

Case Report:**Synchronous dual primary malignancy of urinary bladder and hypopharynx: an extremely rare phenomenon**Jayasree Kuna,¹Pranabandhu Das,¹Rashmi Patnayak,²A. Tyagi³*Departments of¹Radiation Oncology, ²Pathology, ³Urology, Sri Venkateswara Institute of Medical Sciences, Tirupati***ABSTRACT**

The diagnosis of multiple primary malignancy (MPM) is not uncommon. Nevertheless synchronous MPM involving urinary bladder and hypopharynx is an extremely unusual event. No such cases have been reported so far in English literature to our review. We report the case of 62-year-old male patient who presented with haematuria and later dysphagia to solids. Whole body ¹⁸F-fluoro deoxy glucose positron emission tomography- computed tomography (¹⁸F-FDG PET-CT) revealed two distinct lesions one in hypopharynx and another in urinary bladder. Biopsy from the urinary bladder mass and the hypopharyngeal lesion were suggestive of urothelial carcinoma and poorly differentiated squamous cell carcinoma respectively. The patient was treated with concurrent chemo-radiotherapy to hypopharynx. Following treatment he had improvement of dysphagia. Haematuria had also stopped. Because of severe comorbidities the planned radical cystectomy or radiotherapy were deferred. Currently the patient is in symptomatic remission six months following treatment.

Key words: *Synchronous, Dual primary malignancy, Hypopharynx, Urinary bladder*

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INTRODUCTION

The occurrence of multiple primary malignancy (MPM) is not uncommon in present times with the advent of advanced diagnostic imaging modalities as well as increased efficacy of cancer therapy.¹ The risk of association of synchronous MPM including urinary bladder cancer was significantly documented with the stomach, the prostate, the larynx and the liver cancers.² Synchronous MPM involving urinary bladder and hypopharynx is an extremely unusual. We present one such case who was treated with favourable outcome at our center.

CASE REPORT

A 62-year-old male who was a chronic tobacco smoker presented with a 3 months history of nocturia and a 10 day history of haematuria. He did not have any co-morbid conditions.

Complete haemogram was normal. Urine routine and microscopic examination revealed plenty of epithelial and pus cells. On contrast enhanced computed tomography (CECT) of the abdomen and pelvis a mass measuring 6.3 x 3.2 x 1.7 cm was seen in the left posterior lateral wall of bladder with left sided hydro-ureteronephrosis. Cystoscopic evaluation revealed a flat sessile growth measuring about 6 x 3 x 2 cm extending over bladder base and involving left vesicoureteric junction. Transurethral resection of bladder tumor (TURBT) was done. Histopathology was suggestive of poorly differentiated malignancy (Figure 1). Immunohistochemistry markers such as pan cytokeratin (Pan CK), vimentin (Ki-67)(40%), cytokeratin-20 (CK-20), cytokeratin-7 (CK-7) were positive where as S-100, synaptophysin, chromogranin, cluster of

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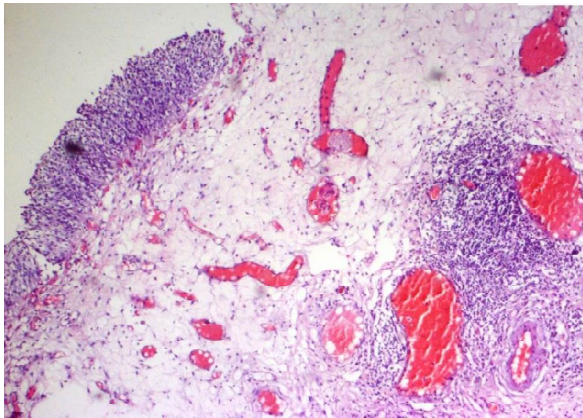


Figure 1: Photomicrograph polygonal neoplastic cells in clusters admixed with inflammatory cells suggestive of poorly differentiated malignancy (Haematoxylin and eosin, $\times 40$)

differentiation 68 (CD-68), human melanoma black 45 (HMB-45) were negative suggestive of poorly differentiated carcinoma of urothelial origin (Figure 2). During this work up period it was found that patient also had complaint of dysphagia to solids. Upper gastrointestinal endoscopy showed proliferative lesion at post cricoid region of hypopharynx. Histopathological examination of biopsy from hypopharynx revealed squamous epithelium with underlying poorly differentiated malignancy (Figure 3). Whole body ^{18}F - deoxy glucose positron emission tomography-computed tomography (^{18}F -FDG PET-CT) was advised as part of metastatic work-up which showed intense ^{18}F -deoxy glucose (FDG)

