An Unusual Case of Gastric Signet-Ring Cell Adenocarcinoma Metastasizing to the Urinary Bladder

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Introduction

Secondary bladder tumors are rare. Only about 1-2% of bladder tumors are secondary[1] – either via direct extension or metastasis from distant primary. Most common primary sites resulting in direct extension into the bladder are from the colon, rectum, prostate, and cervix. Distant metastatic cancer is less common, with metastatic gastric carcinoma only accounting for 4% of secondary bladder tumors [1].

Case report

A 53-year-old Chinese male presented with six months history of cough and increasing breathlessness on exertion. Physical examination was unremarkable. Chest X-ray showed bilateral airspace opacification with small pleural effusions. Investigations for underlying cardiac and infective etiology including tuberculosis and COVID-19 were negative. Computed tomography (CT) pulmonary angiogram was done to look for pulmonary embolism, which revealed a 1.8cm right lower lobe lung nodule and multiple sclerotic bony lesions suspicious for metastases. Subsequent staging CT of the abdomen and pelvis revealed multiple enhancing nodular foci along the bladder wall. Flexible cystoscopy revealed multiple discrete sessile tumors over the lateral walls, trigone and right ureteric orifice (image 1). Patient subsequently underwent transurethral resection of bladder tumors. Histology of the resected bladder tumor was invasive carcinoma with signet ring cells (image 2A).

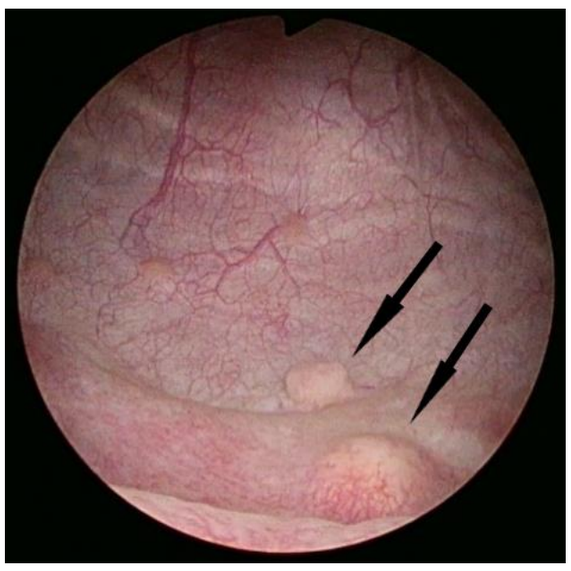

Image 1: Cystoscopy images showing multiple bladder tumors

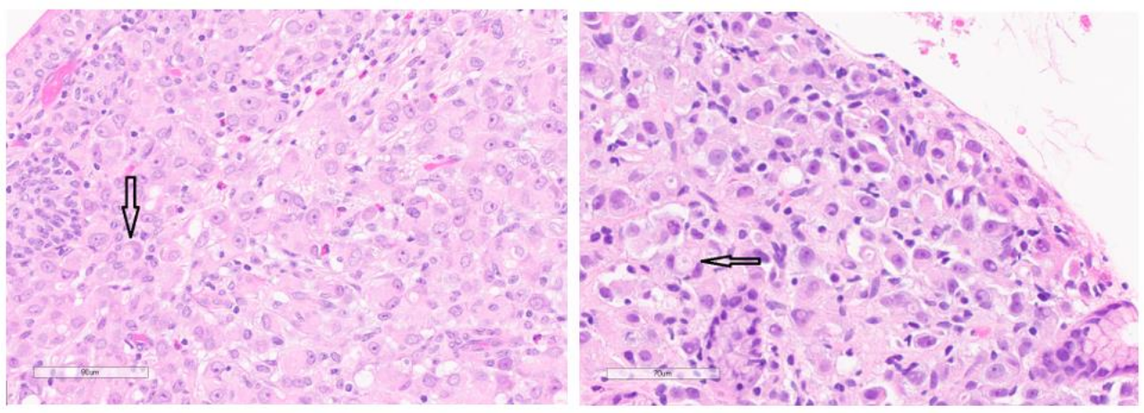

Image 2A (right): Signet ring cells seen from bladder biopsy
Image 2B (left): Signet ring cells seen from gastric biopsy

On further questioning, the patient reported a 6-month history of dyspepsia. Endoscopic evaluation of the gastrointestinal tract showed an erythematous lesion seen at stomach fundus with small ulcerations [image 3], which were biopsied [image 2B]. Histology confirmed signet ring cell adenocarcinoma, which were morphologically similar to the original histology from the bladder tumor. Patient was referred to Medical Oncology and was subsequently commenced on palliative chemotherapy.

