Feasibility of Simultaneous Testicular Microdissection for Sperm Retrieval and Ipsilateral Testicular Tumor Resection in Azoospermic Men

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Male infertility is known to be associated with testicular tumors (Honig et al, 1994). In one recent report (Nobert and Goldstein, 2001), at least a 16-fold increase in the risk of testicular cancer, with seminoma being the most prevalent one, has been reported to be associated with male infertility.

Generally, the standard initial treatment for testicular mass, in view of its high likelihood of malignancy, is inguinal orchiectomy. We hereby report 2 cases of testicular mass discovered during infertility evaluation for azoospermia. In both cases, simultaneous testicular sperm retrieval with microdissection technique, for future use of assisted reproduction, was performed during orchiectomy. The safety and advantages of this management approach for azoospermic patients with incidentally discovered testicular mass are discussed.

Case Reports

Case 1—A 32-year-old male, who had a previous history of bilateral undescended testes and had undergone bilateral orchiopexy at the age of 6 years, presented with primary infertility. He was otherwise healthy. His current partner was a healthy 29-year-old woman. His clinical examination was unremarkable apart from a palpable left testicular mass. He was found to be azoospermic on 2 complete semen analyses performed 2 months apart. Serum follicle-stimulating hormone (FSH) was 13.7 IU/L, luteinizing hormone 13 IU/L (0.9–14.8 IU/L), and serum testosterone 17 nmol/L (10.0–38.5 nmol/L). Genetic evaluations, including a Y-chromosome microdeletion analysis and karyotype, were normal.

Testicular sonogram confirmed a left intratesticular mass of 3.5 × 2.5 cm. Serum tumor markers, including lactate dehydrogenase (LDH), beta human chorionic gonadotrophins (β-HCG), and alpha fetoprotein (α-FP) were within the normal reference ranges. Additional imaging studies included a normal CT scan of the abdomen and pelvis and a normal chest film.

A left inguinal orchiectomy was planned for the patient. Because the couple was interested in assisted reproduction with intracytoplasmic sperm injection (ICSI) in the future, a decision was made to retrieve sperm from the ipsilateral testicle with microdissection technique (Schlegel, 1999) for sperm cryopreservation. Intraoperatively, an inguinal incision was made to mobilize and to clamp the left spermatic cord. The testicle was delivered and removed. The tunica albuginea was opened microscopically, a well-defined solid heterogeneous brown rubbery lesion measuring 3.4 × 2.5 × 2.4 cm was noted. Multiple microsurgical sampling of the seminiferous tubules was obtained. A few nonmotile sperm were noted in one of the samples. The seminiferous tubules were processed for sperm cryopreservation.

The final pathological evaluation revealed a Leydig cell tumor. There were less than 5 mitotic figures per high-power field, with minimal cellular atypia, no necrosis (Figure 1a and b), no vascular invasion and no marginal infiltration, consistent with a nonmalignant Leydig cell tumor. The seminiferous tubules demonstrated germ cell aplasia/Sertoli cell only morphology, with focal spermatogenesis.

The postoperative course was uneventful. In the short-term follow-up of 1 year, there was no clinical or biochemical evidence of recurrence. Subsequently, the couple underwent assisted reproduction with ICSI. Six oocytes were obtained from the female partner. Only 2 motile sperm were subsequently found in the thawed testicular sperm extraction (TESE) sample for ICSI. Four
Figure 1. (A) Leydig cell tumor with adjacent seminiferous tubules. (B) Higher magnification of Leydig cell tumor.
oocytes were injected with freshly retrieved sperm from the contralateral testis. A total of 4 good-quality embryos were obtained (including 1 fertilized by a cryopreserved sperm). Two embryos were transferred to achieve a clinical pregnancy and 2 remaining embryos were cryopreserved.

Case 2—A healthy 28-year-old male and his 28-year-old healthy wife presented with a 3-year history of primary infertility. Clinical examination was remarkable only for a hypotrophic left testis and bilateral varicoceles. He was found to be azoospermic on 2 complete semen analyses performed 2 months apart. Serum FSH was 13.7 IU/L, luteinizing hormone 7.5 IU/L, and serum testosterone 17 nmol/L. Genetic evaluations, including a Y-chromosome microdeletion analysis and karyotype, were normal. On testicular sonogram, in addition to bilateral varicoceles, a lobulated hypoechoic lesion (Figure 2) measuring 1 cm × 1.6 cm was found incidentally on the superior aspect of the left testis. The lesion did not appear to be hypervascular. In addition, there were small microcalcifications in the left testis parenchyma.

A presumptive diagnosis of testicular cancer was made. Serum tumor markers were within normal reference range. Additional imaging studies included a normal CT scan of his abdomen and pelvis and a normal chest film.

