

## MEDitorial March 2010

### Bladder Cancer

Last month, my article addressed the issue of blood in the urine (“hematuria”). A concerning cause of hematuria is **bladder cancer**, a variably malignant tumor starting in the lining of the urinary bladder. Probably due to randomness, I have seen more than my share of this disease, just since the start of this year. Cause of bladder cancer is not always known, but cigarette smoking is an unequivocal risk factor; and industrial exposure to certain organic chemicals, including aniline dyes and benzene-derivatives, may play a role.

Bladder cancer is usually detected by cystoscopy (looking inside bladder, usually in the office under local anesthetic, sometimes with sedation); but occasionally, other tests, e.g., CT scanning, ultrasound and advanced urine tests (cytology, BTA, “F.I.S.H.”, etc.) can suggest this disease. TURBT (transurethral resection of bladder tumor) is the hallmark of diagnosis and treatment. This is an operation under anesthesia to “ream out” the growth from within the bladder. Very large tumors may require several sessions--or simply may not be safe to totally remove in this fashion.

Most urologists can tell, by looking at the growth and its characteristics, whether this is a more “serious” form of bladder cancer. Most cases fortunately involve superficial cancer, i.e., not invading into the deeper

bladder layers including the lamina propria (just below the lining) or the muscularis (thick muscular layer, located even deeper, in which there are numerous blood vessels and lymphatics allowing tumor cells to spread outside bladder and potentially to lymph nodes and other organs). Characteristics of the more innocuous superficial bladder cancers include small size, papillary appearance (like a polyp or “head of broccoli”), lack of focal thickening of bladder wall or involvement of the area where the ureters (tubes entering bladder from above, conducting urine from kidneys). The latter involvement can actually block the ureters, which would be a concerning finding and would favor the diagnosis of a more aggressive/invasive cancer. Multicentricity, or many growths as opposed to one or two, also raises certain red flags. So would a focal or diffuse velvety-red appearance of the bladder lining (possible “flat” cancer).

Once the tumor is resected, it is sent for pathology, from which we derive a definite diagnosis including the type of tumor (most bladder cancers are “transitional cell carcinomas”, named after the cell of origin) as well as its grade (on a pathologic scale of 1-3 or sometimes 1-4, based on malignant appearance of cells microscopically) and depth of penetration, provided we, as urologists, have done biopsies deep enough into the bladder wall. Only exception to having a pathology report would be if I choose to cauterize or laser an obviously superficial/small/minimally malignant tumor (especially a “repeat offender”), which I know--by sight--has no change of causing significant problems. In some frail/elderly patients and those on anticoagulants, use of a Holmium or other laser device may be preferable, even though

doing such will reduce the accuracy or availability of specific pathologic diagnosis.

Most TURBT's (except perhaps those done with a laser) require a few days of catheterization to allow more optimal healing of the surgical ulcer site. Failure to leave in a catheter will increase the chance of postop bleeding and inability to urinate-- especially in male patients.

Once we have back the pathology, we can direct further treatment. Most patients have a fairly low grade superficial pattern which simply can be "watched" with surveillance follow-up office cystoscopies. These tests may occur, e.g., every three months for the 1<sup>st</sup> two years and barring recurrence, every 6 months for out to 5 years--and then yearly. The very minimal low-grade bladder cancers may not need life-long follow-up. More aggressive tumors or repeated episodes of bladder cancer need to be taken more seriously. Removal of the bladder (see below) is always an option to cure such disease and prevent metastases (potentially fatal spread of bladder cancer to other organs). However, intermediate types of bladder cancer including those with more malignant cells or depth of penetration into lamina propria – or another "flat" type of bladder cancer called CIS (carcinoma-in situ) may be managed with **BCG**. BCG is an altered form of mycobacterium (of which tuberculosis is an example) which when placed into the bladder in a liquid form causes a specific type of immunologic response felt to help the body fight off bladder cancer. BCG treatments are one of our best weapons, short of total bladder removal, against recurrence or even progression of bladder cancer. Studies indicate anywhere from

a 50-75% reduction in bladder cancer when BCG is utilized. Side effects, if any, are usually minor and include some pain with urination and bleeding for 1-2 days. More severe side effects from overstimulation of the immune system and rarely absorption of some of the BCG (altered/weakened) bacteria into the bloodstream may make the patient sicker and rarely require hospitalization and anti-tuberculosis antibiotic therapy.

Another "adjuvant" treatment we use to reduce recurrences is a chemotherapeutic agent called Mitomycin-C. This can be used by instillation into the bladder in the office as a series of treatments; but now commonly is placed into the bladder right at the end of the TURBT operation as a solitary treatment, especially in patients with intermediate-risk tumors. It is usually well tolerated and lacks the side effects of the same drug if used intravenously to treat other types of advanced (non-bladder) cancers.

When we talk about worse forms of bladder cancer, we are referring to those where the pathologic features show very malignant cells or deep penetration into the bladder wall. Studies suggest these tumors are genetically altered with lack of cell division regulation--and production of substances that allow invasion through normal barriers and into lymphatic channels and blood vessels. These types of bladder cancer, as well as more intermediate types (such as those involving lamina propria or carcinoma-in-situ) which keep recurring despite TURBT and use of BCG and other adjuvant modalities of treatment are dangerous and are associated with a higher risk of metastases and death from bladder

cancer. It is in these cases we must strongly consider removal of the bladder (radical cystectomy). This is done in conjunction with urinary diversion either with an ileal conduit (intestinal urinary tube ending up as a skin stoma) or continent diversion (internal "new" bladder formulated by use of excess intestines). The latter diversion allows one to still urinate, although control may be less than perfect especially at night and urinating may not be quite the same as with a normal bladder.

In some cases of localized but severe bladder cancer where a cystectomy is not wanted by the patient or there is a very high surgical risk, a Medical Oncologist can coordinate "bladder- sparing" therapy usually incorporating chemotherapy and localized bladder radiation—the results of this are controversial and probably, in my mind, not as successful as removal of the bladder.

Failure to intervene with cystectomy at the proper time or delays in diagnosis of a very malignant bladder cancer can have catastrophic consequences. Although some patients with very advanced bladder cancer can be treated with chemotherapy, many will, unfortunately, succumb to the disease.

It appears that the number of annual cases of bladder cancer in the US is increasing, up 50% over a 20 year period since the late 1980's. Over 75,000 new cases, mostly of the superficial variety, are diagnosed annually, with a 3:1 male predominance.

As you can tell, bladder cancer is actually many diseases. We as urologists have to be very precise in our diagnosis and in advising the best course of action to patients afflicted with this problem.

**Dr. Alan Freedman**

**401 Old Newport Blvd., Suite 101**

**Newport Beach, CA 92663**

**Phone: (949) 645-3434**

**FAX: (949) 645-0277**