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Prognostic factors in women treated for ovarian yolk sac tumour: A retrospective analysis of 84 cases

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ABSTRACT

Background: Ovarian yolk sac tumour (OYST) is a very rare malignancy arising in young women. Our study aimed to evaluate long-term outcomes and to identify prognostic parameters likely to help make appropriate risk-based decisions about therapy in this disease.

Methods: This retrospective study is based on prospectively recorded OYST cases at the Institut Gustave-Roussy. A univariate analysis using the logrank test evaluated possible associations between survival and patient or disease covariates. The multivariate analysis was performed using the Cox proportional hazard regression method.

Results: Between 1976 and 2006, 84 patients were registered. Since 1991, most of the patients have undergone fertility-sparing surgery. With a median follow-up of 71 months, the overall 5-year and event-free survival rates are 84% and 79%, respectively. In the multivariate model only the absence of ascites and a favourable serum AFP decline rate were significantly associated with better overall survival.

Conclusions: Patients with a poor prognosis factor such as an unfavourable serum AFP decline may be considered for aggressive treatment whereas those with good prognostic factors could be given less courses of chemotherapy.

1. Introduction

Ovarian yolk sac tumours (OYSTs) are very rare (incidence rate of 0.048/100,000 women-years) occurring mostly in adolescent and young women. They account for 20% of malignant ovarian germ cell tumours (MOGCTs), and are the second most frequent histological subtype of MOGCTs, after ovarian dysgerminoma. Most OYSTs are pure neoplasms although mixed MOGCTs, including a yolk sac component, are not uncommon. Elevated serum alpha-feto-protein (AFP) is one of the hallmarks of OYSTs and positive staining on tissue microarray sections facilitates the diagnosis. OYSTs may

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carry a worse prognosis amongst MOCGTs.[1] Before the era of modern chemotherapy, overall survival (OS) at 3 years was 13%.[2] Cisplatin-based multi-agent chemotherapy has dramatically improved the prognosis of MOGCTs. In the 1990s, the combination of bleomycin, etoposide and cisplatin (BEP) was shown to be highly active against MOGCTs and became the standard treatment for these tumours.[3,4] We recently confirmed these results for the subset of OYSTs: a 5-year OS rate of 94% was observed after surgery followed by BEP chemotherapy.[5]

In mixed OYSTs, the prognosis is thought to result from the YST component.[6] However, very little is known about prognostic factors for OYSTs because the rare published series of OYSTs usually comprises less than 50 patients.[6]

Here, we aimed to study prognostic factors and long-term outcomes in 84 patients treated for an OYST.

2. Methods

2.1. Patient population

This retrospective study is based on prospectively recorded OYST cases at the Institut Gustave-Roussy (IGR, Villejuif, France). Between 1976 and 2006, 84 patients with pure or mixed OYSTs were either treated at IGR or referred there for advice on therapy after surgery.

We chose to include only postpubertal cases because some studies have reported that the physiopathology of OYSTs occurring in children and young women could be different.[7] Information concerning all patients was abstracted from the medical records in accordance with local regulations. Information on the last physician visit reporting the tumour status, menstrual history, hormonotherapy and reproductive history was requested from the corresponding physicians in a questionnaire, for patients who were not followed up at the IGR.

2.2. Staging and tumour classification

Tumours were staged according to the International Federation of Gynecology and Obstetrics (FIGO) staging system for ovarian cancers.[8] The histological type was defined according to the WHO classification.[9] All pathologic samples were centrally reviewed at the IGR before 1990. Subsequently, the pathologic samples of 12 patients referred for treatment were not reviewed because the diagnosis was made in academic hospitals. Most of the stage I lesions had not been properly assessed according to FIGO recommendations in patients referred after surgery, especially regarding peritoneal cytology. Stage Ia was therefore defined as a tumour strictly limited to one ovary, with an intact capsule, without ascites and no tumour cells in peritoneal cytology when available. Stage Ic tumours were strictly limited to one ovary but exhibited capsular rupture or ascites >100 mL or ascites with tumour cells, when available.

2.3. Treatment and tumour response

Most of the patients underwent initial surgery at the local hospital and were referred to the IGR thereafter. The majority of them were operated on using a single ovarian procedure without staging surgery. In such cases, completion surgery and restaging were reconsidered only after initial chemotherapy. The presence and the size of residual disease were determined based on the analysis of surgical reports and postoperative imaging studies.

In our institution, surgical paradigms evolved over time. Before the era of highly effective chemotherapy, surgical guidelines recommended radical surgery with bilateral salpingo-oophorectomy, hysterectomy, lymphadenectomy and omentectomy. During the 1990s, given the very good results observed with BEP chemotherapy, a less invasive surgical procedure was advocated in order to spare fertility whenever possible in these young patients. Nowadays, in early-stage disease, our surgical guidelines recommend unilateral salpingo-oophorectomy with peritoneal staging procedures (routine peritoneal cytology, multiple peritoneal biopsies and omentectomy). In advanced disease, unilateral salpingo-oophorectomy, omentectomy and resection of macroscopic lesions on the peritoneum with a fertility-sparing intent should be attempted whenever possible.

Chemotherapy was according to standardised protocols. Most patients received platinum-based combination chemotherapy. Some patients were included in a prospective phase II trial conducted between 1985 and 1990 with high-dose cisplatin consisting of two doses of cisplatin along with vinblastine, bleomycin and etoposide (PVeVB).[10] Since 1996, BEP has become our standard chemotherapy regimen.

Patient follow-up included a clinical examination, blood marker measurements and imaging at least every 3 months during the first year following treatment and at gradually increasing intervals thereafter. A 2-year interval from the end of treatment was strongly advised before allowing pregnancy.

2.4. Serum AFP decline

The half-life of serum AFP was calculated at point 1 after surgery before the first chemotherapy cycle and at point 2 immediately before the second cycle of chemotherapy. AFP values were plotted semi-logarithmically, and the half-life of the AFP decline was calculated between each point using a calculation module MONOTOR-IT – REMISOL (Beckman Coulter Inc.). The method of half-life determination used was derived from the Lange half-life formula ($T_{1/2} = 0.693/M$), where M represents the slope of the line between any two marker values (X and Y), using the following equation $M = \ln X - \ln Y/\text{days}$ between X and Y.

Patients were classified as having an unfavourable AFP decline if the half-life of AFP was >10 days. The marker decline was deemed favourable if the half-life of AFP was $\leqslant$10 days. Patients with AFP normalisation prior to chemotherapy were classified in the favourable group.

2.5. Statistical analysis

Survival curves were calculated using the method of Kaplan–Meier. OS was calculated from the date of the diagnosis to the time of the last follow-up or death. Event-free survival (EFS) was calculated from the date of the diagnosis to the date of