The approach to fertility preservation in a single oncofertility centre

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Abstract

Background: The number of young female cancer survivors is increasing due to advances in cancer therapies, but many face infertility as a result of treatment. These fertility issues are often inadequately addressed. Oncofertility has emerged as a new interdisciplinary field to address the issue of gonadotoxicity associated with cancer treatment and to facilitate fertility preservation including oocyte and ovarian tissue cryopreservation. The aim of this study was to report 2 years' experience from the San Raffaele Oncofertility Unit.

Patients and methods: Data from patients treated from April 2011 to September 2013 were analysed.

Results: Sixty-one patients (mean age 26 years; range 3–46). were referred for evaluation to San Raffaele Oncofertility Unit after cancer diagnosis and before gonadotoxic treatment. Twenty-two patients (36%) were affected by breast cancer, 15 (24.6%) by sarcomas, 10 (16.4%) by haematological malignancies, 10 (16.4%) by central nervous system cancers, 3 (4.9%) by bowel tumours and 1 (1.6%) by Wilms tumour. Twenty-four patients were given the option of oocyte cryopreservation before starting chemotherapy; mean level of antimullerian hormone was 1.7 ng/mL (range 0.1–7.8). Four patients failed the procedure, while in 20 patients, a mean number of 7.5 (range 1–21) cryopreserved oocytes was obtained. The mean number of days between patient counselling and oocyte retrieval was 17 (range 2–37). Sixteen patients (26.2%) underwent ovarian tissue cryopreservation. Mean number of days from laparoscopic surgery to the beginning of chemotherapy/radiotherapy was 4 days (range 2–10). Twenty-one patients (34.4%) were not recruited for fertility preservation techniques.

Conclusions: Fertility preservation should be considered an essential component of the patient's treatment plan. A multidisciplinary approach, with constant interaction among the treating oncologist, reproductive gynaecologist and support professionals, is important for prompt referral and treatment.

Key words: cancer treatment, fertility preservation, oncofertility

Introduction

In women, among 10% of cancers occur in those younger than 45 years. Advancements in diagnosis and treatment have substantially improved cancer survival rates in the last few decades. Indeed, during the past 5 years, overall rates of cancer deaths in women have fallen by >1.6% per year [1]. The increasing number of cancer survivors focuses attention on long-term effects caused by cancer treatment and its impact on quality of life. Premature ovarian failure is one of the major sequelae of chemotherapy and/or radiotherapy in female children and young women, depending on the follicular reserve, the age of the patient and the type and dose of drugs used [2, 3].

Sperm banking for post-pubertal males has been available for many years and preservation of fertility in males is well established [4]. In contrast, the options for fertility preservation in females have been developed more recently and are less well known [5]. Consequently, discussion of potential reproductive health issues with this group at the time of diagnosis may occur less frequently than for males. Only a small number of patients at risk for ovarian failure is referred to specialists to discuss fertility preservation options [6].

Embryo cryopreservation is the only well-established method for female fertility preservation; however, this technique is not allowed in Italy. Recently, substantial improvements have increased available options, specifically oocyte cryopreservation and ovarian tissue cryopreservation. Patients should be counselled about fertility preservation strategies [7]. We report the experience of the San Raffaele Oncofertility Unit.

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Conflicts of interest statement
The authors have no conflicts of interest to declare.

CANCER BREAKING NEWS 2014;2(1):20-23

Materials and methods

Data from patients referred to the San Raffaele Oncofertility Unit after cancer diagnosis and before gonadotoxic treatment between April 2011 and September 2013 were retrospectively reviewed. Patients younger than 40 years could be offered fertility preservation strategies. The antimullerian hormone test was proposed as marker of ovarian reserve. Prepubertal girls and women that could not delay chemotherapy were offered ovarian tissue cryopreservation. Ovarian biopsies were obtained during laparoscopic surgery. Oocyte cryopreservation was proposed to patients of reproductive age in whom ovarian stimulation was not contraindicated.

Clinical information including age, type of tumour, stage, planned oncologic treatment, prognosis, hormonal tests, fertility preservation desire, fertility preservation strategy and outcome were collected in a database.

