A RARE COMBINATION OF SYNCHRONOUS DOUBLE PRIMARY MALIGNANCIES – A CASE REPORT WITH LITERATURE REVIEW

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ABSTRACT

Aim: Aim of this study is to report a rare combination of synchronous double primary malignancies and to review the literature with reference to so far reported cases.

Case Report: A 48 years old male patient presented to us with lower abdominal pain and burning micturition of one month duration. Based on clinical presentation and investigation reports he was diagnosed as a case of synchronous double primary malignancies of ascending colon and urinary bladder. After complete workup for both the malignancies, he underwent Trans Urethral Resection of Bladder Tumour (TURBT) and radical right hemicolectomy.

Discussion: The term Multiple Primary Malignant Neoplasms (MPMNs), was first used by Billroth in 1889. They can be synchronous or metachronous. Extensive literature search shows only four cases of synchronous double primaries involving urinary bladder and colon. We are reporting a rare combination of synchronous double primary malignancies of urinary bladder and ascending colon. This is the fifth case report of synchronous double primaries involving bladder and colon & third case report involving bladder and ascending colon to the best of our knowledge.

Conclusion: MPMNs are still elusive for want of proper guidelines regarding correct terminology and classification encompassing varying presentations of chronological, aetiological, clinical and histopathological combinations. Our case adds up to literature for further research. The possibility of occurrence of synchronous multiple primary malignancies should be considered during workup for any malignant condition to institute early intervention to achieve good outcome.

Key Words: Colonic adenocarcinoma, Synchronous primaries, Urothelial carcinoma

INTRODUCTION

The term Multiple Primary Malignant Neoplasms (MPMNs), was first used by Billroth1 in 1889. MPMNs are referred by some authors as multiple primary cancers (MPCs), or as Multiple primary malignancies (MPMs). Though the occurrence of multiple primary cancers has risen due to improvements in diagnostic techniques and treatment, the diagnostic criteria for multiple primary cancers remain the same as advocated by Warren and Gates2 in 1932. i.e. 1) Each cancer must be definitively malignant by histopathology, 2) they must be histologically different and 3) the possibility of metastasis among the cancers must be excluded. Differentiation between multiple primary and multicentric cancers was addressed in the classification by Moertel CG3:

I MPMNs of multicentric origin: a) The same tissue and organ. b) A common, contiguous tissue shared by different organs. c) The same tissue in bilaterally paired organs.

II MPMNs of different tissues or organs.

III MPMNs of multicentric origin plus a lesion (s) of a different tissue or organ.

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In 2002, Howe in ‘A review of the definition for multiple primary cancers in the United States’ classified the association of different cancers in two categories depending on the timing of their discovery; a) synchronous in which the cancers occur at the same time or within two months and b) metachronous in which the cancers follow in sequence of more than two months apart. Vaamonde et al. reckoned the time factor as six months. In 2005, International Agency for Research on Cancer working Group has come out with International Rules for Multiple Primary Cancers.

CASE DETAILS

A 48 years old male patient presented to us with lower abdominal pain and burning micturition of one month duration and was evaluated for the same with ultrasonography abdomen, which revealed well defined isoechoic lesion in the left lateral wall of urinary bladder. Further evaluation with CT urogram showed well defined heterogeneous enhancing lesion with speculations in the urinary bladder suggestive of carcinoma of bladder and incidentally discovered circumferential wall thickening involving the distal part of ascending colon causing partial obstruction with presence of multiple enlarged lymph nodes seen adjacent to the lesion. (Figure 1a & 1b). His serum CEA level was 38 ng/ml. Evaluation with colonoscopy showed circumferential proliferative growth in the distal ascending colon (Figure 2a). Biopsy taken from the growth at colonoscopy reported as adenocarcinoma. He was planned for cystoscopy, which showed a large (6x5cm) papillary growth in the left lateral wall of bladder and rest of the bladder normal (Figure 2b). Transurethral resection of bladder tumour (TURBT) was done and sent for Histopathological examination, which was reported as papillary urothelial carcinoma, low grade with focal invasion and bladder muscle free of tumour (T1G1) (Figure 3a and 3b). Patient was taken up for radical right hemicolecystomy. At laparotomy found to have circumferential growth involving distal ascending colon with few enlarged lymph nodes at the adjacent mesocolon. Radical right hemicolecystomy with ileo-transverse anastomosis was carried out. Right hemicolecystomy specimen is shown in (Figure 4a and 4b). Histopathological examination of the postoperative specimen was reported as well differentiated adenocarcinoma involving muscularis, pT2pN0 (Figure 5a and 5b). Postoperative period went uneventful and patient was advised regular follow up including periodic cystoscopy.

