

Chemotherapy-Induced Infertility in Patients With Testicular Cancer

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A 29-year-old Caucasian married man, Mr. A, is the father of a 1-year-old daughter and is a successful tax attorney who maintains a healthy lifestyle. While performing a testicular self-examination, Mr. A noticed a small, fixed mass in his left scrotum. After medical workup, biopsy, and consultation, a left orchiectomy and retroperitoneal dissection were recommended. Pathology revealed a nonseminoma germ cell testicular tumor, pT4, N4, M-positive; with tumor invading the scrotum; vascular and lymphatic invasion; and a solitary lung lesion noted on computed tomography scan. No additional metastatic lesions were found on bone scan or magnetic resonance imaging. Biopsy confirmed the metastatic lesion in the lung. Postoperatively, Mr. A was scheduled to receive four cycles of bleomycin, etoposide, and cisplatin (BEP), a standard treatment for testicular germ cell cancer.

Mr. A and his wife had been planning to have a second child. In initial consultation with the oncologist, Mr. A brought up the topic. He and his wife wanted to know whether his cancer or any of his treatment would have an effect on their ability to conceive. The oncologist gently explained that a decrease in fertility occurs with testicular cancer, which is compounded by orchiectomy and chemotherapy. The oncologist informed Mr. A that, during chemotherapy, sperm counts usually are low and often undetectable, with only 20%–50% of patients treated with chemotherapy resuming normal sperm counts two to three years after completion of treatment (Kreuser, Harsch, Hetzel, & Schreml, 1986; Nijman, Schraffordt Koops, Kremer, & Sleifer, 1987). Mr. A and his wife were alarmed to learn that it was impossible to predict whether or when he would resume normal sperm counts or whether he would remain azoospermic (i.e., the absence of sperm in the semen). Fertility options were discussed with Mr. A and his wife.

They decided to opt for sperm banking, agreeing that if it did not work, they would consider adoption. Mr. A completed his four cycles of chemotherapy and was in full remission one year later. After attempting to conceive for one year, Mr. A's sperm count remained low at 18 million per ml (normal count is greater than 20 million per ml), identifying the need to use the sperm banked earlier. Two years after Mr. A completed treatment, Mrs. A underwent two cycles of insemination and successfully gave birth to a healthy daughter. Mr. and Mrs. A were grateful that they were made aware of their options and had time to make the necessary fertility arrangements before Mr. A started chemotherapy. Mr. A remains disease free.

Testicular Cancer and Infertility

In 2011, 8,290 estimated cases of testicular cancer will be diagnosed in the United States, with an estimated 350 deaths. The incidence of testicular cancer is increasing for unknown reasons (American Cancer Society [ACS], 2011). As advances with combination chemotherapy and radiation are made, a significant number of patients are being cured of testicular cancer. Unfortunately, a major side effect of treatment includes temporary or permanent loss of fertility. Testicular cancer most frequently occurs in men ages 15–35; therefore, fertility and sexual functioning are important issues to discuss prior to treatment.

Sperm cryopreservation is the only preventative course of action currently available for conserving fertility in young men with cancer (Trottmann et al., 2007). The procedure of cryopreservation is the storing at low temperatures of biologic materials, such as sperm, for long periods of time—as long as 50 years. The process of sperm banking often takes a total of two weeks and requires three to six sperm donations,

all completed prior to beginning chemotherapy. The cost of cryopreservation through a typical sperm bank is \$250 for initial sperm freezing and consultation. Subsequent sperm freezing is \$200 per donation and an additional monthly storage fee of \$70 (Sperm Bank, Inc., 2011).

Although sperm banking is a viable option to spare fertility, it remains elusive for many patients. In a study regarding knowledge and experience regarding infertility, only 24% of young men with cancer were found to bank their sperm and only 51% had been offered sperm banking (Schover, Brey, Lichtin, Lipshultz, & Jeha, 2002b). The most commonly accepted reason for the low percentage of sperm banking was the lack of information given to young men by their healthcare team. In an investigation of oncologists' attitudes and practices regarding sperm banking, barriers for discussing the opportunity with patients were identified. Those included lack of time for discussion, a perception of high cost factors, and a lack of knowledge regarding convenient facilities for referral (Schover, Brey, Lichtin, Lipshultz, & Jeha, 2002a). A survey of 45 men with cancer by Edge, Holmes, and Makin (2006) reported that only 67% of young men aged 13–21 years had banked their sperm prior to gonadotoxic therapy. Reasons given included anxiety at diagnosis, difficulty in talking about fertility, and a lack of understanding about sperm banking.

