CME CREDIT

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BRIEF QUESTIONS AND ANSWERS ON CURRENT CLINICAL CONTROVERSIES

Q: Should we offer semen cryopreservation to men with testicular cancer?

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A: YES, ALL MEN WITH testicular cancer should have the option of banking sperm before starting chemotherapy or radiation therapy if they want to retain the potential to have children.

Semen cryopreservation has become particularly important in recent years for several reasons. Long-term survival rates have increased: more than 90% of patients with testicular cancer now survive longer than 5 years,[1] making treatment-related complications such as infertility more of an issue. Assisted reproductive techniques have also improved, and cryopreserved semen from men with cancer can be used successfully to initiate pregnancies.[2] In addition, semen cryopreservation helps patients maintain their morale during stressful treatment by providing hope that they may still be able to have children.

HOW COMMON IS TESTICULAR CANCER?

The incidence of testicular cancer has increased worldwide during the last 4 to 5 decades. In industrialized countries, testicular tumors are the most common solid malignant disease among men aged 20 to 34.[3,4] About 5,600 cases of testicular cancer are diagnosed annually in the United States.[1]

HOW CANCER TREATMENT DIMINISHES FERTILITY

Treatment can diminish fertility,[1] despite modifications designed to preserve spermatogenesis.

Radiation therapy can be toxic to the gonads, even though shielding the gonads helps preserve spermatogenesis and leads to a certain degree of recovery in spermatogenesis over time.[1,5–7] Many patients who undergo radiotherapy remain azoospermic for extended periods. Although testicular shielding may decrease the scatter radiation dose by 50%, significant doses can still reach the testis by internal body scatter. Thachil et al[8] found that 32% of patients with testicular seminoma became azoospermic and 50% experienced severe oligospermia after receiving a total of 2,500 cGy to the periaortic area in 20 fractions. Of this dose, 325 cGy, or 13% of the total dose, was directed at the upper scrotum, and some of this dose likely reached the gonads by internal body scatter.

Ionizing radiation may also cause genetic mutations that accumulate as the total dose increases and hamper the ability of spermatozoa to initiate a viable pregnancy. An increased frequency of numerical and structural chromosomal abnormalities has been shown to persist up to 5 years after radiation therapy.[9]

Chemotherapy works by interrupting obligatory cell processes such as DNA synthesis and folate metabolism in rapidly dividing malignant cells.[5] But it also interferes with spermatogenesis and the endocrine and exocrine functions of the male reproductive system.[7,10]

A number of factors may influence gonadal function: the drug used, the dose, the number of chemotherapy cycles, and adjuvant therapy after treatment.

Many chemotherapeutic agents are powerful testicular toxins; these include busulfan, chlorambucil, cyclophosphamide, cisplatin, thiotepa, and procarbazine. Alkylating agents can cause irreversible azoospermia. Patients with testicular germ cell tumors often receive cisplatin-based chemotherapy, which causes

Offer the option of sperm banking before radiation or chemotherapy

oligospermia in 16% and azoospermia in 20% of men who have normal sperm counts before chemotherapy.

The depletion of the germinal epithelium is progressive and dose-dependent, and alternations in Sertoli cell and Leydig functions are reflected by elevations in gonadotropin-releasing hormone, luteinizing hormone, and follicle-stimulating hormone.[11]

Recovery of spermatogenesis can be slow and sometimes incomplete after chemotherapy for testicular cancer. At 2 years after chemotherapy, spermatogenesis has returned in only 48% of men.[12]

Retroperitoneal lymph node dissection can cause ejaculatory dysfunction through emission failure, retrograde ejaculation, or both.[1,5,10]

HOW ASSISTED REPRODUCTION HAS IMPROVED

New techniques can overcome poor sperm quality

Some have questioned the use of semen cryopreservation in patients with testicular cancer because these patients have poorer semen quality than men without this disease.[2,12–15] Even before treatment, 50% to 60% of men with testicular cancer have substantial reductions in their total sperm counts[11]; their motile sperm counts are lower before freezing and after thawing, and they have lower sperm motility.[14,15]

However, new assisted reproductive techniques such as intracytoplasmic sperm injection (ICSI) can overcome the poor semen quality and may result in pregnancy.[16,17] Goldschlag et al[18] reported that of 41 partners of patients with testicular cancer who attempted to become pregnant with ICSI using cryobanked semen, 22 (54%) achieved a normal clinical pregnancy, and 19 (46%) went on to delivery. We have seen similar results in our program.

Therefore, even samples from men with testicular cancer that are too poor in quality for traditional assisted reproductive techniques (intrauterine insemination or conventional in vitro fertilization) may still be adequate for ICSI. Only one viable sperm per oocyte is required for ICSI. Semen cryopreservation is thus a viable alternative for any patient with testicular cancer.

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