


Case Report

Urinary Bladder Metastasis from Gastric Cancer: A Case Report and Review of the Literature

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Abstract: Bladder metastasis from gastric cancer is a unique clinical entity, which can be revealed infrequently in patients with metastatic gastric cancer. Secondary neoplasms to the bladder are also a less frequent clinical entity representing only 15% of all bladder neoplasms. Gastric cancers consist of an exceptionally small percentage of all secondary bladder neoplasms. Until now only 27 cases were recorded in the international medical literature. The current work analyzes a 65-year old male patient who presented initially with a locally advanced gastric adenocarcinoma. He was treated with a combination of total gastrectomy and perioperative chemotherapy. Eight months later presented a relapse with bladder metastasis, liver metastasis and peritoneal involvement. Furthermore, in this manuscript, we conducted a review of the recorded cases with bladder metastasis from gastric cancer. In the most of cases the diagnosis of bladder metastasis was metachronous with an average time of presentation in four years after the primary diagnosis of gastric cancer and most of the patients of our review presented with urinary symptoms at the time of diagnosis of bladder metastasis. Concerning the management of the metastatic disease surgical management with total or partial cystectomy was performed in 11% of patients and TUR was performed in 22% of patients. Palliative chemotherapy for the management of metastatic disease was initiated in 46% of patients.

Keywords: Urinary bladder metastasis; metastatic gastric cancer; secondary bladder neoplasms



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1. Introduction

Primary bladder cancer is a frequent malignancy. Bladder cancer is the ninth most common cancer in the world, with 430,000 new cases diagnosed in 2012 [1]. Urothelial (transitional cell) carcinoma is the predominant histologic type in the United States and Europe, where it accounts for 90% of all bladder cancers. In other areas of the world, non-urothelial carcinomas are more frequent. Non-urothelial carcinomas of bladder include squamous cell carcinomas, adenocarcinomas, small cell carcinomas and less frequent metastatic cancers to the urinary bladder.

The urinary bladder may be involved by direct extension of tumors from adjacent sites (secondary involvement) or by metastases from a distant site [2]. Secondary tumors account for approximately 15% of malignant bladder tumors. Cancers extending from the colon or rectum, prostate and uterine cervix are most common and most frequently identified in the bladder neck and trigone. Metastatic lesions from melanomas and stomach, breast and lung cancers are less frequent [3].

We report the case of metastatic bladder cancer from primary gastric adenocarcinoma and hereby present a review with similar cases of the pertinent medical literature.

2. Case Presentation

A non-smoker 65-year old male patient with no occupational exposure to urothelial carcinogens, initially diagnosed 14 months ago with gastric signet ring cell adenocarci-

noma. At the initial staging there were no distant metastatic sites and the patient received perioperative chemotherapy and total gastrectomy with D2 lymphadenectomy. After the abovementioned multimodal treatment approach patient underwent follow up.

After 8 months the patient suffered from severe vomiting and nausea. Moreover, he reported episodes of hematuria. We performed a new CT scan with CT thorax, abdomen and pelvis, which revealed a mass in the area of anastomosis, diffuse peritoneal disease, ascites and 3 hepatic lesions compatible with liver metastases. Furthermore, in the CT scan were revealed two masses in the bladder wall, respectively, measuring 8 mm and 12 mm associated with bilateral hydronephrosis. Due to our patient's background of primary gastric carcinoma, a secondary location of the bladder was suggested. Nephrostomy tubes were placed in both kidneys.

A cystoscopy showed two solid protuberant nodular lesions one in the trigone and the other in the left lateral bladder wall. Multiple biopsies were taken by both lesions.

After pathological examination of the biopsy specimen the diagnosis of metastatic poorly differentiated adenocarcinoma of the bladder from a gastric primary cancer was reached. HER2 testing with FISH revealed over expression of HER2.

We decided to start palliative chemotherapy with fluorouracil, irinotecan and trastuzumab. After four cycles (two months after the diagnosis of the metastatic disease) patient developed ileus and 10 days later succumbed due to the symptomatic.

