

## Births using sperm retrieved via immediate microdissection of a solitary testis with cancer

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**Objective:** To determine the feasibility of achieving births using sperm retrieved from a solitary testis with cancer.

**Design:** Prospective clinical study of azoospermic men with testis cancer in a solitary testis.

**Setting:** Infertility patients in an academic environment.

**Patient(s):** Azoospermic men with previous history of orchiectomy and testis cancer in a remaining solitary testis.

**Intervention(s):** Viable sperm were retrieved by immediate microdissection of paratumor testicular tissue from orchiectomy specimen.

**Main Outcome Measure(s):** Live births were achieved using sperm from immediate microdissection of orchiectomy specimen with testis cancer.

**Conclusion(s):** Azoospermic men with cancer in a solitary testis have potential for fertility. (Fertil Steril® 2005; 84:1508.e1–3. ©2005 by American Society for Reproductive Medicine.)

**Key Words:** Testis cancer, infertility, anorchid, microdissection, azoospermia

Testicular neoplasms are the most common solid tumors of men between 15 and 34 years of age (1). Because most patients with testis tumors are young men of reproductive age and have not yet fathered children, future fertility is of great concern and should be discussed with patients, especially before anticancer treatments such as chemotherapy and radiation therapy. Unfortunately, most men are subfertile and sometimes azoospermic at the time of diagnosis. The mechanisms behind this impaired fertility before the gonadotoxic effects of cancer therapy are poorly understood. However, it is known that seminiferous tubular function is significantly impaired in these men before any treatments (2).

Patients with a unilateral testis cancer have a 1,000 times greater risk of developing metachronous lesions in the contralateral testis compared to the general population (3). Although the natural history of carcinoma-in-situ is uncertain, it is estimated that up to 10% of men with a testis tumor have contralateral carcinoma-in-situ, and, of those, up to 50% may develop clinical germ cell tumors (4). Although the reported incidence of bilateral testis tumors is 2.5%–5% of all testicular malignancies (3, 4), the consequence of either synchronous or metachronous testis tumor is anorchia and sterility.

The advent of IVF with intracytoplasmic sperm injection (ICSI) and testicular sperm extraction (TESE) provides an

opportunity for fertility in azoospermic or virtual azoospermic men with testicular cancer (5, 6). We report herein a novel technique of immediate microdissection of the radical orchiectomy specimen in previously azoospermic men rendered anorchid due to germ cell tumors in a solitary testis. In our ongoing series of two patients, a singleton pregnancy and two live births were achieved in one couple after ICSI using the cryopreserved testicular sperm.

### MATERIALS AND METHODS

Inguinal exploration is performed as previously described (7). Briefly, through an inguinal incision, the external oblique aponeurosis is opened and the spermatic cord is isolated and doubly clamped. The testis is delivered and the gubernaculum is clamped and ligated. The testis is isolated with a rubber dam and cooled with iced saline slush. Using the operating microscope under 6–15 power magnification (8, 9), testis biopsy of the lesion is performed and immediately sent for pathologic evaluation as a frozen section intraoperatively. If malignancy is confirmed on pathology, radical orchiectomy is performed unless the lesion is amenable to a testis-sparing procedure (8, 10). After the orchiectomy, the specimen is taken to a sterile bench with a dissecting microscope.

Using the dissecting microscope, the tunica albuginea is bivalved and normal testicular tissue is dissected off of the tumor. Maximum amounts of normal testicular tissue are

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obtained safely with a clear margin from the tumor under the microscope. The tissue is minced through manual dispersion of the normal testicular tissue. The dispersed testicular tissue is placed in human tubal fluid (HTF) culture media supplemented with 6% plasmanate. Cryopreservation is then performed with a two-step standard cryopreservation (TEST-yolk buffer or glycol buffer) (11).

