CASE REPORT
Urooncology

Doi: 10.4274/jus.galenos.2024.2024-1-4
J Urol Surg 2024;11(4):240-242

Managing the Expected, Diagnosing the Unexpected: A Rare Presentation of Undiagnosed Breast Carcinoma-A Case Report

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Abstract

Metastatic breast cancer (BrC) is a common condition. Primary metastatic sites are lung, liver, and bone. BrC rarely metastasizes to the bladder, and primarily at an advanced stage. We present an unusual case of BrC diagnosed in a woman presenting with gross hematuria and irritative voiding symptoms. Cystoscopy revealed a small benign-looking process at the bladder dome, biopsy was performed, and histology revealed metastatic lobular BrC. Further diagnostics confirmed the diagnosis and medical treatment was initiated. Gross hematuria should always be properly investigated, and bladder biopsies taken at the smallest suspicion, to avoid overlooking malignancy and secure the accurate diagnosis.

Keywords: Breast cancer, hematuria, bladder cancer, pathology, case report

Introduction

Secondary bladder neoplasms are uncommon and account for up to 4.5% of all bladder neoplasms. The most common primary sites are the colon, prostate, rectum, and cervix, which infiltrate the bladder via direct spread, whereas metastatic spread to the bladder is very uncommon (1). In some large series of surgical and postmortem materiel breast cancer (BrC) was found to be the primary site in 2.4% of bladder metastasis although the prevalence of bladder metastasis in BrC varies in the current literature from <1% to 7% (2). Bladder metastasis from BrC presents typically late in advanced metastatic disease and is easily overlooked (2). We present a rare case of undiagnosed BrC in a middle-aged woman with no previous cancer-related symptoms and a history of bilateral urolithiasis with gross hematuria and irritative voiding symptoms. This case report follows the format of the CARE guidelines.

Case Presentation

A 66-year-old woman with a current history of spontaneous passage of a right-sided kidney stone and persistent bilateral urolithiasis without hydronephrosis for 6 months was referred to our outpatient clinic on suspicion of urothelial cancer due to painless gross hematuria and irritative voiding symptoms. The patient had no history of cancer. A non-contrast computed tomography (CT)-scan showed no signs of malignancy in the upper urinary tract. All blood tests were normal. A flexible cystoscopy revealed a small 4-mm exophytic process at the bladder dome, which was negative under NBI lighting and initially interpreted as folding of the mucosa. A biopsy was performed to rule out malignancy.

Microscopic examination revealed an infiltrating epithelial tumor consisting of large, dyscohesive tumor cells arranged in groups varying in size and as single cells. The cells had a high N/C ratio, a small amount of eosinophilic cytoplasm, and a large hyperchromatic nucleus with moderate to high pleomorphism and moderate mitotic activity. Immunohistochemical (ICH) analysis showed strong positivity of malignant epithelial cells for GATA3, CK7, CK7/19, Estrogen receptor (100%), and gross cystic disease fluid protein-15 (GCDFP-15). They were non-reactive to E-cadherin, TTF-1, CDX2, CK20, and synaptophysin. HER2 receptor status was borderline. *In situ* hybridization did not detect gene amplification. Based on these findings, the specimen was a metastatic lobular BrC.

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Received: 08.01.2024 **Accepted:** 29.04.2024

Cite this article as: Dalsborg Madsen SM, Andersen Lynggård L, Stilling C, Skjold Kingo P. Managing the expected, diagnosing the unexpected: a rare presentation of undiagnosed breast carcinoma-a case report. J Urol Surg. 2024;11(4):240-242.

The patient denied having any symptoms related to BrC. Clinical examination revealed no lumps in the breast or axilla. Ultrasound revealed two small suspicious tumors in the right breast measuring 7 and 3 mm, respectively, and multiple enlarged lymph nodes. A biopsy was performed, and histology confirmed the presence of invasive BrC. A diagnostic CT scan revealed small metastatic lesions in the columna, costa, gluteal muscle, liver, and mediastinal lymph nodes.

The patient favored surgical treatment, but due to the metastatic nature of the cancer, no surgical treatment was available at this stage. Oncological palliative treatment with ribociclib (Kisqali®) 600 mg x 1 and Letrozol (Letrozol®) 2.5 mg x 1, was initiated. Prior to each treatment cycle, blood samples and physical examination was performed and a supplementary CT-scan of the thorax, abdomen, and pelvis was conducted at every 3 cycle. The patient responded well to treatment, with no signs of progression and only minor side effects, such as mild paresthesia of the fingertips and toes and transient liver affection only shown on bloodwork. The patient have provided written consent.