3. Discussion

Bladder cancer is the second most common genitourinary cancer and the ninth most common cancer worldwide among all malignities. The predominant histologic type of bladder cancer is urothelial carcinoma and the less frequent are adenocarcinoma, squamous cell carcinoma and small cell carcinoma. Moreover, the urinary bladder may be involved by direct extension of tumors from adjacent sites (secondary involvement) or by metastases from a distant site [2,3]. Secondary tumors account for approximately 15% of the malignant bladder tumors. Adenocarcinomas are the most frequent histological subtypes of such metastatic tumors [2].

Metastasis to the bladder may be a result of direct extension from adjacent organs like prostate, rectum and uterine cervix or can be a result of hematogenous metastatic spread from gastric cancer, melanomas, lung cancer or breast cancer.

Bates et al. found that the most common sites of origin of secondary bladder neoplasms were colon, prostate, rectum and cervix. In this review gastric cancers consist 4.3% of all secondary bladder neoplasms in a series of 282 cases [2].

We performed a review of similar case reports of the pertinent international medical literature. 24 case reports including our case report, involving 28 patients with secondary bladder tumor from primary gastric neoplasm, were included and analyzed in the entire process.

The features of these cases were summarized in Table S1.

Most of the recorded patients were predominantly male representing 19 of the total 28 cases (67%). The age range was 30–90, median of 56-years old. Bladder cancer is typically diagnosed in older individuals, with a median age at diagnosis of 69 years in men and 71 in women [4]. In addition to differences in incidence, sex and race also affect the stage at presentation and prognosis. Even though the overall incidence of bladder cancer is lower in women and African Americans, these groups have more advanced-stage tumors at presentation compared with white men [5].

Metastasis to the urinary bladder from gastric cancer can be synchronous or metachronous concerning the primary presentation of gastric cancer. In our study in 67% of cases (19 of 28 cases) the diagnosis of bladder metastasis was metachronous with an average time of presentation in 4 years after the primary diagnosis of gastric cancer.

57% of the patients (16 of 28 cases) presented also other metastatic sites except of bladder involvement. The most frequent site of metastasis in 12 of 16 cases (including this case report) was peritoneal involvement.

From the 28 cases, 13 patients (46% of patients) presented with metastatic disease at the time of diagnosis (either bladder or another metastatic site).

The most common sites of metastatic gastric cancer are the liver, the peritoneal surfaces and the nonregional or distant lymph nodes. Less commonly, ovary, central nervous system (brain or leptomeningeal), bone, intrathoracic (pleural or parenchymal) or soft tissue metastases can occur.

Most of patients of our review presented with urinary symptoms at the time of diagnosis of bladder metastasis or in some cases were the cause to reveal the bladder involvement. In our study 82% of patients reveal urinary symptoms with hematuria as the predominant symptom. Painless hematuria is the most common presenting complaint, it is found among 85%–90% of patients with primary or secondary bladder cancer. It may be gross or microscopic, intermittent rather than constant. Patient complaints are rare until the tumor penetrates the mucosal lining. Clinical signs include urgency, dysuria, increased frequency. In more advanced tumors, pelvic pain and symptoms related to urinary tract obstruction, exempli gratia flank pain, may be present [6].

Physical examination should include rectal and vaginal bimanual palpation. A palpable pelvic mass can be found in patients with locally advanced tumors. In addition, bimanual examination under anesthesia should be carried out before transurethral resection of the bladder, to assess whether there is a palpable mass or if the tumor is fixed to the pelvic wall.

Diagnosis work-up includes both non-invasive and invasive methods.

Anemia can be present due to blood loss. Azotemia and elevated creatinine levels may be noted in patients with ureteral occlusion.

In 54% of the patients in our review (15 of 28 patients) hydronephrosis was present. The secondary sign of hydronephrosis is associated with advanced disease and poor oncological outcome [7]. It can be assessed by either CT urography or by MRI urography in cases when radiation or iodinated contrast media are contraindicated [8]. CT urography can moreover reveal thickening of the bladder wall.

Examination of voided urine or bladder washings for exfoliated cancer cells has high sensitivity in high-grade tumors and may be a useful indicator in some cases of high-grade malignancy.