## CASE REPORT

JM is a 34-year-old man with prior history of right testicular cancer. He underwent a right radical orchiectomy and subsequently received radiotherapy to the retroperitoneum for stage I seminoma at age 25 years. Attempts were made to bank sperm before his surgery and radiotherapy but virtual azoospermic semen parameters and lack of viable sperm prohibited cryopreservation. Postoperatively, he became absolutely azoospermic. One year later, he underwent microsurgical repair of a large left varicocele with return of rare nonmotile sperm to his ejaculate (12). Six years later, he was found to have a palpable mass in the remaining left testis. Ultrasound confirmed a solid lesion. The  $\alpha$ -fetoprotein (AFP),  $\beta$ -hCG, and LDH levels were normal. Follicular-stimulating hormone and LH levels were elevated (17.6 IU/L and 11.1 IU/L, respectively) with a normal T level (405 ng/dL). Preoperative semen analyses revealed only three nonmotile sperm. He had recently married and expressed a strong desire for future fertility.

The diagnosis of seminoma was made from an intraoperative frozen section. A testis-sparing partial orchiectomy was not possible due to the location and size of the tumor, thus a left radical orchiectomy was performed. After orchiectomy, the specimen was moved to a sterile bench and extraction of normal testicular tissue surrounding the tumor was performed using  $\times 5$ – $\times 10$  magnification. A sample of the dissected tissue was examined under  $\times 400$  magnification and sperm were observed. Analyses of the specimen revealed a sperm concentration of only 150 sperm/mL with 20% motility and C-progression. A total of seven vials were cryopreserved. The ICSI was performed after oocyte retrieval from the partner using the cryopreserved testicular sperm extracted from the solitary testis with cancer. A singleton pregnancy was achieved on the second IVF/ICSI attempt and the couple subsequently delivered a healthy full-term baby boy. Another singleton pregnancy and subsequent live birth of a healthy full-term baby was achieved for the couple during a third IVF/ICSI attempt using previously cryopreserved testicular sperm.

The other patient in our series is the identical twin brother of this patient. He also was azoospermic from bilateral testis cancers and subsequently underwent identical procedures. Viable testicular sperm were successfully extracted by the microdissection technique and cryopreserved to be used for future IVF cycle.

## DISCUSSION

The incidence of testis cancer is increasing worldwide and approximately 7,200 new cases are diagnosed each year, mostly in young men between the ages of 15 and 34 years, in the United States (1). Despite a more than 90% cure rate, infertility has been a persistent enigma to clinicians who are treating these young men of reproductive age (13). It is well known that a history of testicular cancer is associated with a much higher risk of developing a tumor in the contralateral testis. Testicular cancer is often familial, with an especially high incidence in brothers as seen in our case study. Male children of men with testicular cancer and brothers with a history of testicular cancer should undergo testicular examination and sonogram and be taught testicular self-examination.

With increasing incidence and successful treatments for patients with a testicular cancer, a number of men with bilateral testicular tumors, either synchronous or metachronous, are expected to rise (14). Because a majority of testis cancer survivors are already subfertile, either primarily from the tumor itself or secondary to treatment such as radiation, chemotherapy, or surgery, a second tumor in the remaining solitary testis has previously guaranteed absolute sterility.

Traditionally, cryopreservation of semen before treatment has been recommended to allow for future paternity in men with testis cancer. However, poor pretreatment semen quality and even poorer post-thaw survival precludes the use of cryopreserved sperm in many patients (15, 16). Men with bilateral testis tumors, mostly metachronous lesions, with no viable cryopreserved sperm were doomed to absolute sterility.

We have previously reported high pregnancy rates (PR) for men with nonobstructive azoospermia using TESE and ICSI (17). In this report, we demonstrated a novel technique of extracting viable testicular sperm by immediate microdissection of the paratumor testicular tissue in a solitary testis. More important, two pregnancies with live births were achieved with IVF/ICSI using testicular sperm retrieved from an anorchid man. Once doomed to absolute sterility, azoospermic men with cancer in a solitary testis have potential for fertility.

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