Hereditary Urothelial Carcinomas of the Upper Urinary Tract Are Underestimated and Misclassified as Sporadic Tumours: Results of the French Collaborative Database on UUT-UCC

Introduction and Objectives: Hereditary non-polyposis colorectal cancer (HNPCC) is an autosomal dominant multi-cancer syndrome caused by germline mutations of mismatch repair genes. Upper urinary tract urothelial cell carcinoma (UUT-UCC) belongs to the group of HNPCC-related cancers and hereditary cases are estimated to account for 5% of cases. However, many urologists are not aware of this association, and it is presumed some hereditary cancers are misclassified as sporadic and their incidence is underestimated, although there are consequences for detection and surveillance in the relatives of HNPCC patients. The aim of this work was to analyse, using a large cohort from a national collaborative group, the demographic and epidemiologic factors that are associated with suspicion of hereditary UUT-UCC.
Materials and Methods: A multi-institutional, national, retrospective study was conducted, including 1,122 patients from the French national database on UUT-UCC. Patients were considered at risk for hereditary UUT-UCC if they presented one of the following clinical criteria: age at diagnosis < 60 years with no previous history of bladder cancer, previous history of any other HNPCC-related cancer regardless of age, one first-degree relative with HNPCC related cancer diagnosed before 50 years old or two first-degree relatives with HNPCC related cancer regardless of age. Otherwise, they were classified as sporadic cancer. Gender, age at diagnosis, smoking status with the duration of intoxication, professional exposure to carcinogens, tumour characteristics and oncologic outcomes were also analysed.
Results: Among 1,122 patients, 239 (21.3%) were considered at risk for hereditary UUT-UCC: 79 (33%) had a personal history of another HNPCC-related cancer, 14 patients (5.9%) had one first-degree relative with HNPCC-related cancer diagnosed before 50 years old, 6 (2.5%) had two first-degree relatives with HNPCC-related cancer regardless of age and 169 patients (70.7%) were under 60 years old with no previous history of bladder cancer. In the group at risk for heredity cancer, there was a preponderance of female sex (sex-ratio=1.8 vs 2.44, p=0.047). Secondly, tobacco intoxication or professional exposure to carcinogens were less prevalent (respectively 56.7% vs 66.4%, p=0.012 and 13.9% vs 25.9%, p=0.037). Tumour location differed significantly between the two cohorts (p=0.026). In the hereditary cancer at-risk group and the sporadic group, tumours of the ureter, renal pelvis and both occurred in 30% vs. 39.7%, 54.5% vs. 48.4% and 15.5% vs. 11.8%. However, histological characteristics and oncologic outcomes were similar in the 2 groups.
Conclusion: In this study, 21.3% of the patients diagnosed with UUT-UCC were at risk for an underlying associated hereditary syndrome. Demographic and epidemiologic characteristics suggest different mechanisms of carcinogenesis among this population. Upon diagnosis of UUT-UCC assessment of specific clinical information, namely previous personal/family cancer history, should alert clinicians to the possibility of an associated hereditary syndrome such as HNPCC.