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Editorial

Chemotherapy for Ovarian Germ Cell Tumours

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Evaluation of new treatment schemes for rare malignancies represents a major problem in medicine. Collection of a sufficient number of patients always brings with it a heterogeneity of detection methods, histomorphological classifications, surgical treatment and follow-up. In single institutional studies, this is produced by changes in medical practice over decades, and in multicentre studies, by individual differences of the participating centres.

Malignant ovarian germ cell tumours comprise a variety of histologically different types, which are derived from the primitive germ cells of the embryonic gonads (Figure 1). They represent less than 5% of all malignant ovarian tumours, of which dysgerminomas and endodermal sinus tumours are the most frequent subtypes. As they usually occur in adolescence or early adulthood, decisions on treatment represent a challenge to the gynaecological oncologist.

In spite of their different histomorphological features, ovarian germ cell tumours are, in most cases, sensitive to cytotoxic agents. Even extensive metastatic disease can be cured with the use of chemotherapy, and prognosis has been improved drastically. In combination with systemic therapy, less aggressive, fertility preserving, surgical procedures have become possible. Three-year survival in patients with stage II–IV disease is now more than 80% when effective chemotherapy has been given after surgery [4]. Until now, a combination of cisplatin, vinblastine or etoposide and bleomycin (PVB or BEP) is commonly used in these patients [5]. However, toxicity of this regimen is high, and pulmonary fibrosis caused by bleomycin is a common long term side-effect and can even lead to the death of the patient. Thus, the optimal drug combination has not yet been determined. For those few patients who do not respond to first-line chemotherapy, dose intensified regimens with autologous bone marrow transplants or the use of phase II drugs has been recommended.

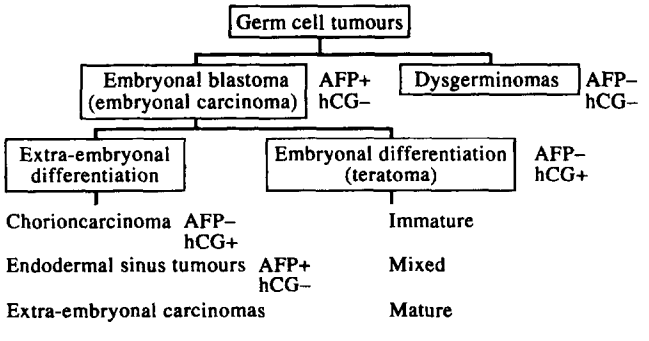

Figure 1. Classification of germ cell tumours of the ovary [1–3] and their secreted markers. AFP, α-fetoprotein; hCG, human chorionic gonadotrophin.

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However, if one reviews the literature on systemic treatment of malignant ovarian germ cell tumours, the aforementioned problem of recruitment of patients with rare disease becomes evident. The majority of the authors report on less than 30 patients. In these small numbers, different stages of disease are included and regimens are used as first- or second-line treatments. As such, the study of Bower and associates in this issue of the Journal (pages 593–597) is of major interest. The number of 59 chemotherapy naive patients is considerably high for a single institution study. While recruitment occurred over 17 years, the authors state that all tumours were staged and evaluated according to the same criteria, and surgical procedures were not changed during this time.

They chose a cytotoxic regimen, according to modern concepts of how to improve the effectiveness of chemotherapies. Development of drug resistance is thought to be the major cause of relapse in ovarian cancer, and can be overcome by dose intensification. As increasing doses would lead to unacceptable toxicity, they combined myelotoxic drugs (actinomycin D, etoposide and cyclophosphamide (ACE)) and alternated this with a combination of less myelotoxic drugs (vincristine, methotrexate, bleomycin and cisplatin, (POMB)). Thus, two distinct regimens could be administered in parallel with tolerable toxicity, and the tumours were

exposed to seven different drugs which are, in part, not cross-resistant. Due to the alternating application scheme, all drugs could be given in an effective dose. Dose intensification was obtained without increased toxicity. Only 1 patient died due to a late toxicity of etoposide by developing a secondary acute myeloid leukaemia.

The achieved result of a 3-year survival rate of 88% with POMB/ACE as first-line treatment excludes patients with stage IA disease and are therefore comparable with published results of PVB or BEP. Fertility was preserved in those patients with conservative surgery and menstruation returned 2–6 months after the end of treatment. As a randomised trial comparing BEP with this new treatment scheme is not suitable due to the small number of patients, we have to wait for reports of experiences in other institutions before POMB/ACE can be considered as a standard treatment option in malignant ovarian germ cell tumours.

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