

A retrospective study of 32 borderline ovarian tumours: The experience of a non-specialized centre

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Summary

Background: We evaluated the clinical features and treatment of patients with borderline ovarian tumors.

Methods: This was a retrospective review of the charts of 32 patients with borderline ovarian tumours that underwent surgery at the Department of Obstetrics and Gynaecology, "Tzaneio" General Hospital of Piraeus, over a 14-year period (1/1990-12/2003).

Results: Of the patients 62.5% were pre- or peri-menopausal. Mean age was 41.6 years. Five patients (15.63%) had undergone pelvic surgery (caesarean section not included) for unrelated reasons prior to the diagnosis of borderline tumour. Mean follow-up was 71.37 months and all patients showed up for their scheduled appointment during the first trimester of 2004. Pain was the presenting symptom in 37.5% (12/32) of patients. Twenty patients were diagnosed either by ultrasound (12.5%, 4/32) or during unrelated surgeries (50%, 16/32) and reported no relevant symptoms at the time of diagnosis. Treatment was conservative, comprised of either cystectomy (3/32), unilateral salpingo-oophorectomy (13/32), and unilateral salpingo-oophorectomy with myomectomy (1/32). Abdominal hysterectomy with bilateral salpingo-oophorectomy was performed in 15 patients for unrelated conditions (uterine pathology). Mucinous borderline tumours were identified in 11 patients (34.38%), serous borderline tumours in 17 patients (53.12%), and non-serous-mucinous borderline tumours in four patients (12.5%). Omentectomy was performed in two cases, biopsy of the contralateral ovary was performed in five cases and peritoneal washing in eight cases. Restaging surgery was performed at the Metaxa Anticancer Piraeus Hospital in 11 patients (34.38%). One patient who did not undergo a restaging operation had a recurrence of the disease.

Conclusion: Suboptimal staging remains a major problem during the initial operation in non-specialized centres in gynaecologic malignancies.

Key words: Borderline ovarian cancer; Staging; Treatment; Biopsy.

Introduction

Epithelial ovarian tumours that present with intermediate biologic behaviour have been identified as a separate group [1]. Since 1929 – when it was observed for the first time – patients who were considered terminal because the ovarian tumours had extended beyond the ovaries with wide peritoneal implants at initial laparotomy survived and were well for many years. The terminology for these tumours since their initial recognition has varied (low-grade non-invasive carcinoma, tumours of borderline malignancy, carcinoma of low-grade malignant potential, or tumours of low malignant potential [2]. The International Federation of Gynaecology and Obstetrics (FIGO) in 1971 characterised this group of tumours as carcinoma of low malignant potential [3]. In 1973 the World Health Organization (WHO) described them as borderline tumours [4]. Histologically, tumours of borderline malignancy display neither the cytologic anaplasia nor the destructive invasive growth typical of carcinoma; however, these tumours (serous in particular) often are associated with extra ovarian lesions of unknown pathogenesis, termed implants [5]. Reduced risk of borderline ovarian tumours is associated with increasing parity and lactation, while elevated risks of serous tumours appear with a high body mass index and use of unopposed estro-

gens. The effect of oral contraceptives used in borderline tumour prevalence is unclear as some investigators have found a positive effect [6] while others found no impact at all [7]. The aim of this study is to present our experience in the management of borderline ovarian tumours over a 14-year period.

Methods

We identified 32 patients who underwent surgery in the Department of Obstetrics and Gynaecology of "Tzaneio" General Hospital of Piraeus, with borderline malignancies of the ovary over a 14-year period (1/1990-12/2003). Inpatient and outpatient charts were reviewed fully and the relevant clinical information was extracted. Missing information was obtained from the patients at the time of a planned follow-up visit. The last follow-up visit was scheduled for all patients during the first trimester of 2004. Our hospital does not have an oncology department thus all patients after the initial diagnosis were sent for evaluation and further treatment at our nearby Oncology Hospital (Metaxa Anticancer Piraeus Hospital). Differences between means were evaluated using the Student's *t*-test with two-tailed *p* values. The level of significance was set at $p < 0.05$.