Results

Sixty-one patients (mean age 26 years; range 3–46) were referred after cancer diagnosis and before gonadotoxic treatment for evaluation to the San Raffaele Oncofertility Unit between April 2011 and September 2013. The number of patients referred increased over time as shown in Figure 1. Twenty-two patients (36%) were affected by breast cancer, 15 (24.6%) by sarcoma, 10 (16.4%) by haematological malignancy, 10 (16.4%) by central nervous system cancer, 3 (4.9%) by bowel tumour and 1 (1.6%) by Wilms tumour.

Twenty-four patients were underwent oocyte cryopreservation before starting chemotherapy (Table 1). Twelve of these (50%) were affected by breast cancer, 6 (25%) by sarcoma, 3 (12.5%) by haematological malignancy, 2 (8.3%) by nervous system tumour and 1 (4.2%) by rectosigmoidal tumour. The mean level of antimullerian hormone was 1.7 ng/mL (range 0.1–7.8 ng/mL). Four patients failed the procedure (1 for premature luteinisation, 3 for failed synchronization). The mean number of total retrieved oocytes in patients with cancer was 8.5 (range 1–26) and the mean number of frozen oocytes was 7.5 (range 1–21). The mean number of days between the patient's counselling and oocyte retrieval was 17 (range 2–37).

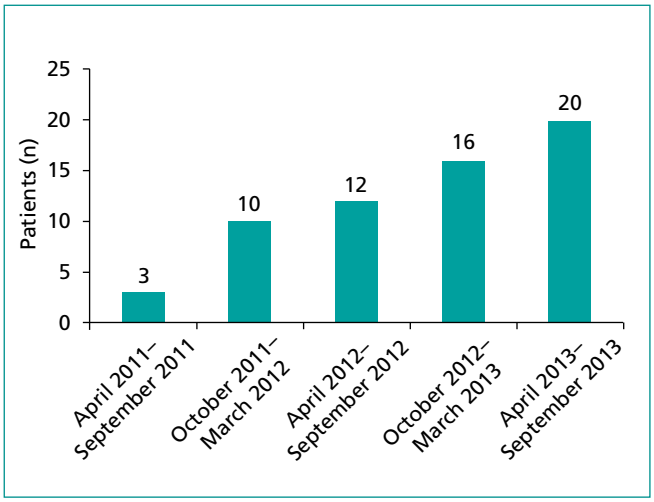

Fig. 1. Patients referred to the San Raffaele Hospital Oncofertility Unit from April 2011 to September 2013.

Table 1. Patient characteristics in those undergoing oocyte cryopreservation

Parameter	N (%)	Median age, years (range)
Oocyte cryopreservation	24 (39.3)	30 (18–35)
Breast cancer	12 (50)	*Mean time from first visit to retrieval: 17 days*
Sarcoma	6 (25)	
Haematological malignancy	3 (12.5)	
Nervous system tumour	2 (8.3)	
Bowel cancer	1 (4.2)	

Sixteen patients (26.2%) underwent ovarian tissue cryopreservation (Table 2). Eight of these (50%) were affected by nervous system tumour, 5 (31.3%) by sarcoma, 1 (6.3%) by breast cancer, 1 (6.3%) by Wilms tumour and 1 (6.3%) by non-Hodgkin lymphoma. The mean number of days from the laparoscopic surgery to the beginning of chemotherapy/radiotherapy was 4 days (range 2–10).

Twenty-one patients (34.4%) were not recruited for fertility preservation techniques. The reasons for non-recruitment are shown in Table 3.

