SECONDARY BLADDER CARCINOMA METASTASIS FROM OTHER ORGAN: A LITERATURE REVIEW

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ABSTRACT

Objective: *This review article discusses the importance of considering metastasis malignancy in the differential diagnosis of high-grade urothelial lesions.* ***Material & Methods:*** *The review presents a summary of metastasis of bladder carcinoma from various organs. The most common sources of secondary bladder tumors are stomach, breast, colon cancer, and melanoma. The article highlights the need for careful evaluation and further workup in patients being treated for metastatic cancer who present with hematuria and symptomatic anemia.* ***Results:*** *Diagnosis of secondary bladder carcinoma involves imaging, cystoscopy, and transurethral resection. Biopsies should be collected from patients with suspected urothelial bladder metastasis from other cancer origins or those with suggestive symptoms. The article emphasizes the importance of differentiating metastatic adenocarcinoma of the lung from primary bladder adenocarcinoma, especially when bladder examination does not correlate with imaging results. It also discusses the increased risk of secondary bladder carcinoma in rectal cancer survivors who have undergone radiation therapy.* ***Conclusion:*** *In conclusion, secondary bladder carcinoma metastasis from other organs presents a diagnostic dilemma and requires comprehensive evaluations. Healthcare professionals should consider metastasis malignancy in the differential diagnosis of high-grade urothelial lesions, especially in the absence of readily available clinical history of primary cancer.*

Keywords: *Bladder cancer, secondary tumors, metastasis, differential diagnosis, primary cancer.*

ABSTRAK

Tujuan: *Artikel tinjauan ini membahas pentingnya mempertimbangkan keganasan metastasis dalam diagnosis banding lesi urotelial tingkat tinggi.* ***Bahan & Cara:*** *Tinjauan ini menyajikan ringkasan metastasis karsinoma kandung kemih dari berbagai organ. Sumber tumor kandung kemih sekunder yang paling umum adalah kanker lambung, payudara, usus besar, dan melanoma. Artikel ini menyoroti perlunya evaluasi yang cermat dan pemeriksaan lebih lanjut pada pasien yang dirawat karena kanker metastasis yang mengalami hematuria dan anemia simptomatik.* ***Hasil:*** *Diagnosis karsinoma kandung kemih sekunder melibatkan pencitraan, sistoskopi, dan reseksi transuretra. Biopsi harus diambil dari pasien dengan dugaan metastasis kandung kemih urotelial dari asal kanker lain atau mereka yang memiliki gejala sugestif. Artikel ini menekankan pentingnya membedakan adenokarsinoma metastasis paru-paru dari adenokarsinoma kandung kemih primer, terutama ketika pemeriksaan kandung kemih tidak berkorelasi dengan hasil pencitraan. Artikel ini juga membahas peningkatan risiko karsinoma kandung kemih sekunder pada penyintas kanker rektum yang telah menjalani terapi radiasi.* ***Simpulan:*** *Sebagai kesimpulan, metastasis karsinoma kandung kemih sekunder dari organ lain menghadirkan dilema diagnostik dan memerlukan evaluasi yang komprehensif. Tenaga kesehatan harus mempertimbangkan keganasan metastasis dalam diagnosis banding lesi urotelial tingkat tinggi, terutama jika tidak ada riwayat klinis kanker primer yang tersedia.*

Kata kunci: *Kanker kandung kemih, tumor sekunder, metastasis, diagnosis banding, kanker primer.*

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INTRODUCTION

Bladder cancer, also known as urothelial or urinary bladder cancer, is ranked as the 7th most common cancer in men and the 17th among women worldwide. Furthermore, in the Western World, it is the 4th most common type in men and the 9th in women, accounting for 3% of all new diagnoses. Several studies have shown that men also face a four fold higher likelihood of being affected by the condition compared towomen. Secondary bladder tumors are an infrequent occurrence, accounting for

only 2% of all bladder tumors. These conditions are characterized by poor prognosis and the majority of cases are identified during autopsy. According to previous studies, the primary tumors causing secondary bladder cancer include gastric, breast, and lung cancer, as well as malignant melanoma. Although bladder metastases from distant organs are rare, direct infiltration of cancerous tissues into surrounding organs, such as the colon, prostate, and cervix is prevalent.[1]

