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Home > Vol 96, No 8 > Jantip

Mutations of Fibroblast Growth Factor Receptor 3 Gene (FGFR3) in Transitional Cell Carcinoma of Urinary Bladder in Thai Patients [Revision-2a]

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Abstract

Objective: Determine the incidence of FGFR3 mutations in Thai patients with bladder transitional cell carcinoma (TCC), and evaluate their correlation with pathological characteristics.

Material and Method: One hundred twenty two frozen tissue samples from TCC patients were analyzed for mutations in exons 7, 10, and 15 of FGFR3 by polymerase chain reaction and direct DNA sequencing.

Results: FGFR3 mutations were detected in 22 of 122 cases (18%) studied, all of which were found within previously identified hotspots, including S249C (13 cases; 59%) and R248C (4 cases; 18%) in exon 7, and Y375C (5 cases; 23%) in exon 10, but no mutations in exon 15. Sixty-five patients (53%) were categorized as non-muscle-invasive TCC (pTa-pT1). The incidence of mutations is significantly higher in non-muscle-invasive tumors (28%) compared to the muscle-invading group (7%) ($p<0.01$). Patients with grade (G) 1 TCC have significantly higher mutation frequency (40%) compared to other grades (4%) ($p<0.01$). When T stage and grade were considered together, mutations were most commonly found in Ta-T1/G1 TCC (18/45 cases, 40%). Mean follow-up period was 45.1 months. Two-year and four-year overall survival (OS) was 70% and 56% respectively. Three-year OS in non-muscle-invasive TCC (80%) is significantly higher than that of muscle invading TCC (41%) ($p<0.01$). However, three-year OS in cases with an FGFR3 mutation (73%) is not significantly different from cases without a mutation (61%). In 16 cases with an FGFR3 mutation and recurrent disease, no mutations were detected in metachronous disease.

Conclusion: The overall incidence of FGFR3 mutations in Thai patients with TCC was lower than similar reports from other ethnic groups. In the presented cases, although FGFR3 mutations were frequently detected in low-grade, non-muscleinvasive TCC, identical mutation was not conserved in metachronous disease, thereby precluding the use of this marker in detection of tumor recurrence.

Keywords: Urinary bladder cancer, FGFR3, Transitional cell carcinoma

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