



## Familial aggregation of bladder cancer

### Familijarna agregacija raka mokraćne bešike

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#### Abstract

**Background.** Except for smoking and certain occupational exposures, the etiology of bladder cancer is largely unknown. Several case reports have described familial aggregation of transitional cell carcinoma of the bladder. Although the majority of patients with bladder cancer do not have family history of transitional cell carcinoma of the urinary tract, the study of familial transitional cell carcinoma may lead to the knowledge on the pathogenesis of this disease. The purpose of this study was to describe three cases of urinary bladder cancer in a single three-member family, i.e. in two generations (mother and son) and a family member related by marriage (the patient's wife). **Case report.** Three cases of urinary bladder cancer occurred in a three-member family within the interval of 5 years. The following common characteristics were detected in our patients: old age (over 60), working as farmers for more than 50 years, negative personal medical history on relevant health disorders, place of birth – village, place of residence – village, the same water supply, similar nutrition, positive family history on urinary bladder cancer or other malignant tumors, the first sign of illness was macroscopic hematuria in all the patients and the same pathohistological type of cancer – *carcinoma papillare transitiocellulare*. **Conclusion.** The stated common characteristics in our cases indicate, above all, the impact of exposure to external surrounding factors on the occurrence of urinary bladder cancer.

#### Key words:

urinary bladder neoplasms; carcinoma, transitional cell; family; carcinoma, papillary.

#### Apstrakt

**Uvod.** Osim značaja uticaja navike pušenja cigareta i profesionalne izloženosti nekim kancerogenima na nastanak karcinoma mokraćne bešike, etiologija tog malignog tumora nije sasvim razjašnjena. Nekoliko epidemioloških studija opisalo je familijarnu agregaciju raka mokraćne bešike – *carcinoma papillare transitiocellulare*. Mada se kod većine obolelih ne registruje pozitivna porodična istorija za tranziciocelularni rak mokraćne bešike, ispitivanje familijarne agregacije može doprineti sagledavanju patogeneze tog malignog tumora. U ovom radu prikazana su tri slučaja raka mokraćne bešike u jednoj porodici, kod dve generacije srodnika (majka i sin) i kod člana porodice koji nije krvni srodnik (supruga obolelog). **Prikaz slučaja.** Tri slučaja raka mokraćne bešike u tročlanoj porodici zabeleženi su u intervalu od pet godina. Oboleli od raka mokraćne bešike imali su sledeće zajedničke karakteristike: stariji uzrast (preko 60 godina), bavljenje poslom poljoprivrednika duže od 50 godina, negativnu ličnu zdravstvenu istoriju ozbiljnih poremećaja zdravlja, mesto rođenja – selo, mesto stalnog boravka – selo, isti način snabdevanja vodom za piće, sličan način ishrane, pozitivnu porodičnu istoriju raka mokraćne bešike i druge maligne tumore, hematuriju kao prvi znak bolesti, isti patohistološki tip malignog tumora – *carcinoma papillare transitiocellulare*. **Zaključak.** Karakteristike obolelih ukazuju na značaj izloženosti faktorima spoljašnje sredine u nastanku raka mokraćne bešike.

