The Clinical Usefulness of DNA Aneuploidy in Borderline Ovarian Tumours

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We read with great interest the article by Ewald-Riegler et al. [1] on borderline ovarian tumours (BOT), which found intraoperative tumour rupture, incomplete staging and fertility sparing surgery to be risk factors for disease recurrence. Previous work has suggested that DNA ploidy is an important prognostic factor in BOT; a study by Kaern et al. [2] contained 370 patients with BOT and found that DNA ploidy, stage, histological type and age were significant prognostic factors. DNA ploidy appeared to be a powerful prognostic indicator; patients with aneuploid tumours had a 19-fold increased risk of death compared to patients with diploid tumours.

With a view to ascertaining the prevalence and prognostic value of ploidy, we identified 70 patients who presented with borderline ovarian tumours at the Nottingham City Hospital, United Kingdom, over a 12-year period. These patients were identified using the hospital pathology database. Of the 70 patients studied, 28 patients had serous BOT 28 (40%) and 42 patients had mucinous BOT (60%). The patients were staged as follows: FIGO stage IA 51 patients (73%), IB 6 patients (9%), IC 6 patients (9%), II 1 patient (1%), III 6 patients (9%). 43 patients (61%) underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy (TAH/BSO). 10 patients (14%) had a bilateral oophorectomy and omentectomy. 17 patients (24%) had a unilateral oophorectomy and biopsy of the contralateral ovary and 11 of these patients had a TAH/BSO after completion of their family planning. No patients developed recurrent disease after a mean follow up period of 69.5 months (range 16–177 months). 7 patients (10%) died of causes other than BOT.

Thirty-micron sections were cut from formalin-fixed, paraffin embedded tissue blocks for each patient and single nuclei suspensions were prepared. Nuclear DNA content was measured in a FACScan flow cytometer using Cell QUEST software. Aneu-

ploidy with a DNA index of 1.9 was detected in only 1 patient. This patient, who had a stage IA serous BOT, is alive without any recurrence after 96 months of observation following TAH/BSO. All the remaining 69 tumours showed diploid DNA content. The coefficient of variation for the diploid peaks ranged from 7.48 to 12.8 (mean 8.67) in diploid histograms despite using a low flow rate.

A recent review [3] stated that the primary treatment modality for the management of BOT is surgery. Based on the prognostic importance of DNA ploidy suggested by Kaern et al. [2], the same review recommends the analysis of DNA ploidy in their management algorithm. Whilst we recognise the prognostic importance of DNA ploidy, in our experience it unlikely to be a useful clinical discriminator due to a low prevalence rate; only 1 of our 70 patients (1.4%) had DNA aneuploidy. The aneuploidy rate was 9% in the study by Kaern et al. [2] which might be attributed to larger sample size, observer bias in identifying and grading BOT, differences in study population, histological type, tumour stage at presentation, study methodology and various biases inherent in retrospective studies. A multicentre prospective study with central pathology review is needed to confirm the prevalence and prognostic value of ploidy before ploidy is used routinely in treatment algorithms.

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Disclosure Statement

None of the authors have any conflicts of interest to declare.

References

- 1 Ewald-Riegler N, du Bois O, Fisseler-Eckhoff A, Kommoss F, Harter P, Traut A, Hils R, du Bois A: Borderline tumors of the ovary: clinical course and prognostic factors. *Onkologie*. 2012;35:28–33.
- 2 Kaern J, Tropé CG, Kristensen GB, Abeler VM, Pettersen EO: DNA ploidy: the most important prognostic factor in patients with borderline tumors of the ovary. *Int J Gynecol Cancer* 1993;3: 349–358.
- 3 Cadron I, Leunen K, Van Gorp T, Amant F, Neven P, Vergote I: Management of borderline ovarian neoplasms. *J Clin Oncol* 2007;25:2928–2937.