Results

Age at presentation ranged from 17-71 years with 62.5% of patients being pre- or peri-menopausal. Average age was 41.6 years. Patients had an average age at menarche of 11.28 years (range 9-15 years). The mean number of gestations was 2.31 (range, 0-9) and the mean parity

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was 1.47 (range, 0-5). Age at menarche, number of gestations, or parity did not appear to correlate with any of the clinical findings analyzed ($p > 0.1$). None of these patients had infertility problems (in the sense of undergoing an infertility investigation). Five patients (15.63%) had undergone pelvic surgery (caesarean section not included) for unrelated reasons prior to the diagnosis of borderline tumour. The average period between the original surgery and the diagnosis of borderline tumour was 13.66 years. The indication for the original pelvic surgery was a benign ovarian cyst in four of the cases. We could not detect any relatives with breast or ovarian cancer in the family history of the patients in the current study. Mean follow-up time was 71.37 months, and all patients showed up for their scheduled appointments during the first trimester of 2004. Pain was the presenting symptom in 37.5% (12/32) of patients. Seven patients presented with acute abdominal pain, consistent with the intraoperative finding of torsion. Twenty patients were diagnosed either by ultrasound (12.5%, 4/32) or during unrelated surgeries (50%, 16/32) and reported no relevant symptoms at the time of diagnosis. Treatment was conservative, comprised of either cystectomy (3/32), unilateral salpingo-oophorectomy (13/32), and unilateral salpingo-oophorectomy with myomectomy (1/32). Abdominal hysterectomy with bilateral salpingo-oophorectomy was performed in 15 patients for unrelated conditions (uterine pathology). Mucinous borderline tumours were identified in 11 patients (34.38%), serous borderline tumours in 17 patients (53.12%), and non serous-mucinous borderline tumours in four patients (12.5%, one endometrioid and three Brenner tumours). The size of the primary borderline ovarian tumours ranged from 25 mm to 220 mm, with a mean size of 103 ± 52.4 mm. The mean diameter of mucinous tumours was 119 ± 60.4 mm, and those of serous tumours were 91 ± 43.2 mm. Mucinous tumours were significantly larger than serous tumours ($p < 0.05$). The size of the endometrioid tumour was 68 mm and the size of the three Brenner tumours was 28, 34 and 39 mm. Because malignancy was not suspected at the initial operation, the abdomen was not properly explored. Omentectomy was performed in two cases, biopsy of the contralateral ovary was performed in five cases and peritoneal washing was performed in eight cases. Restaging surgery was performed at the Metaxa Anticancer Piraeus Hospital in 11 patients (34.38%). One patient who did not undergo restaging surgery presented seven years after the initial operation with a contralateral pelvic mass and underwent contralateral salpingo-oophorectomy with restaging.

Discussion

Borderline tumours of the ovary tend to occur at a younger age than their invasive counterparts [8].

In the current study the mean age at diagnosis was 41.6 years, with 62.5% of patients being pre- or perimenopausal, and 43.75% of the patients presenting prior to the age of 40 years. There was no significant

