Challenges in the Modern Treatment of Muscle-Invasive Bladder Cancer

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Still missing in our treatment of bladder cancer are the tools to accurately predict response to a specific therapy, whether it be chemotherapy, radiation, or transurethral resection alone. Once we have these tools, we will be well on our way to applying a more intelligent, true personalized medicine approach to the treatment of this disease.

Drs. Dickstein and Kamat have written a very nice summary of the issues currently facing the urologist treating a patient with localized invasive bladder cancer. They focus on the toxicity of radical cystectomy, choices for urinary diversion, and the roles of bladdersparing and robotic techniques.

One of the most challenging decisions in the management of invasive bladder cancer arises in the initial treatment of patients with high-grade disease with lamina propria invasion, HGT1. This may occur as the initial tumor in some patients, or it may represent progression from prior carcinoma in situ (CIS) or high-grade Ta disease. This is a well-recognized aggressive tumor, with a risk of progression of up to 70%. Most urologists begin with intravesical bacille Calmette Gurin (BCG), but durable long-term local control is achieved in only about one third of patients.[1] The others either must undergo delayed cystectomy or progress to metastatic disease. Patients who have a cystectomy after the tumor becomes muscle invasive have a worse outcome than those who undergo cystectomy earlier.[2] Cure rates with early radical cystectomy are high in patients with HGT1 disease, but this may represent overtreatment for patients who were destined to respond well to BCG.

A number of predictors of progression of HGT1 disease to muscle invasion while on BCG have been proposed. These include the presence of associated CIS, lymphovascular invasion, and deep lamina propria invasion. Patients with persistent T1 disease after induction BCG are also at high risk for progression. Repeat resection appears to be key prior to proceeding with intravesicle therapy, primarily to help avoid understaging of occult muscle-invasive disease on the initial resection. Unfortunately, there are still not convincing prospective data demonstrating the ability of biologic markers to predict which initial tumors are likely to be resistant to BCG. Until these predictors are determined, young, fit patients with high-grade T1 disease should be seriously considered for early cystectomy.[3]

Once the decision is made to proceed to radical cystectomy, the choice of type of urinary diversion is a complex one. It is relatively rare that absolute medical factors, such as renal insufficiency or the presence of tumor in the prostatic urethra, determine the choice of diversion. More often, the choice is determined by less tangible factors, such as functional status, comorbid conditions, age, social support, and body habitus. It is clear that the physician's own training, experience, and opinions also feed into the decision in a major way.[4] The rate of continent diversion in teaching centers varies from 20% to as high as 70%, depending on the physician and institution. However, in the United States overall, less than 15% of all patients undergoing cystectomy in 2005 had a continent diversion, and even for patients under 65 years of age, the rate was less than 25%.[5]

Finally, the authors nicely outline the current data available regarding the timing and inclusion of systemic chemotherapy for patients undergoing cystectomy or radiation therapy for invasive bladder cancer. From 30% to 70% of patients with clinically localized invasive cancer are not cured with cystectomy, depending on pathologic stage.[6] Most of those in whom cystectomy fails likely had occult metastatic disease at the time of the surgery. Level 1 prospective randomized clinical trials support the benefit of neoadjuvant chemotherapy in patients with muscle-invasive disease, although flaws in those randomized trials have been identified. There is less strong evidence supporting adjuvant chemotherapy for patients with high-risk features on final pathology. Systemic chemotherapy is much better tolerated prior to cystectomy than afterward, and patients who need it are more likely to receive the full dose if it is administered before surgery. Concerns voiced by
patients and physicians alike about surgical complications in the post-chemotherapy setting have not been validated. However, some patients with pathologically organ-confined disease may receive little benefit from the addition of chemotherapy prior to surgery. The risk-adapted strategy described in this review is attractive, but it is still unproven whether it will achieve the same results as a standard approach of neoadjuvant chemotherapy in all patients with > cT2 disease.

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