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Altering the Natural History of Surgical Relapse in Testicular Cancer: Suboptimal Surgery and Pneumoperitoneum

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The overall survival for patients with testicular cancer exceeds 95%, and approaches 100% for stage I disease. Given the high probability of cure, clinical investigators have appropriately focused on reducing morbidity and therapy burden without compromising survival in this young patient population. The 2010 Whitmore Lecture entitled *Testing the lower bounds of efficacy in testicular cancer* addressed this topic and showed how radiation and medical oncologists relied on randomized trials to generate level 1 evidence and establish new treatment paradigms [1].

Unfortunately, urologists have lacked similar rigor when testing the lower bounds of efficacy for retroperitoneal lymph node dissection (RPLND) [1]. First, to preserve antegrade ejaculation, surgical templates were modified on the basis of mapping studies, which always underestimate retroperitoneal disease, either because of lack of follow-up or use of postoperative chemotherapy. Ipsilateral metastasis is predictive for contralateral disease. Second, laparoscopic RPLND (L-RPLND) was introduced with a very superficial understanding of the pathophysiology and effect of pneumoperitoneum in the setting of germ cell tumors (GCTs). In our view, each has resulted in avoidable relapses and preventable deaths.

RPLND remains an essential component in the multidisciplinary management of patients with GCT in both primary and postchemotherapy settings. Properly performed, RPLND is both a staging and a therapeutic procedure, but must always be undertaken with therapeutic intent. Retroperitoneal recurrences should always be considered surgical failures, whether they result from technical error(s) or reduced templates. Surgical failures increase the burden of therapy and potentially compromise survival. The completeness of retroperitoneal resection is an independent prognostic variable for patients with NSGCT [2].

`Data from Memorial Sloan Kettering Cancer Center (MSKCC) and Indiana University (IU) demonstrate lower survival in the reoperative setting [2,3]. Donohue et al [2] reported that "in many of these cases there was a relative lack of RPLND experience". The literature suggests that for complex procedures, higher volume and favorable outcomes are correlated. Even though three surgeons perform 23% of RPLND procedures in the USA, it is troubling that the majority are performed by urologists with minimal experience [4].

In this issue of *European Urology*, the experienced investigators from IU [5] report on the clinical course for five patients who experienced relapse following robotic RPLND (R-RPLND). Excluding the patient who suffered a local recurrence adjacent to an undivided lumbar vessel, we agree that the relapse pattern for the remaining four patients is highly unusual following open RPLND, particularly for patients with low-stage (CS I, CS IIA), or small (2.9 cm and 3 cm) residual postchemotherapy masses. The paracolic recurrence in the patient who required colectomy was caused by tumor implant and not a retained spermatic cord. These relapse patterns have not previously been seen at IU or MSKCC following open RPLND, even though each center performed more than 2000 cases over the past 25 yr.

Three cases of peritoneal carcinomatosis following minimally invasive primary RPLND performed elsewhere for CS I NSGCT have been seen at MSKCC. One patient died from diffuse uncontrollable disease following multiple chemotherapy regimens and reoperative RPLND. Another

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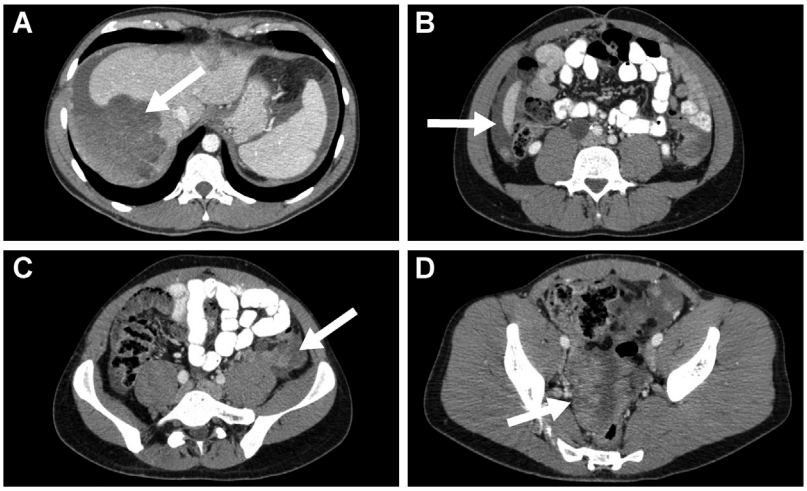

Fig. 1 – Representative computed tomography images at the time of relapse after laparoscopic retroperitoneal lymph node dissection. (A) Large liver metastases (arrow). (B) Peritoneal recurrence involving the bowel (arrow). (C) Paracolic recurrence (arrow). (D) Deep pelvic recurrence (arrow).

