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REFLECTION

Is fertility sparing surgery a treatment option for premenopausal patients with dysgerminoma?

Iavazzo C[1], Vorgias G[2], Iavazzo PE[3], Gkegkes ID[4]

Gynaecological Oncology Department, Northampton General Hospital, Northampton, United Kingdom.
christosiavazzo@hotmail.com

ABSTRACT
Dysgerminoma is the most common ovarian germ cell type ovarian tumour. Primarily, it presents in young women at reproductive age and thus, the preservation of fertility is considered to be fundamental when it is possible for these patients. In comparison to the past the restriction of the extent of the surgical procedure as well as the introduction of innovative chemotherapeutic regimens improved significantly both, the prognosis and the clinical outcomes of this rare neoplasia. As dysgerminomas are extremely radio- and chemosensitive, fertility sparing approach and less aggressive operations should be favoured. We present a narrative review of the multispecialty fertility sparing surgical and medical approach for women with dysgerminoma *(Ref. 21)*. Text in PDF *www.elis.sk.*
KEY WORDS: dysgerminoma, ovarian germ cell tumor, fertility sparing surgery, premenopausal, treatment.

Introduction

From all gyneacological neoplasms ovarian dysgerminoma represents a relative rare entity (< 2 %) (1, 2). Dysgerminoma predominantly affects adolescents and young women being less than 30 years of age at the time of diagnosis (3). In the majority of cases with ovarian dysgerminoma, the affected women will present with clinical stage IA (4). The presence of lymph node metastasis represents an independent predictor of poor survival (5). Ovarian dysgerminoma is extremely radio- and chemosensitive, thus the prognosis is generally excellent even in cases with advanced disease, with an overall survival at 5-year period of over 90 % (3, 6).

The young age of the patients, the rarity of the ovarian dysgerminoma and the absence of randomized trials are factors that influence the final treatment options. The aim of this narrative review is to give some answers on the utilization of fertility sparing surgery as a treatment option for premenopausal patients with dysgerminoma.

Methods

We included studies selected after performing a broad electronic search in the PubMed (27/07/2016) and Scopus (27/07/2016). The search strategy adopted in this narrative review included the combination of the following keywords: treatment AND fertility AND dysgerminoma. The references of the included studies were also hand-searched for additional studies. Studies written in languages other than English were not included. In order to limit the search range, only studies written after 1990 were considered for this review. Our search retrieved 9 studies which were included as eligible for our review. Studies reporting data on fertility sparing management in premenopausal patients with dysgerminoma were regarded as eligible for this review. Abstracts, conference papers, commentaries, animal studies, review articles as well as editorials were excluded from this review.

Discussion

Ovarian dysgerminomas occur in pure or mixed form with other types of germ cell tumours such as embryonal cancer, yolk sac tumour, choriocarcinoma and teratoma. Dysgerminomas are also associated with gonadoblastomas in about 50 % of cases. It should be mentioned that 30 % of the cases can occur in patients with dysgenetic gonads. Dysgerminomas are usually unilateral tumours (90 %) and 70 % of the cases are diagnosed early with stage I disease. However, it should be noted that lymphatic spread to the pelvic and para-aortic lymph nodes can occur very early (7). Recurrences occur within 2 years of diagnosis and are curable (8).

Ovarian dysgerminoma presents histological similarities to testicular seminoma and for that reason the existing chemotherapeutic substances were firstly applied and also were effective in patients with seminoma (9, 10). In particular, dysgerminoma in comparison with other types of germ cell tumours, because at initial diagnosis it is more probable to be at stage Ia, is both chemo- and radiosensitive, the bilateral involvement is more common, from 10 to 15 %, while retroperitoneal lymph nodes are more frequently involved than the intraperitoneal ones, in case of lymphatic dissemination (11).

[1]Gynaecological Oncology Department, Northampton General Hospital, Northampton, United Kingdom, [2]Gynaecological Oncology Department, Metaxa Cancer Hospital, Piraeus, Greece, [3]Department of Paediatrics, Rethymno Hospital, Rethymno, Crete, Greece, and [4]First Department of Surgery, General Hospital of Attica "KAT", Athens, Greece

Address for correspondence: Ch. Iavazzo, MD, MSc, PhD, 38, Seizani Str., Nea Ionia, 14231 Athens, Greece.
Phone: +306948054119

The development of cisplatin-based chemotherapeutics has restricted the extent of the surgical excision offering the patient the possibility of fertility preservation. Fertility-sparing surgery with unilateral salpingo-oophorectomy has become the standard procedure in cases of dysgerminoma. Resection or biopsy is indicated in areas suspected to be involved by the tumour. In particular, biopsy of contralateral ovary might be considered in patients with dysgerminoma (even though there is a probability of secondary infertility related to post-operative adhesions) due to either occult or microscopic tumour dissemination (10–15 %) (12).