Table 2. Patient characteristics in those undergoing ovarian tissue cryopreservation

Parameter	N (%)	Median age, years (range)
Ovarian tissue cryopreservation	16 (26.2)	15 (3–33)
Nervous system tumour	8 (50)	*Mean time from laparoscopic surgery to chemotherapy: 4 days*
Sarcoma	5 (31.3)	
Breast cancer	1 (6.3)	
Wilms tumour	1 (6.3)	
Non-Hodgkin lymphoma	1 (6.3)	

Discussion

Improvements in cancer treatment have had a significant impact on long-term survival. Therefore, quality of life issues such as fertility preservation have become paramount in the lives of reproductive-age women facing malignancy, and are now an integral component in cancer

Table 3. Patients not recruited for fertility preservation techniques

Causes	N (%)
Patient choice	7 (33.4)
Older age	5 (23.8)
Treatment urgency	5 (23.8)
Tumour progression	1 (4.8)
Religious reasons	1 (4.8)
Anaesthesiological contraindication	1 (4.8)
Cost	1 (4.8)
Total	21 (100)

management. Maintaining fertility is very important for many patients diagnosed during their childbearing years. Moreover, women are increasingly postponing childbearing to later in life for social or financial reasons, and the incidence of most cancers increases with age. Only a few patients at risk of premature ovarian failure are referred to specialists to discuss fertility preservation options. Studies have shown that oncologists often do not discuss fertility preservation options with their patients or refer them to infertility specialists [8, 9]. The priority of the oncologists is to treat the cancer and they are reluctant to introduce an issue that could add stress to the patient, especially if the prognosis is uncertain. Patients themselves may be hesitant to delay treatment for any reason. A recent research with young female adult cancer survivors indicates high decisional conflict associated with fertility preservation decisions. In particular, a significantly higher prevalence of high decisional conflict was observed in participants who were not referred for fertility consultation, as well as in participants who reported cost of fertility preservation services to be prohibitive [10]. Moreover, religious, cultural and economic barriers may prevent fertility preservation options from being discussed with the patient. Moreover, for many physicians, there is a lack of training in fertility-sparing procedures or knowledge of new options for fertility preservation [11]. Oncofertility is a new interdisciplinary field that involves the gynaecologic oncologist, the reproductive medicine gynaecologist, the biologist, the general oncologist and the psychologist in a common objective to provide fertility preservation options for cancer patients [12, 13]. In this study, we report 2-years' experience from the Fertility Preservation Unit at San Raffaele Hospital. Several meetings at peripheral hospitals were organized to explain the fertility preservation strategies and the role of the Oncofertility Unit at our hospital. Consequently, the number of patients referred to our Oncofertility Unit for evaluation has increased as shown in Figure 1.

The collaboration between specialists is important to evaluate the best option for the patient. The diagnosis of cancer in a young woman represents a "reproductive" urgency: possibly the first evaluation is dispatched within 24 hours. Short waiting times help to overcome patients' fear of delaying chemotherapy, which is the first cause of refusal of fertility preservation techniques. Oocyte cryopreservation is the option of choice if chemotherapy can be delayed, giving patients with cancer the hope of a successful pregnancy when they have overcome disease. Our patients retrieved a mean 7.5 oocytes for cryopreservation – a number is similar to that reported in the literature [14]. In prepubertal girls and patients who require immediate treatment, ovarian tissue cryopreservation is the only available method. So far, 30 term pregnancies have been reported after reimplantation of cryopreserved ovarian tissue [15].

In our patients undergoing oocyte cryopreservation, the mean time from the first visit to oocyte retrieval was 17 days and in patients undergoing ovarian tissue preservation the mean time from laparoscopic surgery for ovarian biopsy and the beginning of treatment was 4 days. The fertility preservation treatment does not affect the oncologic treatment and this aspect should be stressed during counselling.

An effective multidisciplinary team ensures that fertility preservation is accomplished efficiently and safely while optimizing the time from consultation to treatment. Fertility preservation in the setting of cancer can positively influence a patient's overall feeling of wellbeing by reducing the added stress of potential fertility loss.

Conclusion

Advances in cancer treatment allow many women to be cured. Fertility preservation should be considered an essential component of the patient's treatment plan. Although not all patients will undergo fertility preservation strategies, all women should be counselled about the available options and have the opportunity to maintain their reproductive potential. A multidisciplinary approach, with constant co-operation among the treating oncologist, reproductive gynaecologist and the additional support professionals, is crucial for prompt referral and treatment.

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