Treatment (therapy) of superficial bladder cancer

by Detlef Hoewing - Dienstag, Dezember 29, 2015

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Operative cystoscopy (TUR-B)

Has the urologist after the diagnosis the strong suspicion that a bladder cancer might be present, a relatively small operation, it is first T rans- U rethrale R esection the B ladder (TUR-B, TUR-bladder, or even operative cystoscopy called) Recommend to clarify and confirm the diagnosis.

This is usually performed in a urology clinic. For this purpose, under anesthesia a rigid tube is inserted through the urethra into the bladder, let by the extra surgical instruments such as, eg. As introduce a high frequency current leading wire loop. With their help any existing tumors and tumor-suspicious areas are removed. In the first 24 hours. After TUR-B should be early instillation (flushing the bladder with a drug), to avoid that can colonize new cancer cells in the resected (removed) areas.

The PDD during TUR-B

PDD means P hoto D ynamic D iagnosis and is also known as fluorescence-based diagnosis.

Photodynamic Diagnosis (PDD) under operating conditions is already at the first TUR-B is recommended in order to rule out the possibility that tumor suspicious tissue remains in the bladder.

Hexvix® is currently the only approved drug for photodynamic diagnosis (PDD) to make bladder tumors more visible and determine at a transurethral resection, whether a tumor has been completely removed.

Designed for improved detection of bladder cancer, especially the carcinoma in situ (CIS), the PDD can detect even the smallest tumors that can not be seen with the standard white light method alone under certain circumstances.

After the instillation (introduction into the urinary bladder) Hexvix® is converted to a photoactive porphyrin, which in rapidly proliferating cells (such as tumors) accumulates. Under blue light, these cells fluoresce red.
This phenomenon makes the PDD to a highly sensitive diagnostic method. The additional PDD compared to the sole standard white light TUR-B has the following advantages:

- Detecting 30% more patients with bladder cancer
- Detection of 67% more tumors cis
- Better treatment every fifth patient with confirmed bladder cancer

The PDD is used in conjunction with cystoscopes (endoscopes), which are equipped with filters that allow both a standard white light view and a blue-light fluorescence view of the bladder tissue alternately. The procedure does not entail any additional complications. In addition recommend the EAU guidelines (European guidelines for bladder cancer), the use of fluorescence-assisted TUR-B.

A study of the Franziskus-Hospital in Berlin (teaching hospital of the Charité) in 2006 was able to show (transurethral resection of the bladder) under fluorescent conditions, the effectiveness and the visibility of tumors of the bladder during TUR-B. It proved also that clear benefits with the help of modern camera systems for better visibility of the bladder tumors arise - both under white light, as well as under fluorescent conditions.

**What happens after TUR-B?**

The subsequent histological examination of the removed tissue by the pathologist indicates after TUR-B, how deeply the tumor has grown into the bladder wall and he therefore determines the depth of
penetration of the tumor (the stage), and the extent of malignancy (grading).

**Stage and grade of cancer superficial bladder:**

**Stadium (depth):**

(p) = non-invasive papillary tumor Ta

(p) Cis = carcinoma in situ (flat aggressive tumor)

(p) T1 = Tumor invades superficial bladder inner wall
(p) T2 = tumor invades muscles
(p) T3 = infiltrated outer fat-tissue tumor
(p) = T4 Tumor invades adjacent organs

**Grading (malignancy)**

G1 = Low tendency to relapse (recurrence of the tumor)
G2 = after TUR-B without further therapy often occur recurrences
G3 = highest risk of recurrence. The tumor then often penetrates deeper into the bladder (progression).

If the scars are healed in the bladder, about four to six weeks, a renewed operative cystoscopy (TUR-B) to check first whether all tumorous areas were removed real and the other to the biopsy and subsequent investigation removed tissue to harden the pathological findings.

Because after this finding is directed further therapy (treatment).

**Therapy for superficial bladder cancer**

The superficial bladder carcinomas have a high tendency to relapse, that is, up to 70% of all cases occur after surgery sooner or later tumors. Therefore, is now generally recommended instillation therapy. This is done by flushing a drug into the bladder. After setting of a catheter through the urethra, the drug is introduced into the bladder (instilled). There it can then act on the mucous membrane and the tumor-prone districts. However, the treatment of bladder cancer depends largely on the stage and the grading (malignancy), in which it is located.