Almost 75% of the patients with dysgerminoma will present with clinical stage Ia disease (3). In the past, the majority of these patients were treated post-operatively with radiotherapy. Nevertheless, radiotherapy at pelvis and paraaortic nodes is correlated with a high incidence of ovarian dysfunction or/and sterility, and thus radiotherapy has been recommended at more advanced stage of the disease (13). In addition, the extent of radiation field is in direct correlation with the involved area. Also, the concept of prophylactic mediastinal radiotherapy does not seem to offer any advantage on evolution of the disease and it causes additional toxicity and increases the costs of treatment (11).

The above mentioned facts can lead to fertility sparing type of surgery with excellent oncological and good reproductive outcomes. More specifically, these patients after informed consent can undergo unilateral salpingo-oophorectomy with omental and peritoneal biopsies plus or minus biopsy of the contralateral ovary and pelvic and or para-aortic sampling/dissection in cases with lymph node involvement (14, 15). In cases of bilateral ovarian involvement, uterine preservation should be considered and IVF protocols with donor eggs could be used. According to Sigismondi et al, in dysgerminoma histology, residual disease could be left to spare fertility (16). Stage Ia tumours do not need adjuvant treatment. However, chemotherapy with schemes such as PEB (cisplatin, etoposide, bleomycin) or JEB (carboplatin, etoposide, bleomycin) or PVB (cisplatin, vinblastine, bleomycin) should be offered in patients with higher stage disease (12, 15). Several pregnancies have been reported after surgery and chemotherapy. It was shown that pregnancy outcomes and menstrual function after fertility sparing surgery for pure ovarian dysgerminomas are sufficient (17). In a recent study, 16 out of 50 patients who received fertility sparing surgery (32 %) achieved pregnancy with 14 live births (1). Brewer et al showed that after chemotherapy, 71 % of patients maintained their normal menstrual function during and after chemotherapy, and 93 % had returned to their pre-chemotherapy menstrual pattern while 35 % achieved pregnancy (18). Radiotherapy of the pelvic and para-aortic lymph node areas is rarely used as first line treatment (15). Ovarian transposition of the contralateral ovary is proposed in such cases.

Patients with stage Ia tumours have 95 % five-year disease free survival. The most common areas of recurrence in other stages are the peritoneal cavity and retroperitoneal lymph nodes which highlights the role of pelvic and/or para-aortic lymph node dissection in the fertility sparing approach of such patients. Patients with incomplete staging could undergo surgical restaging or surveillance. More specifically, a recent study showed that only 19.2 % of patients with fertility sparing management had complete surgical staging which included lymph node dissection in 38.5 %, peritoneal and/or omental biopsies in 46.2 % and peritoneal washings in 65.4 % (19). The overall recurrence rate in this group of patients was 11.5 % and it should be noted that all recurrences (mainly in peritoneal cavity or retroperitoneal nodes) occurred in patients who had incomplete staging. All patients with recurrence were cured by salvage therapy (19).

Advanced stage of the tumour ($p = 0.001$) (which is correlated with treatment failure), histologic type ($p = 0.0004$), residual tumour after salvage surgery ($p = 0.0014$) as well as high-dose chemotherapy after primary chemotherapy failed ($p = 0.0405$) were negative prognostic factors for the overall survival (20). Furthermore, the elevation of serum markers b-HCG (β-human chorionic gonadotrophin) and AFP (α-fetoprotein) ($p = 0.009$) and the non-platinum chemotherapy ($p = 0.003$) were significantly associated with relapse whereas the age of the patient at the time of diagnosis has no prognostic value (12, 21).

From the above reviewed results, we suggest that the gold standard treatment of patients with dysgerminomas should be fertility sparing. Management of such patients should be performed in tertiary centres by subspecialists in gynaecological oncology after discussion in MDTs (multidisciplinary team – meetings) and obtaining informed consent from the patients. Genetic counselling is also proposed for such patients.

Conclusion

In conclusion, fertility sparing treatment should be considered as the standard care in case of young patients with ovarian dysgerminoma. In this therapeutic direction assisted the biological characteristics of the tumour, the evolution of the surgical techniques and principally the development of innovative chemotherapeutics. Nevertheless, a multidisciplinary approach that includes a variety of specialists such as gynaecologic oncologists, medical oncologists, psychooncologists, assisted reproduction specialists and paediatricians is essential. Larger, multicenter clinical trials may provide additional clarifications on the management and the treatment options.

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