A left inguinal orchiectomy was planned for the patient. Because the couple was interested in assisted reproduction with ICSI in the future, a decision was made to retrieve sperm from the left testicle with microdissection technique for sperm cryopreservation. Intraoperatively, an inguinal incision was made to mobilize and to clamp the left spermatic cord. The testicle was delivered immediately, isolated, and covered with a sheet of latex and cooled with ice slush. The tunica albuginea was opened microscopically, a firm, white lobulated nodule, with a waxy texture, of 1.8 × 0.9 × 0.8 cm was found within the superior pole of the testicular parenchyma. The mass was removed in toto for pathology frozen section, which revealed fibrotic hyalinized scar with no sign of malignancy. Multiple microsurgical sampling of the seminiferous tubules was obtained. No sperm were found in the tubules. In view of the unusual calcification-like texture of the intratesticular mass and the absence of viable cells on frozen section, a decision was made to perform a partial orchiectomy of the superior part of the left testis (the patient has consented for such an option preoperatively) where the mass was found. The total warm ischemic time was 10 minutes and cold ischemic time 45 minutes.

The postoperative course was uneventful. Follow-up scrotal ultrasound at 3 months and 6 months postoperatively confirmed positive vascular flow in both testes. Final histological evaluation of the mass confirmed the ab-
Discussion

Testicular tumors show an increased incidence among men with infertility. In addition to the ones that were discovered on a thorough clinical examination of the testis, they can be found incidentally on scrotal sonographic examination or other imaging modalities.

Although seminoma is among the most commonly discovered testicular malignant tumor in infertile men (Nobert and Goldstein, 2001), recent literature suggests that many of these incidentally discovered tumors may be of a benign nature. Some investigators advocated conservative management with regular sonographic surveillance when dealing with these incidentally discovered testicular tumors (Tanguay, 2003).

In view of the high likelihood of malignancy in testicular masses, inguinal orchiectomy remains the standard management for testicular masses. In the 2 cases we hereby presented, intraoperative sperm retrieval was performed simultaneously with the orchiectomy. Intraoperative sperm retrieval with testicular microdissection for sperm extraction was performed with testicular microdissection for sperm extraction. In the second case, it was possible to confidently rule out malignancy, the finding on the intraoperative frozen section of the testicular mass being compatible with the testicular mass classified as a testicular tumor with active spermatogenesis. In the first case, the finding on the intraoperative frozen section of the testicular mass was that of a testicular tumor with active spermatogenesis. In the second case, the finding on the intraoperative frozen section of the testicular mass was that of a testicular tumor with active spermatogenesis. Hence, a decision was made to perform only a partial orchiectomy.

Obviously, we have considered the possibility that the presence of viable cells. The seminiferous tubules revealed Sertoli cell-only pattern (Figure 3) with nodular Leydig cell hyperplasia.

Figure 3. Germ cell aplasia with Sertoli cell-only morphology seen in both cases.
final pathology may indicate the presence of malignancy. Thus, these risks and the various options must be clearly discussed with the patients and well-documented prior to performing the surgery, as we did in this case.

Several issues of concomitant testicular sperm retrieval during orchiectomy for testicular mass should be addressed. Because the tunica albuginea is to be opened to access the seminiferous tubules, the pathologist should be properly informed when staging the lesion. When in doubt, the presence of the pathologist may be necessary when opening the tunica.

If the lesion turns out to be malignant, clinicians may wonder about risks of transferring malignancy when using the retrieved sperm for assisted reproduction. We believe such a risk is minimal. It should be noted that, with the use of microdissection, only individual seminiferous tubules are retrieved (Schlegel, 1999). This is in contrast with traditional TESE when pieces of testis parenchyma are removed for processing. Thus, the risk of transferring a mass of malignant tissue is greatly reduced with the former technique. In addition, during processing of the seminiferous tubules, only a single viable sperm is isolated for each oocyte by ICSI procedure. The residual parenchymal cells are not used. These practices minimize the risk of malignant cell contamination during ICSI. Further studies with longer follow-ups both on the health of the men and in the outcomes of the ICSI offspring, however, are required to fully establish the safety of this approach.

Thus, for men presenting with infertility with incidental finding of testicular mass, we suggest that intraoperative sperm retrieval during orchiectomy should be offered to men who are not able to produce sperm for banking, who are interested in fertility with assisted reproduction (either presently or in the future), who are likely to have healthy residual testis parenchyma for sperm retrieval (such as those with small lesion or nonpalpable lesion discovered by imaging studies, as opposed to those with a testicular mass that has occupied the entire testis, as in most malignant cases). In men in whom the testicular mass is likely to be malignant (based on rate of growth, size of the mass, imaging findings, serum marker levels), radical orchiectomy should be performed. If intraoperative sperm retrieval is to be attempted, we suggest performing it ex vivo after the testis is resected to avoid tumor cell spillage, as we did in case 1.

Conclusions
We presented 2 azoospermic cases with incidental findings of testicular mass during infertility work-up. Intraoperative testicular sperm retrieval for assisted reproduction was performed during orchiectomy. This approach, in selected cases, is safe and allows for the opportunity to preserve residual spermatozoa, particularly in men who are not able to ejaculate sperm for banking, for current or future use of reproduction.

References