Can Reflex UroVysion fluorescence in situ hybridization predict tumor recurrence during follow-up?

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Yoder BJ, Skacel M, Hedgepeth R, Babineau D, Ulchaker JC, Liou LS, et al. Reflex UroVysion testing of bladder cancer surveillance patients with equivocal or negative urine cytology: A prospective study with focus on the natural history of anticipatory positive findings. Am J Clin Pathol 2007;127:295-301.

SUMMARY

The primary aim of this study was to demonstrate the usefulness of multitarget fluorescence in situ hybridization (FISH UroVysion) testing in the early detection of recurrent urothelial carcinoma (UC). The study population comprised patients with bladder tumor on follow-up, who had negative or atypical urine cytology with no evidence of recurrence by cystoscopy. Some of these patients had positive UroVysion FISH in the urine cell sample. The paper looks at the course of these “anticipatory positive” cases with special reference to the recurrence and the time to tumor recurrence. Fifty-six (26.5%) of the 211 patients with negative cystoscopy and negative or atypical cytology had positive FISH results. This group formed the anticipatory positive subset of patients. Recurrent urothelial carcinoma developed in 35 (62.5%) of these 56 patients. Of these recurrent tumors 22 were high-grade UC and 12 low-grade UC. In about 65% of this anticipatory positive group, recurrent bladder UC bladder developed within 29 months. The recurrence rate was 48% in six months and 54% within 10 months of the positive FISH result. In contrast recurrent UC developed in only eight (5.2%) of the 155 cystoscopically negative, cytologically negative or atypical and FISH negative cases.

COMMENTS

Urothelial carcinoma has a high rate of recurrence and progression, necessitating frequent patient surveillance by follow-up is by cystoscopy and urine cytology.[1] The invasive nature of cystoscopy and the relative low sensitivity of cytology are the limitations of this approach. This has led to many adjunctive assays to stratify individuals into high- and low-risk categories.[2] UroVysion is a multitarget FISH assay to detect chromosomal alterations by three DNA probes directed
Abstracts

The primary objective of this multicentric prospective randomized trial[1] was to determine whether pretreatment with dutasteride, a dual 5α-reductase inhibitor (5ARI), reduces surgical blood loss in patients who undergo transurethral resection of the prostate (TURP) for benign prostatic hyperplasia (BPH) with prostates ≥ 30 ml volume. The secondary objectives were to assess bleeding after TURP and postoperative complications like clot retention, blood transfusions, urinary tract infection (UTI), incontinence and acute urinary retention (AUR) following TURP. Two hundred and thirteen men aged 52-85 years (mean 67) with prostate volume of ≥ 30 ml were recruited from 23 centers across six countries. Two hundred and two had TURP and 197 completed the study. They were randomized to three groups: Group I receiving placebo for four weeks preoperatively and two weeks postoperatively, Group II receiving placebo for two weeks followed by dutasteride 0.5 mg for two weeks preoperatively and two weeks of dutasteride 0.5 mg daily postoperatively and Group III with dutasteride 0.5 mg four weeks preoperatively and two weeks postoperatively. Prior prostate surgery, history or evidence of prostatic disease other than BPH, those who had 5ARI within 12 months, those on aspirin and NSAIDS and those with severe medical conditions like liver disease, unstable cardiovascular diseases and bleeding disorders were excluded. All the patient events four weeks before and four weeks after TURP were recorded using daily diary. Subsequently, weekly diary was maintained for 10 weeks. Blood loss was measured from irrigation fluid drained using HemoCue low hemoglobin system-photometer. Serum testosterone, dihydrotestosterone (DHT) were measured during recruitment, during TURP and four weeks after TURP. Microvessel density (MVD) and intraprostatic levels of hormones were measured from prostatic chips after TURP. The mean operative duration was 45 min and about 25 g of prostate was resected. Mean blood loss during TURP was 2.15 to 2.55 gm Hb/gm of resectate in the three groups. There were no statistically significant differences in the blood loss during surgery towards the pericentromeric regions of Chromosome 3,7 and 17 and a fourth probe to 9p21 locus. This molecular cytology by the combination of probes allows detection of chromosomal aneusomy and or deletion of 9p21.[3] Though FISH analysis is currently the most sensitive marker for bladder tumors, the cost of the DNA probes and the laboratory equipment required, limits its use in the everyday routine.[4] However, it is useful for the early identification of patients who are likely to progress. It also helps to lengthen the surveillance period in those with low-risk disease.[3] There is no improvement of FISH over cytology in the cytology-positive cases for detection of recurrence during follow-up.[6] It is worth noting here that many low-grade lesions do not shed cells and do not exhibit chromosomal changes detected by FISH testing. The data presented in the study shows that reflex UroVysion on urine specimens helps to identify the anticipatory positive case so that more aggressive therapeutic options can be planned.

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