13 (17)	3 (4)	10 (13)	2 (3)	28 (37)		
Bilateral ovarian tumors	11 (14)	3 (4)	1 (1.3)	1 (1.3)	16 (21)	.00027	0.27
Ovarian endometriotic cyst	1 (1.3)	29 (38)	7 (9)	3 (4)	40 (53)	.0000001	23.33
Pelvic endometriosis	1 (1.3)	14 (18)	1 (1.3)	1 (1.3)	17 (22)	.038	6.05
Endometrial carcinoma	1 (1.3)	17 (22)	1 (1.3)	–	19 (25)	.0086	7.0
EC Well differentiated (G1)	–	2 (3)	–	–	2 (3)		
EC Moderately differentiated (G2)	–	7 (9)	1 (1.3)	–	8 (11)		
EC Poorly differentiated (G3)	1 (1.3)	4 (5)	–	–	5 (7)		
Ovarian Adenofibroma	1 (1.3)	5 (7)	2 (3)	–	8 (11)	n.s.	
Endometrial EP/EH	3 (4)	11 (14)	2 (3)	2 (3)	16 (21)	n.s.	

Note: OSPC = Ovarian serous papillary carcinoma; OEC = ovarian endometrioid carcinoma; OCCC = ovarian clear cell carcinoma; MC = mixed endometrioid and clear cell carcinoma; RR = relative risk; EP/EH = endometrial polyp/endometrial hyperplasia, n.s. = not significant.

[a] Incidence in OSPC compared to nonserous papillary carcinomas.

Deligdisch. Stage I ovarian carcinoma. Fertil Steril 2007.