#### Ključne reči:

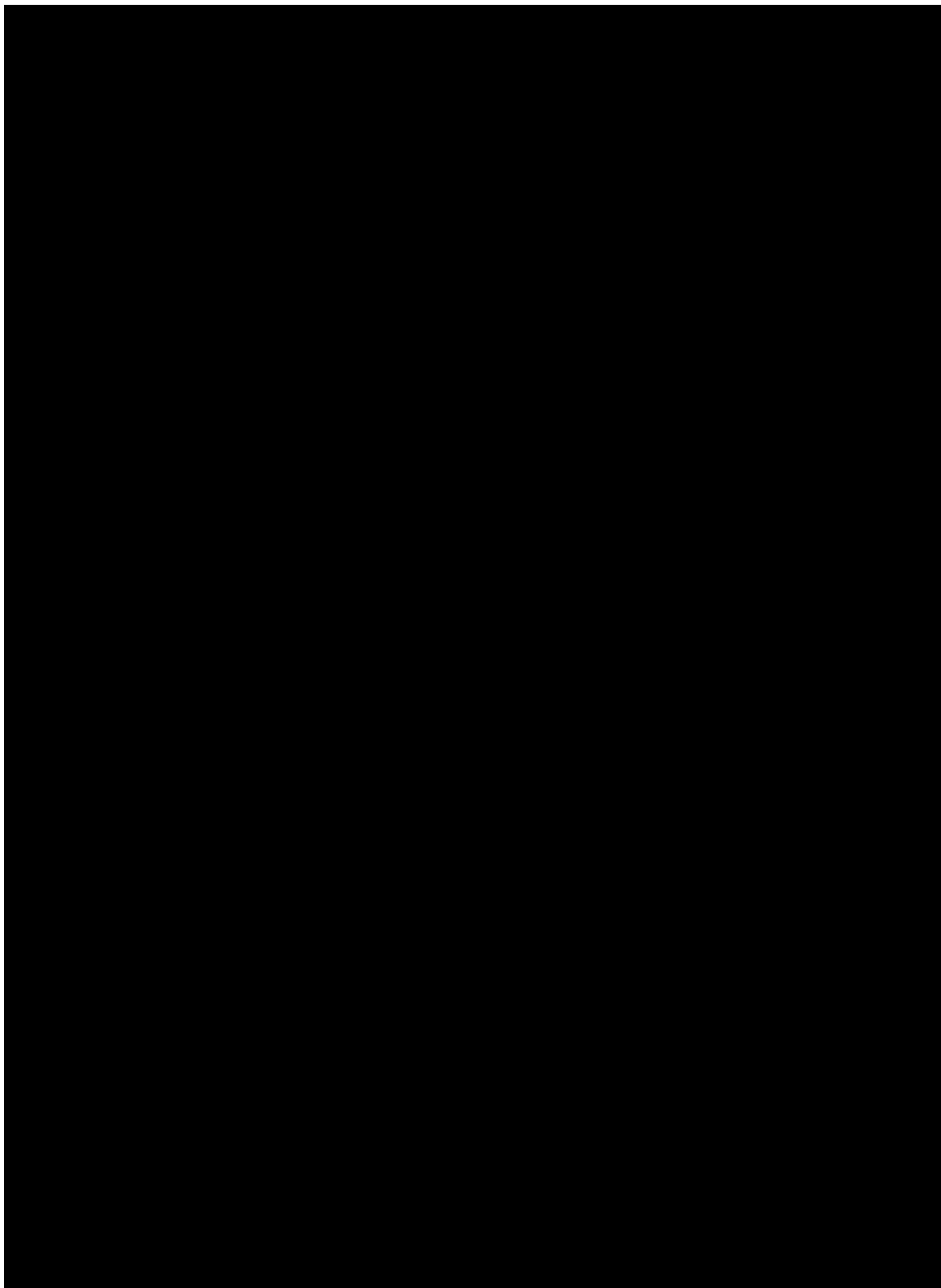
mokraćna bešika, neoplazme; karcinom prelaznih ćelija; porodica; karcinom, papilarni.

#### Introduction

According to a large number of hypotheses on etiology, urinary bladder cancer is considered to be an illness with more possible causes<sup>1-5</sup>. Smoking is a single greatest risk factor for bladder cancer<sup>3,5-7</sup>. Smokers have more than twice the risk of developing bladder cancer as nonsmokers<sup>1,2,5,7,8</sup>. Organic chemicals called aromatic amines are particularly

linked with bladder cancer<sup>3,9</sup>. Arsenic is a known bladder carcinogen and populations exposed to high arsenic levels in their water supply have reported elevated bladder cancer mortality and incidence rates<sup>10,11</sup>. The reason for high incidence of urinary tract cancer in individuals suffering from Balkan nephropathy has yet to be determined<sup>12</sup>.