Men with testicular cancer often are young and may not be thinking about having children at the time of diagnosis; however, oncology healthcare professionals must discuss fertility issues and raise the topic of cryopreservation. In a study aimed at identifying the psychological impact of sperm banking, the majority of patients interviewed who banked sperm on their own initiative experienced a noticeable positive psychological effect (Saito, Suzuki, Iwasaki,

Yumura, & Kubota, 2005). Sperm banked on the patient's own initiative was found to encourage patients during and after treatment. Despite the personal anxiety associated with surviving cancer, men have reported that the experience of diagnosis increases the value they place on family closeness (Schover et al., 2002b). Those emotions add to the importance of discussing fertility options prior to treatment.

Chemotherapy-Induced Infertility

Alkylating agents and nitrogen mustard derivatives are known to have the most damaging effect on the quantity and quality of sperm production (Dohle, 2010). The total number of chemotherapy cycles and the dosages are important variables to consider when evaluating the risk for infertility (Lass et al., 1998). Cisplatin is an alkylating agent that currently is the main chemotherapeutic agent in the oncologic protocol of BEP for treating testicular cancer (Dohle, 2010; Trottmann et al., 2007).

Cisplatin has been found to be the most common sterilizing agent for germ cell tumors (Gaffan et al., 2003). If a patient is to receive more than four cycles of cisplatin-based chemotherapy, spermatogenesis (i.e., the process of sperm development and becoming capable of fertilizing an ovum) is negatively affected (Lass et al., 1998). The cumulative dose

predictive of cisplatin-based infertility is 400 mg/m² (Pont & Albrecht, 1997). When patients are treated with cisplatin-based therapy, azoospermia can be anticipated seven to eight weeks after the initiation of treatment because of the chemotoxic action of the drugs on rapidly proliferating spermatogonia and on the germinal epithelium of the testis, from which the spermatozoa develop (Dohle, 2010). The degree of recovery depends on the number of surviving germ cells and pretreatment fertility.

Spermatogenesis resumes about 12 weeks after completion of therapy and has been found to occur in 55%–80% of patients treated with cisplatin-based chemotherapy. Normal sperm counts (normospermia) may take up to five years to recover and some patients may always experience subfertile levels of sperm (oligospermia) (Dohle, 2010).

Available Options for Infertility Treatment

The primary fertility option available for men is cryopreservation or sperm banking. Once the sperm sample has been collected for cryopreservation, the semen is analyzed for sperm number and motility. Although patients with testicular cancer are at risk for poor semen quality before treatment, any sperm sample containing motile spermatozoa should be frozen, regardless of its quality (Lass et al., 1998). Three to six separate donations typically are required, depending on the initial sperm count and analysis of initial sperm. The more sperm a patient is able to produce, the greater the chance of conception.

A study by Lass et al. (1998) demonstrated that if, for some reason, no option existed but to start chemotherapy immediately because of the seriousness of the illness, attempting semen cryopreservation during or after the initial treatment still is worthwhile. Although men with testicular cancer may have reduced sperm quality at the time of diagnosis, many patients still have enough acceptable spermatozoa for freezing. Evaluation of chemotherapy dosages and cycles make it difficult to predict the risk of post-treatment infertility, but pretreatment fertility has been shown to be of significant prog-

nostic value for future sperm recovery (Dohle, 2010).

If after completion of treatment a patient does not regain a sufficient sperm count of greater than 20 million per ml, frozen sperm can be used in modern assisted reproductive techniques. The options currently available are: intrauterine insemination (sperm injected into uterus), invitro fertilization (IVF) (sperm and ovum cultured in petri dish), and micromanipulation or intracytoplasmic sperm injection (ICSI) (one sperm microscopically inserted into an ovum). A cryopreserved spermatozoa extracted from an orchidectomized seminoma-bearing testis has been used successfully (Lass et al., 1998). The quantity and quality of semen cryopreserved will determine the individual option chosen. Intrauterine insemination works best if a large amount of cryopreserved semen is available. If the quality and quantity of the cryopreserved semen is poor, then IVF or ICSI are the best options. Successful pregnancies have been achieved using all of those options without congenital abnormalities reported (Dohle, 2010). Future therapeutic options may consist of male germ cell and testicular stem cell transplantation or banking of testicular tissue from prepubertal boys (Trottmann et al., 2007).

Implications for Nursing

A patient's ability to acquire knowledge about available fertility options prior to initiating chemotherapy can be a difficult process. Unfortunately, treatment can lead to an untimely loss of fertility. Oncology nurses are advocates for their patients and, by becoming knowledgeable about treatment-related risks of infertility and resources available to patients, nurses can help patients with their concerns related to infertility and their search for alternative ways to build a family. A valuable resource for both nurses and patients can be found at www.fertilehope.org.