Several studies have shown that metastases to the urinary system are rare, with only a few reports examining their occurrence. Furthermore, Alsolama et. al reported a case with concurrent bladder and testicular seminoma, and Gurbuz and colleagues documented a case with simultaneous bladder carcinosarcoma and testis seminoma. In another report,an orchiectomy was performed for testis seminoma, but biopsy of the paraaortic and inguinal lymph nodes during a kidney transplant in the patient showed the recurrence of seminoma.[2]

Symptomatic patients typically present with painless gross hematuria, and the most common sites of metastases include regional lymph nodes, lungs, liver, and brain. This article underscores the importance of including metastasis malignancy in the differential diagnosis of high-grade urothelial lesions. Although a clinical history of primary cancer often serves as the initial diagnostic clue, this clinical information is not always readily available.[3]

OBJECTIVE

Therefore, this review aimed to discuss the possible mechanism of bladder carcinoma metastases.

MATERIAL & METHODS

A comprehensive literature reference search was conducted through PubMed, Google Scholar, Proquest, and Cochrane Library. Published articles were identified through computer search and literature review, and identical results were excluded. Furthermore, the remaining articles were independently screened for relevance based on their abstracts. The titles and abstracts were then scanned for potential relevance and inclusion eligibility was reviewed.

RESULTS

In this review, there were several case reports of metastasis into the bladder from other organs but were relatively limited. Table 1 presents a summary of metastasis of bladder carcinoma from other organs.

Author, Year	Design	Population	Major Finding	Main Organ	Comment
Katz, et al (2017).[4]	Case Report	One case	H&E stain from liver biopsy with morphologically similar cells to the esophagus biopsy. Immunohistochemical (IHC) stains showed cytokeratin 7 positive, cytokeratin 20 positive, Caudal Type Homeobox 2 (CDX2) positive	Esophageal	This case underscored the importance of comprehensive evaluations and further workups in patients being treated for metastatic esophageal cancer who presented with hematuria and symptomatic anemia.The mechanism was not stated
Feldman et al (2017).[1]	Retrospective study	66 cases of secondary bladder tumor	Colorectal origin was most common in the research series (15/66, 22.7%) followed by cervix (10/66, 15.2%) and ovary (10/66, 15.2%). In the female cohort, cervix (10/44, 22.7%) and ovary (10/44, 22.7%) were most common followed by endometrium (8/44, 18.2%). In the male	Mentioned before	Women were more likely to have metastatic tumors to the bladder, and those with cervical SCC presented at earlier ages. In addition to IHC, clinical and radiological correlation was helpful to avoid the diagnostic pitfall.