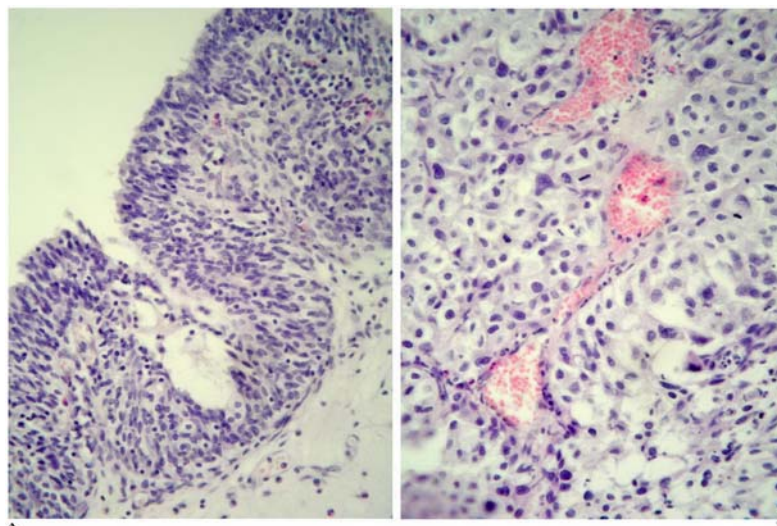
Several epidemiological studies have indicated a possible familial component to bladder cancer<sup>13-16</sup>. Kiemeny and



At the beginning of 1997, the patient's mother (born in 1915) was admitted to the hospital for hematuria and frequent urination. Transurethral resection was performed in January 1997, followed by radiation therapy. A biopsy specimen revealed *carcinoma papillare transitiocellulare*, histological grade 2, with signs of submucosa infiltration (Figure 3). In July 1997, recurrence was diagnosed and cauterized. In August 1998, the second recurrence was diagnosed, followed by another transurethral resection in January 1999. Death occurred in 2000.

the smooth muscle. Infiltration of lymph vessels and moderate necrosis points were detected. Transurethral resection was performed in August 2001, followed by radiation therapy. Twenty five months later the patient had no recidives. According to family tree (Figure 1), her father died at the age of 70 of lung cancer, and his relative died of stomach cancer at the age of 66. No other family members were affected by cancer.

The patient's mother and wife in their personal medical histories had no evidence of several diseases (urinary infec-

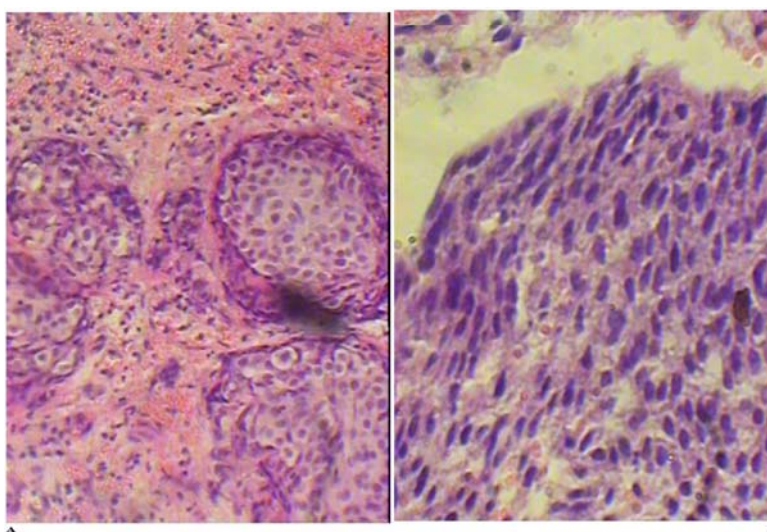


**Fig. 3 – Histologic analysis of bladder cancer in the patient's mother – A) *carcinoma papillare transitiocellulare* (hematoxylin-eosin, original magnification  $\times 100$ ); carcinoma papillare transitiocellulare (hematoxylin-eosin, original magnification  $\times 400$ )**