Nurses should respond sensitively when caring for patients at risk for infertility or who are indeed infertile. Nurses must recognize that patients diagnosed with infertility will experience a normal process of grief and loss (Schoener & Krysa, 1996). The grieving response includes phases of shock, denial, bargaining, guilt, anger, depression, and acceptance. Infertility can be an emotional reaction related to the loss of an expected way of living, the loss of self-concept, the loss of sexual identity, and the loss of

- A** **Awareness and Advice**
Being aware reminds nurses of the emotional aspects of infertility. Knowing the kind of advice to give patients is a key element of effective care.
- B** **Blame and Balance**
Blame or anger can be a driving emotion experienced by couples; nurses must encourage couples to talk about their feelings. Talking about their fears and emotions may help patients and spouses to be open and supportive of each other, finding balance.
- C** **Competence and Compassion**
Nurses should be knowledgeable and keep in touch with how their patients are coping throughout the process of infertility. Compassionate intervention includes making patients feel cared for by providing education needed for them to effectively cope.

Figure 1. The ABCs of Supportive Strategies for Infertility

Note. Based on information from Sherrod, 2004.

closeness in relationship with a partner (Sherrod, 2004). The ABCs of support strategies are a way that nurses can serve in an emotionally supportive role for patients (Sherrod, 2004) (see Figure 1). Hope is essential for effective cop-

ing and nurses can provide that needed supportive care through education and appropriate referrals.

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Digital Object Identifier: 10.1188/12.ONF.27-30

Clinical Highlights: Infertility in Patients With Testicular Cancer

Definition and Pathophysiology

Infertility is the inability to conceive offspring; a couple may be considered infertile after two years of regular sexual intercourse without contraception that does not result in pregnancy (World Health Organization, 2011). Chemotherapy can damage developing cells such as ova and sperm. Chemotherapy-induced infertility in men is caused by a decrease or absence of the quality and quantity of sperm production. Infertility occurs because of damage to the lining of the testicles where sperm is produced. The formation of sperm occurs by means of a process called spermatogenesis (i.e., the sperm become mature and are able to fertilize an ovum). When this process is altered because of testicular exposure to chemotherapy, oligospermia or azoospermia results. The process may or may not be reversible and full recovery of spermatogenesis can take as many as five years (Dohle, 2010).

Chemotherapy-Induced Infertility

Alkylating agents have the greatest negative effect on infertility in patients with testicular cancer. They cause damage to the seminiferous tubules and destroy spermatogonia. Bleomycin, etoposide, and cisplatin (BEP) is a standard first-line treatment for testicular cancer (Trottmann et al., 2007). Cisplatin is an alkylating agent that has proven to be effective against germ cell tumors (Gaffan et al., 2003). The cumulative dose predictive of infertility for cisplatin-related infertility is 400 mg/m² (Pont & Albrecht, 1997). Most patients undergoing the combination chemotherapy regimen (BEP) will experience azoospermia seven or eight weeks after the initiation of treatment because of the action of chemotoxic drugs on rapidly proliferating spermatogonia. If the cells survive, spermatogenesis restarts 12 weeks after treatment and the degree

of recovery depends on the number of surviving germ cells. Spermatogenesis may eventually occur in 20%–50% of patients (Padron, Sharma, Thomas, & Agarwal, 1997).

Risk Factors for Infertility

In addition to chemotherapy, testicular cancer itself contributes to low sperm count and infertility. Hypotheses include the tumor invasion of the testes, malignancies that result in malnutrition causing deficiencies needed for optimal gonadal function, malignancy-induced fevers that negatively influence spermatogenesis, and tumor released cytokines that affect spermatozoa function, resulting in low sperm motility (Dohle, 2010). Other risk factors include age at the time of diagnosis, pretreatment sperm count, and orchiectomy.

Treatment Interventions

Sperm banking or cryopreservation is the only intervention currently available to treat infertility in patients with testicular cancer. Sperm banking needs to be done prior to the start of chemotherapy but, if not possible, samples should still be collected during or after treatment (Lass et al., 1998). Three to six sperm donations often are recommended. Sperm donations are frozen and, for a storage fee, can be stored for as long as 50 years. The cost of sperm banking ranges from \$200–\$500 (Sperm Bank, Inc., 2011).

Implications for Nursing

Unfortunately, many patients who undergo chemotherapy for testicular cancer are not aware that infertility is a risk. Educating patients about the possibility of infertility following chemotherapy is crucial. Lack of knowledge about infertility risks, misinformation about the costs of sperm storage, and confusion about the process of cryopreservation are some of the reasons men do not pursue sperm banking

(Trottmann et al., 2007). Education should be carried out at the time of diagnosis and prior to treatment so that patients may have ample time to prepare. Discussing the issue of infertility must be done with sensitivity.

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