Most bladder cancers (about 80%) are in the early stages discovered (in tumor stage Ta or T1) and as non-invasive (superficial - not deeply penetrated into the bladder wall) designates. They often have a low to moderate aggressiveness (malignancy). This means that the tumor is limited to the innermost layers of the bladder wall and did not attack the muscular wall of the bladder.

Despite all the treatment measures, however, of cases (50-70%) can again bladder cancer occur within 5 years in more than half. Therefore, regular visits to the urologist by a cystoscopy (cystoscopy) is required. In 60-70% of cases, superficial bladder cancer can be cured by long-term repeated TUR B’s and Instillationstherapien because of the risk of the remote settlement can be estimated at an early stage to be low to other organs (metastasis).
Instillation of a chemotherapeutic agent

For the treatment of superficial bladder tumor, which is still in its infancy (Ta-T1) and a low to medium aggressiveness (grading = G1 - G2) which is used as standard therapy often a chemically synthesized therapeutic instilled into the bladder (introduced).

Here it has been shown that mitomycin has the best results of instillation. Mitomycin has also established itself in the Frühinstillation after TUR-B as a standard treatment, since it has a smaller range of side effects than other drugs. Nevertheless, there are also scattered here incompatibilities that may require the use of other chemotherapeutic.

Immunotherapy with BCG

BCG stands for "B acillus C Almette G uérin" and refers to an attenuated, no longer disease exciting Rindertuberkelbakterium. By BCG immunotherapy the natural defense system of the body against the bladder cancer is stimulated and activated directly into the bladder.

BCG produces special defense cells, called "BCG-activated killer cells" that attack targeted bladder tumor cells. Supportive the release of immune mediators (cytokines) is excited.

BCG is a very effective for bladder cancer patients treatment by instillation into the urinary bladder. This treatment of superficial bladder cancer is popular with medium to high aggressiveness (malignancy) of the tumor and has shown in this the greatest success of treatment.Unfortunately, this method of treatment has sometimes severe to severe side-effects and can therefore lead to the termination of the treatment often several years.

When failure of BCG treatment, ie particularly when recurrence (relapse) of a highly aggressive bladder tumor, such as the T1 G3 or a Cis (carcinoma in situ), but only one bladder removal (Zysterkomie) may be recommended.

Cis = Carcinoma in situ

The carcinoma in situ (CIS) of the urinary bladder is a flat located in the mucosal lesion level, which is not raised and leaves his entire extent difficult to distinguish from the healthy bladder wall. Today we know that it is highly aggressive tumors that can grow deep into the tissue of the bladder.

Immunotherapy with Immunocyanin

For some years there are for patients in whom the instillation with mitomycin or BCG was unsuccessful or showed intolerance, an alternative treatment option with Immunocyanin. This is a stable form of the blood pigment keyhole limpet hemocyanin (KLH) of sea snail Megatura crenulata.

Therapy with Immunocyanin (product name: IMMUCOTHEL®) takes, similar to the therapy with BCG in total a year, but has far fewer side effects.

Unfortunately this drug is not yet approved in Germany and is therefore not listed in the list of drugs in
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**Synergo- treatment**

Synergo is a new advanced technology for treating the superficial bladder cancer.

Basis of the treatment is a controlled hyperthermia (overheating) of the urinary bladder walls, along with instillation of a chemotherapeutic substance (usually by means of mitomycin-C) into the bladder.

The core is a high-frequency generator which heats the bladder wall to an optimum temperature. About a catheter allows a small pump chemotherapeutic solution between the bladder and a drug reservoir to circulate.

The information is transmitted to an embedded computer, which monitors all system functions and controls.

The Synergo- treatment is currently only available in a few urological centers, so the developers of the University Hospital Giessen, University Hospital Erlangen, Tübingen University Hospital, Charité Berlin (CM), University of Munich. This consistently report very positive results of the treatment, which means that in the treated patients had significantly lower recurrence tendency is observed and get the final chance of recovery.

**Limiting case of treatment**

Borderline cases in treatment methods make the T1 G3 tumors and Cis (carcinoma in situ) of the urinary bladder. Although still referred to as superficial bladder tumors, they have already penetrated into the bladder wall and tended greatly because of their malignancy recurrence (relapse) of the tumor and also used to grow deeper in the bladder wall. This reduces the risk of metastasis increases (remote settlement in other organs).

These findings, both the complete removal of the bladder (cystectomy), as well as a means of BCG instillation is recommended. If this fails, that is, occurs during treatment of recurrence, all physicians
themselves agree that the bladder has to be removed, if this is possible with the individual patient.

The treatment methods should always be tailored to the individual patient.

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