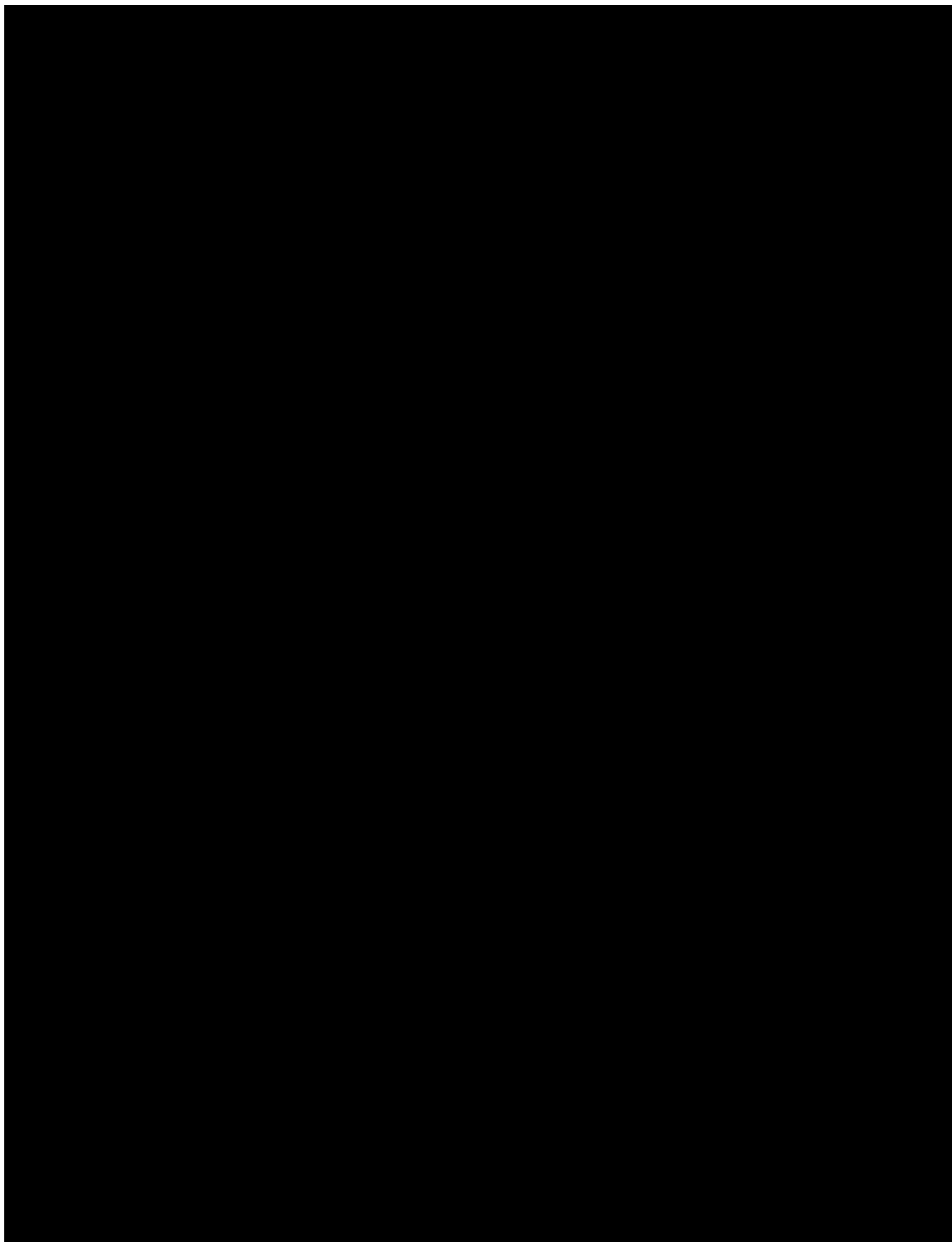
The patient's wife (born in 1938) and got urinary bladder cancer at the age of 63. She was admitted to the hospital for hematuria and frequent urination in August 2001. A biopsy specimen revealed *carcinoma papillare transitiocellulare*, histological grade of 2 and nuclear grade 3 (Figure 4). The tumor was infiltrating submucosa and the fragments of

tions, lithiasis, bladder cancer, tumors of the kidney, diabetes mellitus, sexual diseases and of any form of cancer). They were both non-smokers.

Our subjects lived in a village about 10 kilometers away from Kragujevac. Kragujevac is a town with almost 200,000 people in the center of Šumadija Region in Central Serbia. In



**Fig. 4 – Histologic analysis of bladder cancer in the patient's wife – A) *carcinoma papillare transitiocellulare* (hematoxylin-eosin, original magnification  $\times 100$ ); B) *carcinoma papillare transitiocellulare* (hematoxylin-eosin, original magnification  $\times 400$ )**



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