Recurring multifocal leiomyosarcoma of the urinary bladder 22 years after therapy for bilateral (hereditary) retinoblastoma: A case report and review of the literature

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SUMMARY
We report on a case of urinary bladder leiomyosarcoma in a 23-year-old woman, 22 years after therapy for bilateral retinoblastoma. The tumor presented with dysuria and macroscopic haematuria. Cystoscopy revealed a tumor localized in the trigonum covered by an ulcerated urothelium. The patient underwent a transvesical tumor resection. Eight months later, a second leiomyosarcoma developed in the vertex, at a site different from the previous one. A cystoscopic trans-urethral tumor resection was performed, followed by combined chemotherapy. One year later another recurrence occurred at the site of the primary resection. Open laparotomic resection of the involved bladder wall was performed. The patient remains both recurrence and metastases free after twenty months of follow-up. Molecular analysis of the peripheral blood showed rare germline point mutation in the intron 24 of the RB1 gene. FISH analysis of the tumor tissue revealed polyploid cells with relative loss of normal RB1 gene locus, indicating deletion and second hit loss of the second RB1 allele function. Along with the ten previously reported cases, this report suggests a non-random association between the hereditary retinoblastoma and urinary bladder leiomyosarcoma. Therapy with cyclophosphamide seems to be an important risk factor. Life-long surveillance for second malignancies, including bladder leiomyosarcoma is therefore mandatory in these patients.

Keywords: retinoblastoma – urinary bladder – leiomyosarcoma – secondary cancer – cyclophosphamide

Recidivujúci multifokálny leiomyosarkóm močového mechúra 22 rokov po liečbe bilaterálneho (hereditárneho) retinoblastómu: popis prípadu a prehľad literatúry

SÚHRN
Popisujeme prípad leiomyosarkómu močového mechúra u 23 ročnej ženy, 22 rokov po liečbe bilaterálneho retinoblastómu. Nádor sa prezentoval dysúriou a makroskopickou hematúriou. Cystoskopicky bol zistený ulcerovaný nádor lokalizovaný v trigone. Následne bola vykonaná jeho transvezikálna resekcia. Osem mesiacov neskôr na inom mieste močového mechúra, vo vertexe , vznikol u pacientky druhý leiomyosarkóm. Bola vykonaná cystoskopická transuretrálna resekcia nádoru s následnou kombinovanou chemoterapiou. Po jednom roku sa objavila recidíva v mieste prvej resekcie. Bola vykonaná otvorená resekcia postihnutej steny mechúra. Dvadsať mesiacov po poslednej operácii je pacientka bez známok recidívy alebo metastáz. Molekulárnou analýzou periférnej krvi bola dokázná vzácna zárodočná bodová mutácia v intróne 24 RB1 génu. FISH analýza nádorového tkaniva dokázala polyploiditu nádorových buniek s relatívnou stratou lókusu RB1, indikujúc ,,second hit" deléciu a tým stratu funkcie druhej RB1 alely. Spolu s desiatimi doposiaľ popísanými prípadmi, náš prípad svedčí pre nenáhodnú asociáciu medzi hereditárnym retinoblastómom a leiomyosarkómom močového mechúra. Dôležitým rizikovým faktorom je pravdepodobne liečba cyklofosfamidom. U týchto pacientov je dôležité celoživotné sledovanie na výskyt sekundárnych malignít, vrátane leiomyosarkómu močového mechúra.

Kľúčové slová: retinoblastóm – močový mechúr – leiomyosarkóm – sekundárna malignita – cyklofosfamid

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Leiomyosarcoma is the most common malignant mesenchymal tumor of the urinary bladder, but it accounts for less than 1 % of all malignant bladder neoplasms (1,2). The treatment with cyclophosphamide currently represents the only known risk factor (1,3–5). To date, only ten cases of bladder leiomyosarcoma have been reported as a second malignancy in retinoblastoma survivors (4,6–14). We describe an additional case of bladder leiomyosar-