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Serous and mucinous borderline ovarian tumors: are there real differences between these two entities?

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ABSTRACT

Objective: To evaluate the clinical outcome and pathological features of patients with borderline ovarian tumors (BOT) with special emphasis on serous and mucinous histology.
Study design: Medical and anatomopathological records were reviewed in the Gynecological Oncology Department of the Canarian University Hospital between 1990 and 2005. Survival rates were analyzed by using the Kaplan–Meier technique.
Results: The study included 163 patients. Serous tumors corresponded to 68 cases and mucinous tumors to 91 cases. Eighty-nine percent of patients were at FIGO stage I, 1.2% at stage II and 9.8% at stage III. Serous histology was significantly related to the presence of peritoneal implants (22.4% vs 3.6%; $p = 0.001$), positive peritoneal cytology (35.7% vs 8.5%; $p = 0.001$) and bilaterality (27.9% vs 1.1%, $p < 0.0001$). Event-free survival (EFS) rates at 2, 5 and 10 years were 96.7%, 92.7% and 90.5%, respectively, with a mean survival time of 183 months (CI 95% 172–193). Thirteen recurrence cases were found (7.9%) with a mean time to recurrence of 39.6 months (range 4–140). Overall survival (OS) rates at 2, 5 and 10 years were 100%, 96.4% and 93.6%, respectively, with a mean time of 189 months (CI 95% 179–198). Mucinous BOT were associated with significantly lower OS rates than serous BOT (10 years OS: 88.5% vs 98.2%; $p = 0.01$).
Conclusions: Serous tumors present more unfavorable anatomopathological characteristics but are associated with better prognosis than mucinous tumors. If mucinous BOT diagnosis is retained physicians should be aware that their aggressive potential is not negligible.

1. Introduction

Borderline ovarian tumors (BOT) or tumors of low malignant potential were first described by Taylor in 1929 [1]. They are characterized as tumors with proliferative activity of the epithelial cells, nuclear atypia, and absence or presence of intraepithelial carcinoma or microinvasion without obvious invasion of the stroma [2]. The last criterion is the basis on which BOT is actually distinguished from ovarian carcinoma. These tumors account for 10–15% of all ovarian tumors; they typically affect younger women, as compared with invasive epithelial ovarian tumors, and are mostly diagnosed at earlier stages, which results in a more favorable prognosis, however a small fraction of them are associated with poor prognosis and high mortality rates of 20–50% [3,4].

BOT can be histologically classified, according to their epithelial characteristics, as serous, mucinous, endometrioid, clear cell or Brenner tumors. Serous and mucinous tumors are the most frequent histotypes, accounting for more than 95% BOT [5]. Besides different histological appearances, these subtypes seem to have different etiology and behavior. In contrast to serous tumors – which seemingly have a sporadic origin – evidence suggests that mucinous ovarian cancer may arise via an adenoma-carcinoma sequence, from benign tumor through borderline tumor to invasive cancer [6]. However, published reports comparing serous and mucinous BOT are too scarce to reach firm conclusions about their clinical differences. The goal of the present report was to review the clinical outcome and pathological features of patients with BOT with special emphasis on serous and mucinous histology in order to assess whether real differences exist between both histological types.

2. Materials and methods

This is a retrospective analysis of women with BOT who were diagnosed and treated at the Gynecological Oncology Department of the University Hospital of Canary Islands over the 16-year period

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elapsing between January 1990 and December 2005. One hundred and seventy-four patients with borderline epithelial tumors were selected from an initial review of the gynecological cancer database and the clinical and histopathology records. Eleven of these patients were subsequently excluded: nine of them with concurrent neoplastic disease (4 endometrial carcinoma, 2 cervical carcinoma, 1 primary fallopian tube carcinoma, 1 breast carcinoma and 1 colon carcinoma), 2 cases of tumors with extraovarian origin—1 of them with a borderline tumor of the fallopian tube and 1 primary tumor of the appendix. Eventually, 163 women were included in this study. Mucinous histotype was the most frequently reported with 55.8% (91/163) of cases, while serous histotype corresponded to 41.7% (68/163) of cases. The remaining 2.5% corresponded to 4 patients—3 of them with endometrioid tumor and 1 with clear cell tumor.