Discussion

Our case differs from most previously described cases because these patients had a known primary BrC, which was initially treated prior to the discovery of bladder metastasis. To our knowledge, only one other case describes a patient with undiagnosed BrC who presented with more pronounced symptoms; bilateral hydronephrosis, pitting edema, and renal failure. Cystoscopy merely revealed an irregular thick bladder wall. Random biopsies were then performed, and undifferentiated adenocarcinoma was found. The primary site was a lump in the right breast (3).

Regarding our patient, there was only a minor suspicion of malignancy in the urinary tract given the fact that she had a known benign condition that could possibly explain the gross hematuria and irritative bladder symptoms. In addition, she underwent mammography screening every 2 years, and she had no previous history of cancer. Moreover, CT scan showed no signs of malignancy in the urinary tract, and the cystoscopy findings were almost classed as normal.

Patients with known benign causes of gross hematuria, such as urinary tract infection, prostate hyperplasia, or urolithiasis, pose a potential pitfall in diagnosing malignancy in the urinary tract, as these patients might not be referred to further urologic diagnostic workup despite having relevant risk factors. Existing guidelines dictate that patients with gross hematuria or symptomatic microscopic hematuria should undergo CT urography and cystoscopy to rule out urinary tract malignancy because patients with gross hematuria have a substantial risk

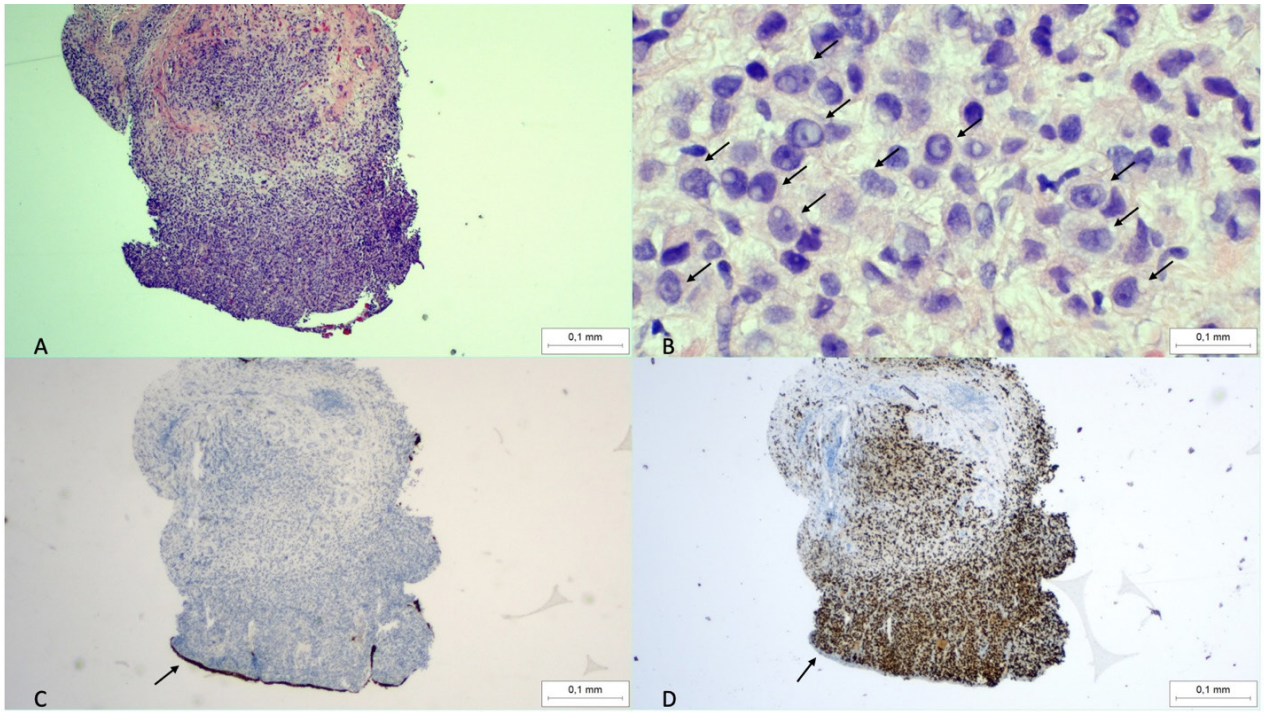

Figure 1. A) Low power hematoxylin and eosin (H&E) of the patient's biopsy showing section of large dense cell groups. B) High power (40x) H&E of same section as A. Arrows pointing at some of the multiple dyscohesive large tumor cells, containing large, atypical nuclei and distinct nucleoli. C) Immunohistochemical (IHC) E-cadherin. Tumor cells has lost normal expression. Brown staining of preserved normal urothelium is seen on the surface of the biopsy serving as an internal control (arrow). D) IHC; gross cystic disease fluid protein-15 staining positive in tumor cells, whereas urothelium is negative (arrow)

of developing urinary tract cancer. Previous studies have shown that >10% of patients presenting with gross hematuria are diagnosed with malignancy in the urinary tract (4).

