European Journal of Cancer 91 (2018) 30–37

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Paediatric dysgerminoma: Results of three consecutive French germ cell tumours clinical studies (TGM-85/90/95) with late effects study

Gwénaëlle Duhil de Bénazé [a], Hélène Pacquement [a], Cécile Faure-Conter [b], Catherine Patte [c], Daniel Orbach [a], Nadège Corradini [b], Claire Berger [d], Hélène Sudour-Bonnange [e], Cécile Vérité [f], Hélène Martelli [g], Brice Fresneau [c,h,*]

[a] *Institut Curie, Pediatric Adolescent Young Adult Department, Paris, France*
[b] *Institut D'Hemato-oncologie Pediatrique, Department of Pediatric Oncology, Lyon, France*
[c] *Gustave Roussy, Department of Pediatric Oncology, F94805 Villejuif, France*
[d] *Centre Hospitalier Universitaire, Department of Pediatric Oncology, St Etienne, France*
[e] *Anti-Cancer Center Oscar Lambret, Pediatric Oncology Unit, Lille, France*
[f] *Pellegrin Hospital, CHU Bordeaux, Pediatric Hematology-Oncology Unit, Bordeaux, France*
[g] *Centre Hospitalier Universitaire, Department of Pediatric Surgery, Le Kremlin-Bicêtre, France*
[h] *Université Paris-Saclay, Univ. Paris-Sud, CESP, INSERM, Villejuif, F-94805, France*

Received 21 July 2017; received in revised form 4 October 2017; accepted 27 November 2017

KEYWORDS
Dysgerminoma;
Ovarian tumours;
Clinical study;
Late effects;
Children

Abstract ***Methods:*** French patients (≤18years) treated for dysgerminoma between 1985 and 2005 in TGM-85, 90, 95 protocols were included. Treatment was based on primary unilateral oophorectomy followed by prophylactic lymph node irradiation (1985–1998) or a wait-and-see strategy (1998–2005) for localised completely resected tumours (pS1) or by platinum-based chemotherapy for advanced diseases.

Results: Forty-eight patients (median age 12.8 years) were included. Six patients had gonadal dysgenesis. Two had bilateral dysgerminoma. Twenty-eight patients had loco-regional dissemination, seven with para-aortic lymph nodes. None had distant metastases. Primary surgery was performed in 47/48 patients. Among the 15 patients with pS1 tumour: seven did not receive adjuvant treatment, six had lymph node irradiation and two received chemotherapy. Among the 32 patients with advanced tumour, 31 received cisplatinum-based (n = 25) or carboplatin-based (n = 8) regimen with lymph node irradiation for one of them and one did not receive adjuvant treatment. With a median follow-up of 14 years, all patients are alive

* *Corresponding author*: Department of Pediatric Oncology, Gustave Roussy, 114 rue Edouard Vaillant, 94805 Villejuif, France. Fax: +33 (0)1 42 11 53 28.
E-mail address: brice.fresneau@gustaveroussy.fr (B. Fresneau).

https://doi.org/10.1016/j.ejca.2017.11.030

in complete remission. Five events occurred: 2 contralateral dysgerminomas, 1 peritoneal relapse and 2 second neoplasms (teratoma and melanoma). Bilateral oophorectomy was necessary for 12 patients. Desire of pregnancy was expressed for 17/36 patients with unilateral oophorectomy, which succeeded in 13 cases (5 medically assisted). 2/17 had ovarian failure. The renal function was normal in 24/25 evaluated patients treated with platinum, ifosfamide or irradiation. The hearing function was evaluated on 17/36 patients treated with platinum: 12 Brock grade-0, 3 brock grade-1 and 2 grade-4.

Conclusion: Dysgerminoma has an excellent prognosis even in advanced cases with conservative surgery and platinum-based chemotherapy. However the disease and/or treatment resulted in a high rate of bilateral oophorectomies and a significant impact on future fertility.

1. Introduction

Malignant germ cell tumours (GCT) are rare and represent 3% of the malignant tumours in children [1,2]. Among ovarian GCT, pure dysgerminoma is the most frequent histological type in adults [3] but is rare in children [4–6]. Treatment of dysgerminoma is based on conservative surgery [7]. Radiation therapy used to be the standard adjuvant treatment. Since 1985, the French Society of Pediatric Oncology (SFOP) then called SFCE (*Société Française de Lutte contre les Cancers et les leucémies de l'Enfant et de l'adolescent*) progressively replaced radiotherapy by adjuvant chemotherapy to limit long-term sequelae [8]. Moreover, the SFOP reduced indications of adjuvant treatment to patients with advanced disease. We report here the results of the combined analysis of the three successive SFOP-SFCE germ cell tumours clinical studies for patients treated for pure dysgerminoma and present long-term survival and late effects data.

2. Patients and methods

Between 1985 and 2005, French children and adolescents (aged ≤18 years) with pure dysgerminoma were prospectively registered in the three successive SFOP-SFCE clinical studies for GCT: TGM85 (01/1985-12/1989), TGM-90 (01/1990-12/1994) and TGM-95 (01/1995-12/2005). Results of these protocols regarding non-seminomatous GCT and sex cord tumours have already been published [9–13].

The diagnosis of dysgerminoma was made histologically, based on the surgical specimen. No systematic but on-demand central histological review was organised. Serum tumour markers assessment was recommended before any surgery: alpha-fetoprotein (αFP), human chorionic gonadotropin (HCG) and free beta unit of HCG (HCG-β). A karyotype was performed if a disorder of sexual development was suspected. Loco-regional and metastatic tumour spread was assessed by abdominal ultrasound, chest X-ray and/or CT scan.

Primary resection of the tumour was recommended when disease was localised and when a complete and conservative surgery (without a contralateral oophorectomy nor a hysterectomy) was feasible. The recommended surgical procedure was an oophorectomy or a salpingo-oophorectomy after sampling of peritoneal fluid for cytology and careful evaluation of the contralateral ovary and peritoneal surfaces. A protected biopsy was performed if conservative surgery was unfeasible. The therapeutic guidelines for adjuvant treatment were based on the tumour stage, including the post-operative tumour nodes metastases staging system (Table 1) for patients with primary resection. For localised completely resected tumours (pS1), adjuvant radiation therapy (20 Gy to ipsilateral iliac and lumbar-aortic lymphatic chains, +/−supraclavicular area irradiation) was recommended in TGM85, 90 and 95 until 1998. After 1998, a wait-and-see strategy was proposed. For advanced diseases (incompletely resected tumours, loco-regional invasion or metastasis), three cycles of an adjuvant platinum-based chemotherapy were recommended, according to protocol (Table 2). A 'second look' surgery was recommended only in the TGM-85.

All data were prospectively registered in the TGM databases. To obtain long-term follow-up data, patients were contacted by letter after agreement of their reference

Table 1
SIOP (International Society of Pediatric Oncology) post-operative staging system.

Stage PS1	Disease limited to the primary gonadic site and completely excised. Negative peritoneal washing for ovarian tumours. No clinical, radiological, surgical or histological evidence of disseminated disease.
Stage PS2	Disease spread beyond the primitive gonadic site, with or without lymph node involvement, and completely excised. Negative peritoneal washing for ovarian tumours. No metastatic disease.
Stage PS3	Disease spread beyond the primitive gonadic site but not completely excised. No metastatic disease.
- PS 3a	With microscopic residuals.
- PS 3b	With macroscopic residuals or positive peritoneal washing.
Stage PS4	Metastatic disease.