BOT diagnosis was based on the histological criteria established by Hart and Norris and detailed by Skully [6,7]. All anatomopathological diagnoses were made by pathologist-gynecologists working at the University Hospital of Canary Islands. Microinvasion was defined as one or more foci of obvious stromal invasion $\leq 10\ mm^2$ area [8]. Peritoneal implants were classified as non-invasive or invasive depending on the absence or presence of stromal invasion of the peritoneum, respectively. Surgery was considered conservative when the uterus and at least a portion of one ovary were preserved. Conservative surgery was performed when early-stage disease was diagnosed and the patient desired to preserve fertility. Staging was considered complete when all peritoneal surfaces were carefully inspected and peritoneal washing, multiple random or oriented biopsies, omentectomy and appendectomy – in cases of a mucinous tumor – were performed. Staging was considered incomplete in all other cases, independently of the radical or conservative nature of the treatment. Surgical access was laparotomic or laparoscopic depending on the size of the tumor—tumors less than 10 cm were initially managed laparoscopically, independently of their bilaterality. Patients were staged according to classification of ovarian carcinomas established by the International Federation of Gynecology and Obstetrics [9]. All cases were clinically managed following a multidisciplinary approach.

Tumor markers were determined before surgical interventions. The levels of cancer antigen (CA) 125 were considered positive when >35 ng/ml. The CA19-9 and the carcinoembryonic antigen (CEA) were considered positive when >37 ng/ml and >5 ng/ml, respectively. Patient follow-up consisted in clinical examination, blood test for determination of tumor markers and ultrasonographic scan. Follow-up visits were scheduled every 4 months during the first 2 years following treatment; every 6 months during the following 3 years; and once a year afterwards. Event-free survival (EFS) was defined as the time, in months, from the date of the initial treatment to the date of recurrence. Overall survival (OS) was defined as the time, in months, from the date of the initial treatment to the date of the last medical review or to the date of death caused by the disease.

Statistical analysis was performed with the SPSS software, version 12.0 for Windows. Quantitative variables were compared by using Student's *t*-test or the Mann–Whitney test; categorical variables were compared by using the Chi-squared test or Fisher's exact test; survival rates were analyzed with the Kaplan–Meier technique; p values <0.05 were considered statistically significant.

Table 1
Clinical characteristics of patients with BOT with emphasis on serous and mucinous histotype (FH = family history, BMI = body mass index).

	All BOT	Serous BOT	Mucinous BOT	*p* (between histotypes)
Total number of patients	163	68	91	
Mean follow-up (months)	76.8 ± 47.8	80.3 (SD 48.4)	74.3 (SD 47.7)	0.4
Mean age at diagnosis	43 ± 15.6 (15–77)	40 (SD 13.7)	45.4 (SD 16.8)	0.03
Oncological PH	8 (4.9%)	2 (2.9%)	6 (6.7%)	0.5
Smoker	45 (27.6%)	13 (19.1%)	31 (34.8%)	0.03
Nulliparous	56 (34.4%)	30 (44.1%)	25 (27.8%)	0.03
Menopause status	49 (30.1%)	12 (17.6%)	37 (41.1%)	0.002
Average BMI	26 ± 5.1 (16.7–45.4)	26.1 (SD 5.2)	25.8 (SD 5)	0.7
Complaint upon admission				
Asymptomatic	54 (33.1%)	33 (52.4%)	19 (21.8%)	<0.0001
Abdominal pain	58 (36.7%)	21 (30.9%)	37 (41.1%)	0.2
Enlarged abdominal perimeter	31 (19%)	7 (10.3%)	23 (25.6%)	0.01
Other	10 (6.1%)	2 (2.9%)	8 (8.9%)	0.1
No data	10 (6.1%)	5 (7.4%)	4 (4.4%)	0.2
Tumor markers				
Normal	68 (41.7%)	24 (35.3%)	41 (45%)	0.2
Elevated	69 (42.3%)	31 (45.6%)	38 (41.7%)	0.2
Ca125	55 (79.7%)	30 (54.5%)	25 (31.6%)	0.007
Ca 19.9	34 (49.3%)	12 (21.8%)	24 (30.4%)	0.1
CEA	7 (10.1%)	0	7	0.1
No data	26 (15.9%)	13 (19.1%)	11 (12.1%)	0.2
Surgical approach				
Laparotomic surgery	110 (67.5%)	34 (53.1%)	73 (84.9%)	<0.0001
Laparoscopic surgery	28 (17.2%)	21 (32.8%)	7 (8.1%)	<0.0001
Conversion	16 (9.8%)	9 (14.1%)	6 (7%)	<0.0001
No data	9 (5.5%)	4 (5.9%)	5 (5.5%)	0.7
Treatment				
Conservative surgery	64 (39.3%)	28 (41.2%)	34 (37.4%)	0.3
Radical surgery	99 (60.7%)	40 (58.8%)	57 (62.6%)	0.3
Surgical staging	90 (55.2%)	39 (57.3%)	53.8% (49)	0.6
FIGO stage				
I–II	147 (90.2%)	54 (79.4%)	89 (97.8%)	<0.0001
III	16 (9.8%)	14 (20.6%)	2 (2.2%)	