			cohort, colorectal origin (10/22, 45.5%) was most common followed by prostate (7/22, 31.8%)		
Turkogiu et al (2015).[2]	Case report	One case	Histopathology evaluation showed pleomorphic tumor cells with a hyperchromatic nucleus and a one-by one arrangement infiltrating the bladder wall. There was widespread necrosis and occasional lymphocytes	Testicular	Testis tumors must be followed up according to the guidelines. History must be carefully queried and the possibility of solid organ metastasis at the very late stage must always be considered.
Khoury et al (2019).[5]	Case report	One case	Histopathology showed a preserved epithelium with infiltration of the chorion, lymphatic permeation, and signet ring cells in the bladder	Gaster	Focal thickening suggested transitional cell carcinoma (90% of primary bladder tumors) and other bladder neoplasms (lymphoma, for instance)
Yoneyama et al (2018)[6]	Case report	One case	The tumor was biopsied, and a histopathological examination showed a proliferation of cells with eosinophilic cytoplasm and a rounded dentate macronucleus in the mucosal lamina propria	Breast	Routine screening of the lower urinary tract was not necessary for all patients, but women with a history of breast cancer presenting with urinary symptoms must undergo a thorough examination of the urinary tract.The prognosis of secondary bladder carcinoma was very poor. Most of the patients (4/7, 57%) died within 1 year after diagnosis of bladder metastasis.
Guan et al (2021)[7]	Cohort Study	Second bladder carcinoma from non radiation therapy group (461), Second bladder carcinoma from radiation therapy group (249)	In the final Colorectal multivariable analysis, radiation therapy was an independent risk factor of developing secondary bladder carcinoma in radiation rectal cancer survivors (HR, 1.443; 95% CI, 1.209-1.720; adjusted P< 0.001). In addition, subgroup analyses were performed to further evaluate the risk of developing sec ondary bladder carcinoma by competing risk regression.		Radiation was associated with an increased risk of developing secondary bladder carcinoma in rectal carcinoma patients, and special attention must be paid to the surveillance of these patients
Modh et al, (2013)[8]	Case Report	One case	Adenocarcinoma comprising the muscularis propria with benign urothelial mucosa and reactive changes. Immunophenotypically, this was most compatible with a lung primary. The tumor was immunoreactive for CK7 and Napsin A, partially immunoreactive for p53, and nonreactive for CK20, TTF-1.	Lung cancer	Metastatic adenocarcinoma of the lung is important to distinguish from primary adenocarcinomas of the bladder, specifically when cystoscopic examination of the bladder does not correlate with diagnostic imaging results

DISCUSSION

The results showed that secondary tumors of the urinary bladder could present a diagnostic dilemma in considering a differential diagnosis of primary bladder cancer. However, the occurrence of the condition was uncommon, accounting for less than 2% of all bladder cancers. The most common primary sources were stomach, breast, colon cancer, and melanoma. The majority of these secondary tumors were due to direct extension from another pelvic neoplasm, such as sigmoid, prostate, or cervical cancer. Metastases from distant organs were sporadically reported in the literature, with the most common being the stomach, lung, and melanoma.[9] The pattern of spread to urinary bladder carcinoma from breast cancer was because of tumor embolus, which did not seed in the lung but passed through pulmonary circulation and reached the target organ and soiled, causing metastasis. Pontes and Oldford postulated that breast cancer metastasized to the bladder through retroperitoneal engagement. Furthermore, patients receiving steroids could develop metastasis at unusual sites due to the possible influence of the immunosuppressive effect of the drugs.[10-11]

For rectal carcinoma survivors after treatment of radiotherapy, there was no obvious increased incidence of secondary bladder carcinoma in the early latency, but the increased and peaked after a latency of over 20 years. This result showed that long-term follow-up was necessary for the detection of the condition. Considering the influence of the age of rectal carcinoma patients on the risk of secondary bladder carcinoma, a tendency of decreased incidence for the condition was observed with increasing age. This suggested that young rectal carcinoma patients who underwent radiotherapy were at a higher risk of secondary bladder carcinoma compared to the elderly.[7,12]

In this review,the collection of biopsies was recommended in a patient suggestive of urothelial bladder metastasis from other cancer origin or having symptoms. This was because of a missed examination of masses or the absence of early diagnosis programs. Following the diagnosis of urothelial bladder metastasis, transurethral resection of the bladder lesion must be undertaken to stop hematuria. This also facilitated the stenting of ureters in the case of ureter obstruction. Percutaneous nephrostomy could also be performed to normalize renal function.

CONCLUSION

In conclusion, secondary bladder metastases were usually rare and detected after the manifestation of symptoms, with the majority of cases occurring in invasive lobular cancer. In addition to asymptomatic presentations, most cases presented with hematuria and voiding dysfunction. After diagnosis with imaging, cystoscopy must be part of the workup in the lesion biopsy, followed by transurethral resection.

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