Even though bladder cancers may be detected by various imaging techniques, their presence should be verified by undergoing cystoscopy, biopsy and transurethral resection for histopathological diagnosis and staging [9]. Distinction between metastatic bladder lesion and primary tumor may be hard from an imaging viewpoint which makes cystoscopy and histological examination the gold standard in making the diagnosis. Endoscopic findings and macroscopic features of bladder tumors consist crucial part of the characterization of the disease.

The presence of changes in the bladder mucosa is useful in distinguishing a primary bladder tumor from a metastatic bladder tumor. A submucosal tumor is suggestive of a secondary bladder tumor, but ulcerative lesions can be seen in some cases. Solid tumors are more suspicious of metastatic lesions. Superficial, low-grade tumors appear as single or multiple papillary lesions, usually of urothelial pathology. Higher grade lesions are larger and sessile [9]. In our study several endoscopic findings were described like extensive vegetative session, protuberant mass, extensive bullous oedema of the bladder mucosa and diffuse papillary nodular lesion.

The metastatic bladder tumor can be described macroscopically as diffuse or protuberant similar to typical transitional cell carcinoma [10]. In our study 16 patients revealed diffuse wall thickening (57% of patients) and 12 patients revealed protuberant mass (43% of patients).

Concerning the management of metastatic disease with bladder involvement in patients with gastric cancer require the coordination of both a urologist and an oncologist in purpose to diagnose, assess the pathology and the staging and determine further therapeutic actions and, moreover, to improve the patient's quality of life. In our study surgical

management with total or partial cystectomy was performed only in three patients (11% of patients) and TUR was performed in six patients (22% of patients). Palliative chemotherapy for the management of the metastatic disease was initiated in 13 patients of the study (46% of patients).

Advanced gastric cancer has a poor prognosis with a 5-year of 3.1% [11]. In our study the median survival of our patients from the time of diagnosis of bladder metastasis was 5.1 months, a fact that points out the unfavorable prognosis of this entity.

Supplementary Materials: The following are available online at <https://www.mdpi.com/article/10.3390/reports4020014/s1>, References [12–33].

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Abbreviations

CT	Computer Tomography
MRI	Magnetic Resonance Imaging
TUR	Transurethral Resection
FISH	Fluorescence in Situ Hybridization