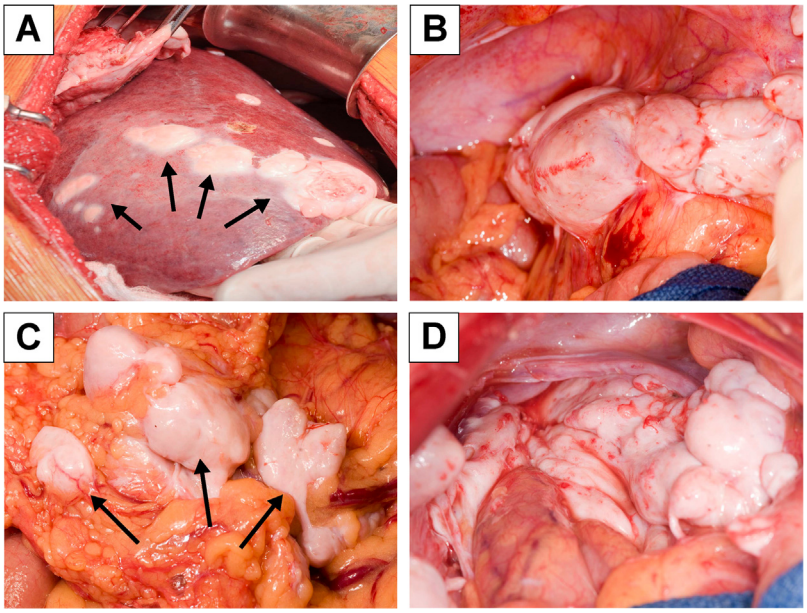

Fig. 2 – Representative intraoperative images at the time of reoperative surgery. (A) Multiple hepatic metastases (arrows). (B) Tumor implants in segment of the colon. (C,D) Diffuse implants in the omentum, mesentery, and pelvic side wall.

CS I patient with one positive node experienced relapse 5 mo after L-RPLND with rising markers, diffuse carcinomatosis, liver metastases, and a frozen pelvis (Fig. 1). Following four chemotherapy regimens including high-dose chemotherapy, he underwent desperation surgery (Fig. 2) requiring bowel resection, multiple liver resections, splenectomy, omentectomy, partial resection of the right and left diaphragm, and resection of multiple implants along both pelvic side walls and cul de sac. Pathology revealed diffuse teratoma and a focus of yolk sac. Hepatic metastases and bulky masses encasing the celiac trunk as an initial site of relapse following open RPLND are also extremely unusual for low-stage and/or low-volume retroperitoneal disease. We have also seen at least four such cases following either L-RPLND or R-RPLND.

These extremely unusual surgical failures cannot be explained by technical error(s) alone. Animal models suggest that the tumor biology may be variably influenced by pneumoperitoneum [6]. Aerosolization of tumor cells is not a theoretical risk. The cohesive properties of germ cell tumors vary widely. Many tumors are friable and implant easily, which cannot be predicted preoperatively. A testis cancer workshop comparing L-RPLND to its open counterpart included multiple live surgeries by high-volume surgeons. The audience witnessed a tumor “sandstorm” that persisted for the duration of the primary L-RPLND. The

patient required four cycles of bleomycin, etoposide, and platinum postoperatively, and approximately 13 yr later underwent reoperative surgery for diffuse teratomatosis.

R-RPLND has largely replaced L-RPLND as a minimally invasive approach. Improved three-dimensional optics and superior instrument dexterity appear to have flattened the steep learning curve. However, as for L-RPLND, therapeutic efficacy, the most important consideration in this highly curable disease, remains difficult to assess and appears to be overstated in the initial reports. First, the number of patients is quite small; second, the majority of node-positive patients received postoperative chemotherapy; and third, the follow-up is relatively short [7–9].

The aberrant recurrences described in the Indiana report represent an important addition to the literature on surgical failure due to a minimally invasive approach [10,11]. This case series suggests that the natural history of surgical recurrence(s) is altered in a subset of patients following R-RPLND. Although the denominator for R-RPLND is unknowable, it is certainly much smaller than that for open RPLND, and its reported outcomes are subject to the bias of much shorter follow-up. It is currently not possible to predict which patients are vulnerable to such events. We agree that these unusual relapses are probably under-reported, and the possibility of their occurrence should probably be addressed during the informed consent process. These cases are very challenging to manage, the treatment burden and secondary toxicities are extremely high, and patients with low-stage disease have died. Reducing surgical morbidity is certainly important, but survival is paramount for patients whose life expectancy often exceeds 40 yr.

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