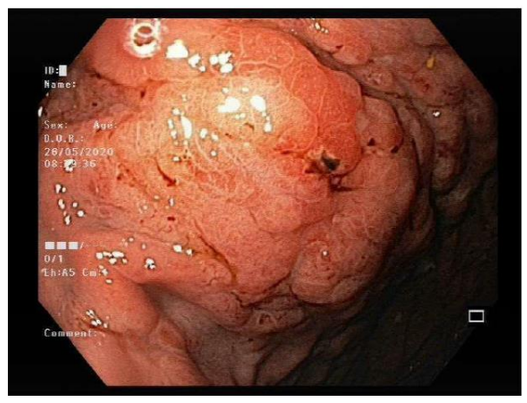

Image 3: OGD showing stomach fundus erythema with small ulcerations

Discussion

Bladder involvement by a secondary tumor is rare (1-2%), with a higher incidence of secondary involvement by direct extension from the surrounding visceral organs (e.g. Colon, Prostate, Cervix) as compared to lymphatic, hematogenous, or peritoneal spread. Tumours that metastasize to the bladder most commonly arise from the stomach (4.3%), skin (3.9%), lung (2.8%), and breast (2.5%)[1]. The diagnostic challenge arises as many of these secondary tumors are also commonly adenocarcinoma in histology, requiring it to be differentiated from a primary adenocarcinoma of the bladder.

Primary adenocarcinoma of the bladder is also rare, and primary signet ring cell carcinoma (SRCC), first described in 1955 by Saphir, accounts for only 0.2% of all primary bladder cancers[2]. The presence of signet ring cells indicates the presence of a poorly differentiated aggressive subtype of mucin-producing adenocarcinoma. More than 95% cases of SRCC arise from the gastrointestinal tract, and less commonly from the breast, lung, and prostate.

In this patient, the immunohistochemical stains that were performed on the initial bladder tumour specimen (including p63, 34BE12, GATA3, E-cadherin, CDX2, NKX3.1, PSA and PSAP) were not helpful in elucidating the primary site. The presence of multiple solid tumours within the bladder unlike the usual papillary urothelial carcinoma morphology, as well as lung and bone lesions on the CT scan, increased the suspicion of metastatic disease. The unusual histology with a patient-reported history of dyspepsia prompted further search for an underlying gastrointestinal primary, and histological confirmation of the presence of SRCC in gastric fundal biopsies confirmed the diagnosis.

Differentiating secondary bladder tumours from primary bladder SRCC is essential as treatment and prognosis is vastly different. The treatment for secondary bladder tumours would depend on the site of the primary and the extent of the metastatic disease. Radical surgery is usually not indicated and endoscopic resection can be considered to manage symptoms such as gross haematuria if any. The treatment for localized primary bladder SRCC, however, would involve extensive surgical resection and adjuvant chemotherapy and radiotherapy. Due to the rarity of primary bladder SRCC, there has been no standardised chemotherapy regimen, with many following the guide of treatment used for SRCC of the stomach, using platinum-based drugs, 5-fluorouracil derivatives and anthracyclines[3,4]. The overall 2-year survival rate for patients with localised bladder SRCC is only 43%, and patients with metastatic disease had a median survival of only 8 months[3]. Metastatic SRCC has a poor prognosis and the approach is palliative. In view of significant chemotoxicity which could further impair patient's quality of life, early discussion on goals of care is essential.

Bladder metastasis from gastric signet ring cell adenocarcinoma is extremely rare, and immunohistochemistry has a limited role in differentiating it from primary bladder adenocarcinoma in the biopsy specimen. A thorough clinical history and a high index of suspicion is key. Signet ring cell adenocarcinoma in the bladder should prompt early endoscopic evaluation to exclude a gastrointestinal primary.

References

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