References

1. Torre, L.A.; Bray, F.; Siegel, R.L.; Ferlay, J.; Lortet-Tieulent, J.; Jemal, A. Global cancer statistics, 2012: Global Cancer Statistics, 2012. *CA Cancer J. Clin.* **2015**, *65*, 87–108. [\[CrossRef\]](#) [\[PubMed\]](#)
2. Bates, A.W.; Baithun, S.I. Secondary neoplasms of the bladder are histological mimics of nontransitional cell primary tumours: Clinicopathological and histological features of 282 cases. *Histopathology* **2000**, *36*, 32–40. [\[CrossRef\]](#)
3. Silver, S.A.; Epstein, J.I. Adenocarcinoma of the Colon Simulating Primary Urinary Bladder Neoplasia. A report of nine cases. *Am. J. Surg. Pathol.* **1993**, *17*, 171–178. [\[CrossRef\]](#)
4. Lynch, C.F.; Cohen, M.B. Urinary system. *Cancer* **1995**, *75*, 316–329. [\[CrossRef\]](#)
5. Scosyrev, E.; Noyes, K.; Feng, C.; Messing, E. Sex and racial differences in bladder cancer presentation and mortality in the US. *Cancer* **2009**, *115*, 68–74. [\[CrossRef\]](#)
6. Tanagho, E.A.; McAninch, J.W. (Eds.) *Smith's Handbook of General Urology*, 17th ed.; McGraw-Hill Medical: New York, NY, USA, 2007.
7. Messer, J.C.; Terrell, J.D.; Herman, M.P.; Ng, C.K.; Scherr, D.S.; Scoll, B.; Boorjian, S.A.; Uzzo, R.G.; Wille, M.; Eggener, S.E.; et al. Multi-institutional validation of the ability of preoperative hydronephrosis to predict advanced pathologic tumor stage in upper-tract urothelial carcinoma. *Urol. Oncol. Semin. Orig. Investig.* **2013**, *31*, 904–908. [\[CrossRef\]](#)
8. Takahashi, N.; Glockner, J.F.; Hartman, R.P.; King, B.F.; Leibovich, B.C.; Stanley, D.W.; Fitz-Gibbon, P.D.; Kawashima, A. Gadolinium Enhanced Magnetic Resonance Urography for Upper Urinary Tract Malignancy. *J. Urol.* **2010**, *183*, 1330–1336. [\[CrossRef\]](#)
9. The European Association of Urology Guidelines Office. *Eau Extended Guidelines on Bladder Cancer*; The European Association of Urology Guidelines Office: Arnhem, The Netherlands, 2020.
10. Sharma, P.K.; Vijay, M.K.; Das, R.K.; Chatterjee, U. Secondary signet-ring cell adenocarcinoma of urinary bladder from a gastric primary. *Urol. Ann.* **2011**, *3*, 97–99. [\[CrossRef\]](#)
11. Brenner, H.; Rothenbacher, D.; Arndt, V. Epidemiology of Stomach Cancer. *Methods Mol. Biol.* **2009**, *472*, 467–477. [\[CrossRef\]](#)
12. Nakamura, K.; Hihara, T.; Nishiumi, T.; Yoneyama, T. A case of metastatic urinary bladder tumor from gastric carcinoma. *Hinyokika Kyo. Acta Urol. Jpn.* **1992**, *38*, 845–847.
13. Saba, N.F.; Hoenig, D.M.; Cohen, S.I. Metastatic Signet-Ring Cell Adenocarcinoma to the Urinary Bladder. *Acta Oncol.* **1997**, *36*, 219–220. [\[CrossRef\]](#) [\[PubMed\]](#)
14. Ota, T.; Shinohara, M.; Kinoshita, K.; Sakoma, T.; Kitamura, M.; Maeda, Y. Two Cases of Metastatic Bladder Cancers Showing Diffuse Thickening of the Bladder Wall. *Jpn. J. Clin. Oncol.* **1999**, *29*, 314–316. [\[CrossRef\]](#)

