MedCrave
Step into the World of Research

Urology & Nephrology Open Access Journal

Case Report

Open Access

CrossMark

Metachronous bilateral urothelial carcinoma in a patient with hereditary nonpolyposis colorectal cancer syndrome - a case report

Abstract

We present a case of metachronous upper urinary transitional cell carcinoma in a 62 year old man found to have hereditary nonpolyposis colorectal cancer syndrome (HNPCC/ Lynch syndrome). We then bring a short review of the literature.

Volume 5 Issue 2 - 2017

Arnon Lavi, Sharon Tzemach, Michael Cohen
Department of Urology, Haamek medical center, Israel

Correspondence: Arnon Lavi, Department of Urology, Haamek medical center, 21 Rabin BLVD, Afula, Israel, Tel 523294388, Email arnonmlavi@gmail.com

Received: July 15, 2017 | **Published:** July 18, 2017

Case report

A 62-year-old man presented to our ward for evaluation of right hydronephrosis found on imaging performed for a new onset acute or chronic kidney disease evaluation. Medical history revealed a sub-total colectomy performed for colon cancer 8 years ago and subsequent chemotherapy. Ureteroscopy revealed an intraureteric pappilary lesion found to be Transitional cell carcinoma (TCC) T2 high grade (HG) on histology. The patient underwent a right radical nephroureterectomy. 3 months later he presented with new onset acute or chronic kidney failure. Computed Tomography (CT) revealed left hydronephrosis and a suspected tumor in the left pelvis. Multiple lesions and a huge renal pelvic tumor were found on left ureteroscopy. Histology revealed TCC HG disease. The patient underwent a left nephroureterctomy and radical cystectomy and was put on hemodialysis. Histologgy revealed a T3N1HG disease.

This patient's 52 year old younger sister presented later with right upper tract urothelial carcinoma (UTUC) in her right pelvis. Ureteroscopic biost revealed TCC T1HG disease. After receiving neoadjuvant chemotherapy (Gemctibine + Cisplatinum) imaging showed a near to complete response in the renal pelvis and paraortic mass. She underwent a right nephroureterectomy with modified lymph dissection which showed no evidence of disease. Genetic investigation revealed a Q158X mutation on MSH2 Gene consistent with the diagnosis of Lynch syndrome/HNPCC (hereditary nonpolyposis colorectal cancer). A family tree of the patients' family is shown in Figure 1. Yamada et al.[1] recently reported a similar case of metachronous upper tract TCC associated with hereditary nonpolyposis cancer (HNPCC) requiring radical surgery. Hubosky et al.[2] reported that of 13 HNPCC patients treated for upper tract TCC, 6 had bilateral disease.

Short review of the literature

In 1913 Warthin first described a hereditary pattern of carcinoma's affecting several families. The susceptibility was particularly for lip, mouth, breast, stomach, intestine and uterus carconaoma's.[3] It was not until a few decades later that Dr. Henry Lynch described families with predisposition to hereditary malignancy and brought the syndrome to the awareness of the medical community.[4,5] Due to his colossal contribution, the term "Lynch syndrome" is now more commonly used to describe HNPCC.

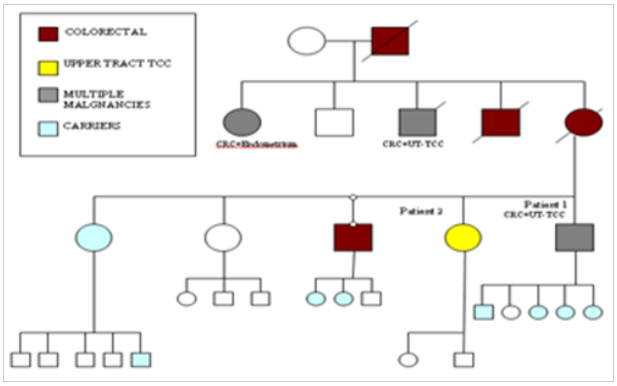

Figure 1 The patients' family tree.