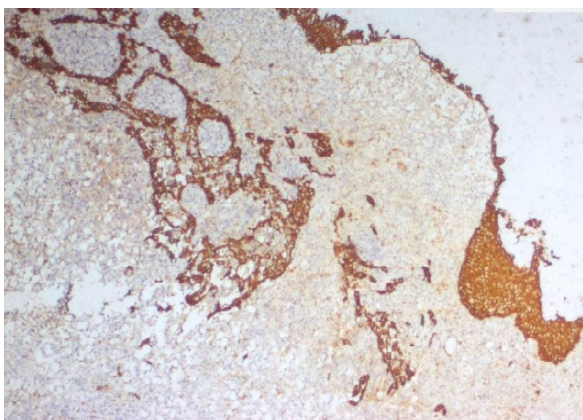


Figure 2: Photomicrograph showing Pancytokeratin positivity in transitional epithelium in bladder and underlying neoplastic islands suggestive of poorly differentiated poorly differentiated carcinoma of urothelial origin (Immunohistochemistry $\times 100$)

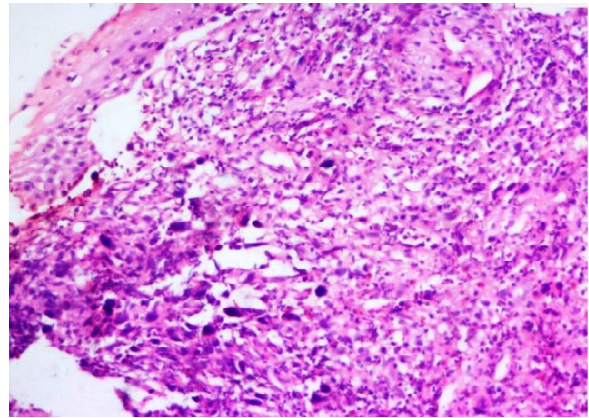


Figure 3: Photomicrograph squamous epithelium with underlying poorly differentiated malignancy (Haematoxylin and eosin, $\times 100$)

concentration in post-cricoid region with dimensions $5 \times 3 \times 1$ cm as well as in right paratracheal and left level V cervical lymph nodes (Figure 4). Intense FDG concentration was noted in the bladder wall on postero-lateral aspect with left sided hydrouretero nephrosis (Figure 4).

The diagnosis of synchronous dual malignancy involving urinary bladder (clinical staging T2N0M0) and hypopharynx (clinical staging T3N2cM0) was thus conferred. Patient was planned to receive radical radiotherapy to hypopharynx as the primary concern was progressive dysphagia. It was to be followed by radical cystectomy. The patient received 59.4 Gy in 33 fractions, 1.8 Gy per fraction and five fractions per week within seven weeks to hypopharynx along with concurrent cisplatin chemotherapy 40 mg per week. Following this treatment he had symptomatic improvement of dysphagia as well as haematuria. Radical cystectomy was planned to be accomplished four weeks after chemo-radiation. But because of difficulty in tracheal intubation for general anaesthesia was detected, surgery was deferred and he was planned for radical radiotherapy treatment to the urinary bladder. Later with progressive deterioration of his general condition, he expressed his unwillingness to afford further treatment. He opted for close observation and supportive care at home.