Bladder metastasis from BrC is believed to be spread hematogenously via the pulmonary circulation without establishing metastasis before reaching the bladder or retroperitoneum (2). The metastasis has an outside-in growth pattern and involves the outer bladder wall through the detrusor muscle before reaching the mucosal lining, which explains the vague or absent symptoms before mucosal involvement. Early symptoms originate from the detrusor muscle and comprise primarily irritative voiding symptoms (5). As observed in our patient, no obvious affection of the mucosa was recognized during cystoscopy, although a minor part of the mucosa was bulging into the bladder.

Despite cystoscopy being an excellent tool for identifying potential malignant conditions in the urinary bladder, even after biopsies and histological examination, the diagnosis can be uncertain. Primary and secondary malignancies of the urinary bladder can be difficult to differentiate because invasive urothelial carcinoma is known for its diversity of morphological appearances. Therefore, it is important to be aware of the specific subtypes of urothelial carcinoma and the divergent differentiation of other epithelial lineages, such as squamous, glandular, and small cell neuroendocrine carcinoma. ICH markers can support the diagnosis of urothelial lineage, but the presence of precursor lesions are also helpful in recognizing primary nature (6). Metastasis from BrC resembles the histological features of the plasmacytoid variant of urothelial carcinoma (7). In our case, the tumor was positive for estrogen receptor and GCDFP-15 and exhibited loss of E-cadherin, which revealed the diagnosis.

Therefore, the importance of using a broad panel of antibodies cannot be overstated. Patients with secondary neoplasms to the urinary bladder generally have a poor prognosis, as the primary cancer is typically at a very advanced stage with multiple sites of metastasis (8). The general survival time for BrC patients with bladder metastasis have been reported as between one month to two years, although survival times longer than 5 years have been reported (2).

Conclusion

In conclusion, our case illustrates the importance of performing an accurate diagnostic workup and performing biopsies at the slightest suspicion; thus, neoplasms of the urinary tract should not be overlooked, especially in patients with known benign conditions in the urinary tract, vague symptoms, or no history of previous cancerous disease.

Ethics

Informed Consent: The patient have provided written consent.

Footnotes

Authorship Contributions

Concept: S.M.D.M., P.S.K., Design: S.M.D.M., P.S.K., Data Collection or Processing: S.M.D.M., L.A.L., P.S.K., Analysis or Interpretation: S.M.D.M., L.A.L., P.S.K., Literature Search: S.M.D.M., Writing: S.M.D.M, L.A.L., C.S., P.S.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Bates AW, Baithun SI. Secondary neoplasms of the urinary bladder are histological mimics of nontransitional cell primary tumors: Clinicopathological and histological features of 282 cases. Histopathology. 2000;36:32-40. [Crossref]
2. Sanguedolce F, Landriscina M, Ambrosi A, Tartaglia N, Cianci P, Di Millo M, Carrieri G, Bufo P, Cormio L. Bladder metastases after breast cancer: managing the unexpected. A systematic review. Urol Int. 2018;101:125-131. [Crossref]
3. Shah KG, Modi PR, Rizvi J. Breast carcinoma metastasizing to the urinary bladder and retroperitoneum presenting as acute renal failure. Indian J Urol. 2011;27:135-136. [Crossref]
4. Khadra MH, Pickard RS, Charlton M, Powell PH, Neal DE. A prospective analysis of 1,930 patients with hematuria to evaluate current diagnostic practices. J Urol. 2000;163:524-527. [Crossref]
5. Hanley M, Rezaee M, Ren B, Sverrisson E. An unusual location for metastasis-breast cancer in the bladder. Urol Case Rep. 2022;45:102215. [Crossref]
6. Lopez-Beltran A, Henriques V, Montironi R, Cimadamore A, Raspollini MR, Cheng L. Variants and new entities of bladder cancer. Histopathology. 2019;74:77-96. [Crossref]
7. Feldman A, Borak S, Rais-Bahrami S, Gordetsky J. Secondary malignancies of the bladder: Avoiding the diagnostic pitfall. Int J Surg Pathol. 2018;26:120-125. [Crossref]
8. Xiao GQ, Chow J, Unger PD. Metastatic tumors of the urinary bladder: A clinicopathological study of 11 cases. Int J Surg Pathol. 2012;20:342-348. [Crossref]