CRC: Colorectal Cancer; UT-TCC: Upper Tract Transitional Cell Carcinoma; Patient 1: First Presented Male Patient with Metachronous Upper Tract; TCC: Patient 2-Patient 1's sister with upper tract TCC

Lynch syndrome is a hereditary disease inherited in an autosomal dominant manner. The underlying defect involves the mismatch repair (MMR) system, comprised of 4 genes producing the MMR proteins: MLH1, MSH2, MSH6 and PMS2. These mutations result in microsatellite instability (MSI). Up to 70-90% of the cases are attributed to mutations in MLH1 and MSH2.[6-8] MSH2 mutation seems to hold the highest risk factor for several cancer types including UTUC.[9,10]

The most common manifestations are colon, Endometrial and ovarian cancers with prevalence of up to 70%, 40 and 11% respectively. Other manifestations include gastric, urotheial carcinoma, small bowel, hepatobiliary, pancreas, brain and sebaceous cancers with prevalence much lower ranging 3-13%.[11] UTUC has been reported to have up to 22 fold increased risk of occurring in Lynch syndrome individuals compared to the general population. The age of occurrence is substantially younger with a median of 56 years.[12] The revised Amsterdam criteria have become widely used to identify high risk families suitable for further genetic investigation. The criteria identify families with 3 closely related members of 2 generations with colon/ extracolonic Lynch syndrome manifestations. One member should be diagnosed before the age of 50.[13] Sporadic UTUC might also benefit from genetic testing. Inactivation of hPMS2 & hMLH1 has been

proposed to be independent markers of good prognosis and occurs in a quarter of sporadic UTUC cases.[14]

Conclusion

UTUC is a lethal disease. High level of suspicion can lead to early diagnosis of Lynch syndrome and hence prompt early screening for different malignancies in order to improve survival.

Acknowledgments

None.

Conflicts of Interset

None.

References

1. Yamada Y, Ueda Y, Higuchi Y, et al. [Metachronous urothelial cancer in bilateral upper urinary tracts and bladder associated with hereditary nonpolyposis colorectal cancer]. *Hinyokika Kiyo*. 2011;57(10):559–563.
2. Hubosky SG, Boman BM, Charles S, et al. Ureteroscopic management of upper tract urothelial carcinoma (UTUC) in patients with Lynch Syndrome (hereditary nonpolyposis colorectal cancer syndrome). *BJU Int*. 2013;112(6):813–819.
3. Classics in oncology. Heredity with reference to carcinoma as shown by the study of the cases examined in the pathological laboratory of the University of Michigan, 1895-1913. By Aldred Scott Warthin. 1913. *CA Cancer J Clin*. 1985;35(6): 348–359.
4. Lynch PM, Lynch HT, Harris RE. Hereditary proximal colonic cancer. *Dis Colon Rectum*. 1977;20(8):661–668.
5. Fitzgibbons RJ, Lynch HT, Stanislav GV, et al. Recognition and treatment of patients with hereditary nonpolyposis colon cancer (Lynch syndromes I and II). *Ann Surg*. 1987;206(3):289–295.
6. Palomaki GE, McClain MR, Melillo S, et al. EGAPP supplementary evidence review: DNA testing strategies aimed at reducing morbidity and mortality from Lynch syndrome. *Genet Med*. 2009;11(1):42–65.
7. Egoavil C, Alenda C, Castillejo A, et al. Prevalence of Lynch Syndrome among Patients with Newly Diagnosed Endometrial Cancers. Suzuki H, editor. *PLoS One*. 2013;8(11):e79737.
8. Weissman SM, Burt R, Church J, et al. Identification of individuals at risk for Lynch syndrome using targeted evaluations and genetic testing: National Society of Genetic Counselors and the Collaborative Group of the Americas on Inherited Colorectal Cancer joint practice guideline. *J Genet Couns*. 2012;21(4):484–493.
9. Ramsoekh D, Wagner A, van Leerdam ME, et al. Cancer risk in MLH1, MSH2 and MSH6 mutation carriers; different risk profiles may influence clinical management. *Hered Cancer Clin Pract*. 2009;7(1):17.
10. Lin-Hurtubise KM, Yheulon CG, Gagliano RA, et al. Excess of extracolonic non-endometrial multiple primary cancers in MSH2 germline mutation carriers over MLH1. *J Surg Oncol*. 2013;108(7):433–437.
11. Cohen SA, Leininger A. The genetic basis of Lynch syndrome and its implications for clinical practice and risk management. *Appl Clin Genet*. 2014;7:147–158.
12. Watson P, Lynch HT. The tumor spectrum in HNPCC. *Anticancer Res*. 2017;14(4B):1635–1639.
13. Vasen HF, Watson P, Mecklin JP, et al. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative group on HNPCC. *Gastroenterology*. 2017;116(6):1453–1456.
14. García-Tello A, Ramón de Fata F, Andrés G, et al. DNA repair genes and prognosis in sporadic forms of urothelial carcinoma of the upper urinary tract. Actas Urol Esp. 2014;38(9): 600–607.