DISCUSSION

MPMNs/MPCs/MPMs, whether synchronous or metachronous are rare as such. Of late, the occurrence of multiple primary cancers has risen due to improvements in diagnostric techniques and treatment. According to study by Suzuki et al., most diagnosed synchronous double primary malignancies (SDPM) were lung cancer and head-neck cancers; metachronous double primary malignancies (MDPM) were lung cancer and breast cancer. They labelled the first of the MDPMs as MDPM-F and second one as MDPM-S. Double primary malignancies occurring at the same time or at the interval of 2-6 months apart are labelled as SDPMs. Our case presented as synchronous double primary malignancies presenting at the same time. MPMNs prevalence ranged from 0.7 to 11.7% in various publications. According to SEER (Surveillance, Epidemiology and End Results) data, the risk of developing subsequent MPMN varies from 1% for an initial liver primary diagnosis to 16% for bladder cancer primaries. Ishimaro et al. published that at least 1.2% of patients referred to PET/CT with cancer diagnosis have a second cancer. Although the mechanism involved in the development of multiple primary cancer has not been clarified, some factors such as heredity, constitution, environmental and immunological factors, oncogenic viruses, radiological and chemical treatments have been implicated. Hereditary susceptibility explains only a small proportion of all second cancers though many hereditary cancer syndromes have been described. MPMNs can occur at any age. However, from the reviewed series, patients with MPMNs tend to be older than those with a single primary malignant neoplasm. In many autopsy series and clinical reports, the median age of 50-94% of MPMN patients was over 50 years. Our case is a 48 years old male. The ratio of male/female patients with MPMNs in several publications varies between 0.9 and 3.5 with male predominance. There are no established therapeutic rules for multiple primary cancers, but the type, progression, response to therapy and patient’s general health status should be considered. If each of the cancers has the possibility for cure, radical therapy is indicated. If radical therapy of the one primary cancer is impossible, conservative therapy is indicated. If radical therapy of the one primary cancer is impossible, conservative therapy is indicated for the other cancers. Multiplicity of primary malignancies itself does not necessarily indicate a poor prognosis as long as adequate diagnosis and treatment are performed. A review of 837 cases of colorectal carcinoma showed 32 cases (3.8%) of colorectal multiple primary malignant tumors and 11 cases (1.3%) of colorectal primary malignant tumour associated with extra colonic primary malignant tumour. There are many reports in literature about double synchronous malignancies. In addition, there are many reports relating to MPMNs of more than two, up to eight MPMNs in the same patient, but almost all of them are metachronous. Colonic primary with extra colonic primary along with other multiple primaries have reported earlier in the literature. They are all metachronous in nature. In 2001 Sari R et al., has reported a case of synchronous double primary malignant neoplasms of colon and bladder. In 2014, Liu Z et al. reported five patients diagnosed with synchronous bladder cancer and Colo

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Rectal Cancers (CRCs) between May 1997 and September 2010. In this series, the primary colorectal tumors included three sigmoid cancers, one ascending colon cancer and one rectal cancer\footnote{Howe HL (Ed) A review of the definition for multiple primary cancers. Ann Surg Oncol 2003;26(1):104-6.}. All the patients in this report underwent simultaneous radical cystectomy and CRC resection. Out of three sigmoid cancers, one was associated with recurrent bladder cancer. Hence, up to date literature search reveals only four cases of synchronous double primaries involving bladder and colon. Our case is unique due to its rare combination of synchronous primaries of urinary bladder ($T_1N_0M_0$) and ascending colon ($T_1N_0M_0$) presenting at the same time in 48 year old male, treated with transurethral resection of bladder tumour and radical right hemicolectomy in immediate consecutive sittings.

**CONCLUSION**

We have reported a rare combination of synchronous double primary malignancies of urinary bladder and ascending colon. This is the fifth case report of synchronous double primaries involving bladder and colon & third case report involving bladder and \textit{ascending} colon to the best of our knowledge. MPMNs are still elusive for want of proper guidelines regarding correct terminology and classification encompassing varying presentations of chronological, aetiological, clinical and histopathological combinations. Influence of one primary over other & suggestions for best possible management are also yet to be defined properly. Our case adds up to the previously available ones for further research. The possibility of occurrence of synchronous multiple primary malignancies should be considered during workup for any malignant condition. As long as appropriate early interventions are performed in the synchronous multiple malignancies, good outcome is expected.

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Authors declare that they do not have any conflict of interest.

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Figure 3a & Figure 3b: Histopathology of bladder cancer.

Figure 4a & Figure 4b: Right hemicolectomy specimen.

Figure 5a & Figure 5b: Histopathology of colonic cancer.