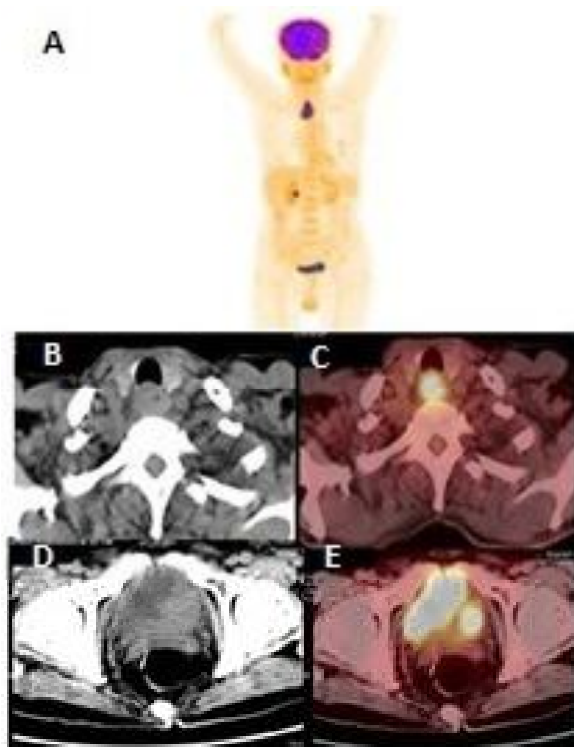


Figure 4: Maximum intensity projection image (A), CT axial image (B) and fused PET-CT image (C) showing intense FDG uptake in post-cricoid region of hypopharynx. CT axial image (D) and Fused PET-CT image (E) showed increased FDG concentration in posterolateral urinary bladder wall causing hydronephrosis

Currently the patient is in symptomatic remission six months after completion of the above treatment.

DISCUSSION

MPMs appear more frequently in the upper digestive tract, respiratory system, head and neck region and urogenital system.^{2,6} A review on 1,104,269 cancer patients concluded that the prevalence of MPM is between 0.73% - 11.7%.³ MPM are divided into two categories depending on the interval between tumour diagnosis. “Synchronous malignancies” are second neoplasms occurring simultaneously or within six months after the diagnosis of first neoplasm while “metachronous malignancies” are second neoplasms that developed after more than six months from the diagnosis of first malignancy.⁴ The aetiological risk factors of MPM include genetic predisposition, exposure

to environmental carcinogens, immunodeficiency and as a long-term complication of chemotherapy or radiotherapy received in the past or a varying combinations of all these risk factors.⁵ A significant association with the development of MPM is also linked to smoking and alcohol consumption.⁶ The median age at diagnosis of bladder cancer is above 70 years. As the tumour is often related to smoking, it is associated with significant comorbidities posing risks for radical surgery. Survival rates are poor in muscle invasive bladder cancer patients surviving five years irrespective of any treatment modality.^{7,8} Many hypopharynx cancer patients also carry significant medical comorbidities that present additional challenges to successful delivery of aggressive cancer therapy despite advances in diagnosis and treatment of hypopharynx cancer. The overall outcome for these patients is relatively poor compared with other head and neck cancers.⁹

The treatment of synchronous dual malignancy poses a great challenge in regard to which entity should be addressed as its primary concern. In our case, the primary concern being moderate dysphagia we had considered treatment of the hypopharynx first with concurrent cisplatin based chemoradiation therapy. This was with intent that chemoradiation can ameliorate the symptoms of dysphagia as well as facilitate down staging the urinary bladder neoplasm which in turn may contribute towards better locoregional control and survival. Our plan towards treatment of second malignancy involving urinary bladder was to do either radical cystectomy or radical radiotherapy. Because of progressive deterioration of his general condition, he could not undergo radical cystectomy or radiotherapy and was kept under close observation and best supportive care at home. There are no standard guidelines for management of MPM. Various factors such as type of malignancies, progression of disease, response to treatment and general condition of

patients should always be taken into consideration. We carried out an online MEDLINE search using medical subject heading (MeSH) terms: “synchronous, dual malignancy, hypopharynx and urinary bladder”. The search revealed that no such cases has been reported so far. We feel that this may be the first case documenting this entity to the best of our knowledge. Previously we have reported 13 cases of multiple primary cancers from our institution.¹⁰ However none of the cases were found to have synchronous malignancies involving hypopharynx and urinary bladder.

While dealing with a cohort of patients with known malignancy this is always customary to keep in mind the possibility of occurrence of a second neoplasm in view of any additional signs or symptoms. Hence a high index of suspicion of second malignancy should warrant an aggressive work up for early detection of malignancy and treatment intervention for an improved outcome. This case is being reported because of its extremely rare occurrence, and the diagnostic as well as therapeutic challenges being encountered during the management.

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