difference in mean age observed between patients with serous and mucinous types of tumours. Independent prognostic factors in patients with epithelial ovarian borderline tumours without residual tumour after primary surgery are: DNA ploidy, morphometry, FIGO stage, histologic type, and age [9]. Reproductive potential is a major concern to many patients with borderline tumours. Conservative surgery has a positive influence on the quality of life of those patients who can become pregnant and deliver. In our study 11 patients (34.37%) at the time of surgery were nullipara, and five of them had never been pregnant (15.63%). Eight patients of the nullipara group became pregnant after treatment with conservative management, with one patient developing recurrent disease seven years after the initial surgery and two years after delivery. Surgical resection is the preferred treatment for recurrent disease. Nearly all patients with recurrent borderline ovarian tumours have recurrent disease inside the abdominal cavity. Distant metastasis is an exception. In some patients, borderline ovarian tumour recurs as borderline ovarian tumour (as happened in our case in the contralateral ovary), but in some cases it progresses to invasive carcinoma. Invasive recurrences should be treated identically to recurrences of ovarian carcinoma. The presence of persistent or recurrent disease correlated with multifocality and involvement of resection margins. Multifocality may be a strong predictor of the failure of cystectomy to control the disease. In our study multifocality was present in two cases that underwent abdominal hysterectomy. No recurrence of disease was seen in ovaries from which a single cyst had been removed with negative resection margins. In our study all three patients that underwent cystectomy had negative resection margins. Four patients with serous borderline tumours had bilateral disease at the time of diagnosis, with one recurring in the contralateral ovary seven years after diagnosis. None of the patients with mucinous tumours or non serous-mucinous borderline tumours had bilateral disease. Large differences have been reported in the distribution of the different histological subtypes. In our study serous tumours seemed to be the majority of borderline tumours, but other reports with an efficient number of patients found mucinous tumours to be the majority of borderline tumours [10, 11]. In our study we found a high prevalence of Brenner tumours of borderline malignancy compared with other studies, but due to the low number of patients involved in this study, no conclusive comments can be made. Mucinous tumours were significantly larger than serous tumours ($p < 0.05$) in our study. This observation is similar to that reported in another study [12], though the mean size in our study was lower for both subtypes. All our patients underwent laparotomy. A minimally invasive surgical procedure is regarded as the appropriate therapeutic approach for borderline ovarian tumours. Ovariectomy is preferred to cystectomy since establishing the diagnosis of a borderline ovarian tumour requires histological evaluation of the stroma. It seems

that laparoscopic treatment in borderline ovarian tumours should be reserved for masses not greater than 5 cm. When conservative therapy is desired, the entire affected ovary should be removed. If the neoplasia is bilateral, cystectomy could be allowed in women who wish to preserve fertility, although they are at high risk of relapse [13]. Unlike port-site metastasis in other gynaecologic malignancies, the prognosis in patients with a port-site implantation after laparoscopic management of a borderline ovarian tumour is excellent. The treatment of this complication is surgical resection [14]. Thirty of the patients (93.75%) in our study did not have visual implants of any kind in the abdominal cavity. In two patients who were scheduled for hysterectomy for unrelated conditions, omentectomy was performed due to multiple peritoneal implants. Restaging surgery was performed at the Metaxa Anticancer Piraeus Hospital in 11 patients (34.38%), and only one patient was staged as Stage II. If borderline ovarian tumours are localised to one or both ovaries (FIGO, Stage I), the prognosis is excellent [15]. Women who initially were diagnosed with Stage IA disease and who had serous borderline tumours or underwent cystectomy appeared to derive the most benefit from restaging surgery. Nonetheless, the indications for restaging surgery remain controversial, as no difference in recurrence rate was observed between women who underwent restaging and those who did not [16]. Restaging could probably be omitted if the peritoneum is clearly reported as "normal" during the initial surgery, in the absence of a micropapillary pattern, and if the patient agrees to be carefully followed-up [17]. None of our patients underwent adjuvant chemotherapy, since chemotherapy has not been proven to prolong long-term survival. None of our patients died during the study period, but it should be mentioned that 11 of them underwent surgery during the previous five years. Sub-optimal staging is one of the major problems of this study. Because malignancy was not suspected at the initial operation, even in cases scheduled for operation, biopsies and peritoneal washing were not part of our protocol. The reasons for a relatively low rate of staging biopsies among obstetrician-gynaecologists worldwide remain unclear. Possible explanations include a view that ovarian serous borderline tumours behave in a benign fashion regardless of stage, a view that postoperative treatment is unnecessary or ineffective for patients with peritoneal implants, or the fact that training with respect to the biologic behaviour of borderline ovarian tumours has been ineffective [18].

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