15. Uemura, M.; Inoue, H.; Nishimura, K.; Mizutani, S.; Miyoshi, S. Metastatic bladder tumor disseminated lymphogenously from gastric cancer: A case report. *Hinyokika Kyo Acta Urol. Jpn.* **2000**, *46*, 723–725.
16. Valero Puerta, J.A.; Medina Pérez, M.; García Carriazo, M.; Valpuesta Fernández, I.; Sánchez González, M.; Mompean, F.O. Me-tástasis vesical de adenocarcinoma de células en anillo de sello de origen gástrico [Bladder metastasis of signet-ring cell ade-nocarcinoma from the stomach]. *Arch. Esp. Urol.* **2000**, *53*, 839–841.
17. Kim, H.-C.; Kim, S.H.; Hwang, S.-I.; Lee, H.J.; Han, J.K. Isolated bladder metastases from stomach cancer: CT demonstration. *Abdom. Imaging* **2001**, *26*, 333–335. [[CrossRef](#)]
18. Antunes, A.A.; Siqueira, T.M., Jr.; Falcão, E. Vesical metastasis of gastric adenocarcinoma. *Int. Braz. J. Urol.* **2004**, *30*, 403–405. [[CrossRef](#)]
19. Matsushashi, N.; Yamaguchi, K.; Tamura, T.; Shimokawa, K.; Sugiyama, Y.; Adachi, Y. Adenocarcinoma in bladder diverticulum, metastatic from gastric cancer. *World J. Surg. Oncol.* **2005**, *3*, 55. [[CrossRef](#)]
20. Farhat, M.H.; Moumneh, G.; Jalloul, R.; El Hout, Y. Secondary adenocarcinoma of the urinary bladder from a primary gastric cancer. *Leban. Med. J.* **2007**, *55*, 162–164.
21. Lim, E.-K.; Lin, V.C.-H.; Shu, C.-T.; Yu, T.-J.; Lu, K. Gastric Cancer with Bladder Metastasis: Case Report and Literature Review. *Urol. Sci.* **2011**, *22*, 80–82. [[CrossRef](#)]
22. Neves, T.R.; Covita, A.; Soares, M.; Monteiro, P.; Nogueira, R.; Lima, M.S.; Monteiro, H. Bladder metastasis of gastric adenocarcinoma. Report of 2 cases and bibliographic review. *Arch. Esp. Urol.* **2011**, *64*, 544–550.
23. Andras, C.; Tóth, L.; Pósán, J.; Csiki, E.; Tanyi, M.; Csiki, Z.; Garami, Z.; Enyedi, A.; Flaskó, T.; Horváth, Z. Occurrence of bladder metastasis 10 years after surgical removal of a primary gastric cancer: A case report and review of the literature. *J. Med. Case Rep.* **2013**, *7*, 204. [[CrossRef](#)]
24. Vigliar, E.; Marino, G.; Matano, E.; Imbimbo, C.; Rossella, D.C.; Insabato, L. Signet-Ring-Cell Carcinoma of Stomach Metastatic to the Bladder: A case report with cytological and histological correlation and literature review. *Int. J. Surg. Pathol.* **2012**, *21*, 72–75. [[CrossRef](#)]
25. Kalra, S.; Manikandan, R.; Dorairajan, L.N.; Badhe, B. Synchronously detected secondary signet ring cell urinary bladder malignancy from the stomach masquerading as genitourinary tuberculosis. *BMJ Case Rep.* **2015**, *2015*. [[CrossRef](#)]
26. Okutur, K.; Eren, O.O.; Demir, G. Metastasis of Gastric Signet-Ring Cell Carcinoma to the Urinary Bladder: A Case Report and Review of the Literature. *Case Rep. Oncol. Med.* **2015**, *2015*, 1–6. [[CrossRef](#)]
27. Seow-En, I.; Seow-Choen, F. Intestinal type gastric adenocarcinoma with unusual synchronous metastases to the colorectum and bladder. *World J. Clin. Cases* **2015**, *3*, 533–537. [[CrossRef](#)]
28. Da Silva, R.; De Araújo, G.N.; Hommerding, C.C.L.; Censi, K.C.; Garcia, S.P.; Casarotto, F.C.; Sprinz, E.; Neto, B.S. Signet-Ring Cell Gastric Carcinoma Metastatic to Bladder. *J. Clin. Case Rep.* **2015**, *5*. [[CrossRef](#)]
29. Hung, C.-Y.; Ueng, S.-H.; Lin, Y.-C.; Chou, W.-C. Metastatic carcinoma of the urinary bladder in a 67-year-old female with underlying triple primary cancers. *J. Cancer Res. Pract.* **2016**, *3*, 49–53. [[CrossRef](#)]
30. Sima, R.R.; Babu, G.S.N.; Rao, A.N.; Malipatel, R. Bladder metastasis: An unusual presentation of stomach cancer. *IJSS J. Surg.* **2016**, *2*, 42–45.
31. Lodh, B.; Sinam, R.; Singh, K. Adenocarcinoma of urinary bladder in patient with primary gastric cancer: An unusual synchronous distant metastasis. *Indian J. Cancer* **2016**, *53*. [[CrossRef](#)] [[PubMed](#)]
32. Khoury, R.; Dragean, C.; Annet, L. Bladder metastasis of gastric adenocarcinoma. *J. Belg. Soc. Radiol.* **2019**, *103*, 24. [[CrossRef](#)]
33. Nouioui, M.A.; Saadi, A.; Chakroun, M.; Oueslati, A.; Ksentini, M.; Bouzouita, A.; Derouiche, A.; Ben Slama, M.R.; Rammeh, S.; Ayed, H.; et al. Unusual Bladder Metastasis from a Primary Gastric Carcinoma: Two Case Reports and Review of Literature. *Case Rep. Urol.* **2020**, *2020*, 1–7. [[CrossRef](#)] [[PubMed](#)]