

Giant Cell Osteoclast-Like Bladder Carcinoma: A Case Report

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Abstract: *Introduction:* Osteoclast-like giant cell bladder carcinomas are an extremely unusual and aggressive histological subtype of urothelial carcinomas. Only 30 cases have been reported globally. *Clinical case:* A 79-year-old male patient was presented to our Urology Department due to macroscopic hematuria that persisted for six months. As part of his diagnostic protocol, a CT scan of the abdomen and pelvis with elimination phase was performed, finding a filling defect of 12 mm at the level of the posterior wall of the bladder. A cystoscopy was subsequently performed, confirming the presence of a 1.5 cm bladder tumor, which was resected in its entirety. Pathology analysis with hematoxylin and eosin stain revealed a composition of mononuclear cells and osteoclast-like giant cells. Immunohistochemistry was positive for epithelial markers cytokeratins AE1/AE3, EMA, P53, and CD68. *Conclusion:* Osteoclast-like giant cell bladder carcinomas are extremely unusual and aggressive. The only diagnostic method is through immunohistochemistry, confirming the presence of epithelial markers for urothelium in the neoplastic cells. Radical surgical treatment is recommended and there has been no proven effective adjuvant treatment to date. The patients' median survival is 15 months.

Keywords: Bladder; Urinary neoplasms; Urogenital; Hematuria; Urology

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1. Introduction

We present a case of a 79-year-old male patient diagnosed with osteoclast-like giant cell carcinoma of the bladder, an extremely unusual and aggressive histological subtype of the urothelial carcinomas. There are only 30 cases reported worldwide, so the information available is very limited. Its presentation, management, and outcome, as well as pathology and immunohistochemical findings will be discussed in this report.

2. Presentation of the case

A 79-year-old male patient was referred to the Urology Department of National Medical Center Northeast Specialty Hospital in July 2020, with macroscopic hematuria that persisted for 6 months, amorphous clots were formed intermittently, and the patient was non-anemic, with no other associated symptoms. When questioned about his history, he reported that he was a smoker for 50 years, at a rate of 60 packs per year, but stopped smoking 6 years ago. He also reported 15 years of occupational exposure to different types of

solvents, such as petrol, thinner and acetone, and his hereditary family history of cancer was denied.

As part of his study protocol, a computed tomography (CT) scan with intravenous contrast was performed on the chest, abdomen, and pelvis, which revealed multiple bilateral pulmonary nodules of peripheral predominance, with an average diameter of 8 mm each, which suggested a metastatic disease (**Figure 1**). At the bladder level, posterior wall thickening was observed with enhancement to 76 Hounsfield Units (HU) in the arterial phase, and a 12 mm filling defect in the elimination phase (**Figure 2**).

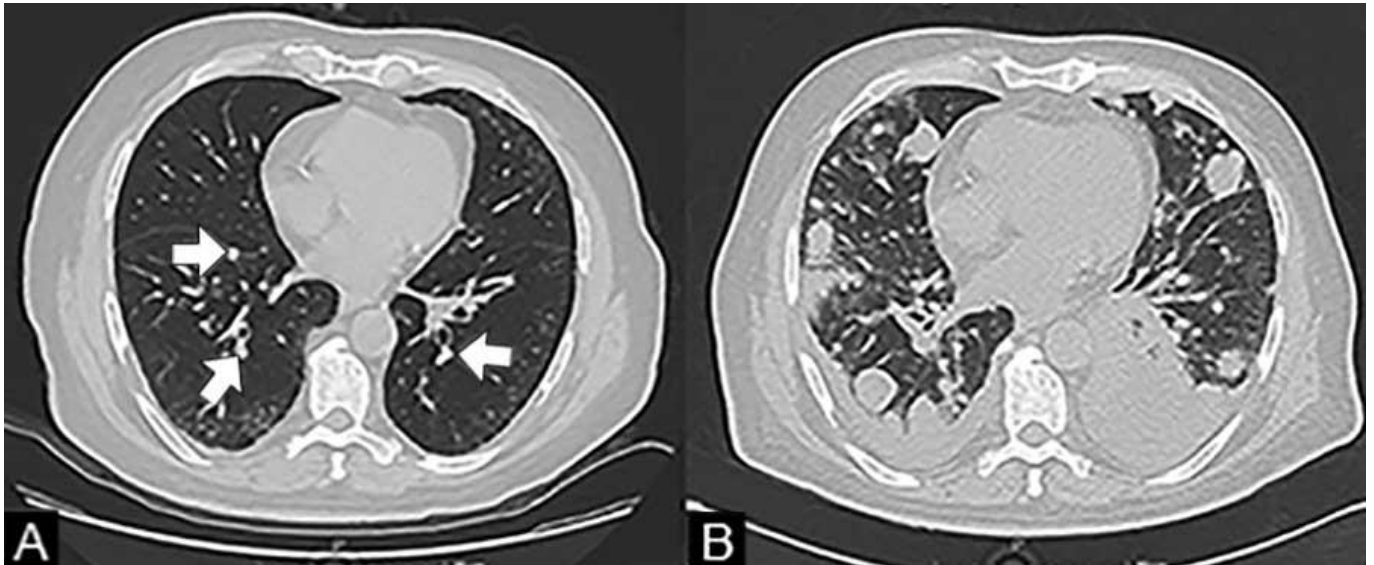


Figure 1. Chest CT scan with lung window in axial reconstruction. Panel A: Initial CT scan with multiple bilateral nodules of 8 mm diameter each (arrows). Panel B: Same CT scan segment months after transurethral resection of the bladder, indicating rapid progression of metastatic disease, as well as bilateral pleural effusion and interstitial pattern secondary to COVID-19 infection in the patient at that time.



Figure 2. CT scan of the abdomen and pelvis with elimination phase in axial (panel A) and coronal (panel B) reconstruction. A 12 mm filling defect in the posterior wall of the bladder (arrow). No evidence of extension into the upper urinary tract or adjacent structures.

Based on the findings in **Figures 1 & 2**, an urgent transurethral resection of the bladder (TURBT) was

performed, and a tumor of 1.5 cm in diameter with a sessile appearance was found at the trigone level, with extensive and friable necrosis. The tumor was resected completely. Following the surgical procedure, complete remission of the hematuria was achieved, and the patient was discharged after 48 hours, with an outpatient follow-up plan.

Pathology analysis of the surgical specimen revealed a composition of two cell populations through hematoxylin and eosin (H&E) staining: the first one was composed of mononuclear cells with scant eosinophilic cytoplasm and a spindle-shaped morphology, their nucleus contained vesicle-shaped chromatin and discrete nucleoli (**Figure 3A**); the second population was composed of giant cells with multiple nuclei, compatible with osteoclast-like giant cells, with obvious atypia (**Figure 3B**). Both cell populations were surrounded by a highly vascularized stroma, with areas of erythrocyte extravasation and extensive necrosis.

Immunohistochemistry was positive for epithelial markers cytokeratins AE1/AE3, EMA and P53 in the mononuclear cells and CD68 in the osteoclast-like giant cells (**Figure 3C**). Both cell populations were positive for vimentin (**Figure 3D**).

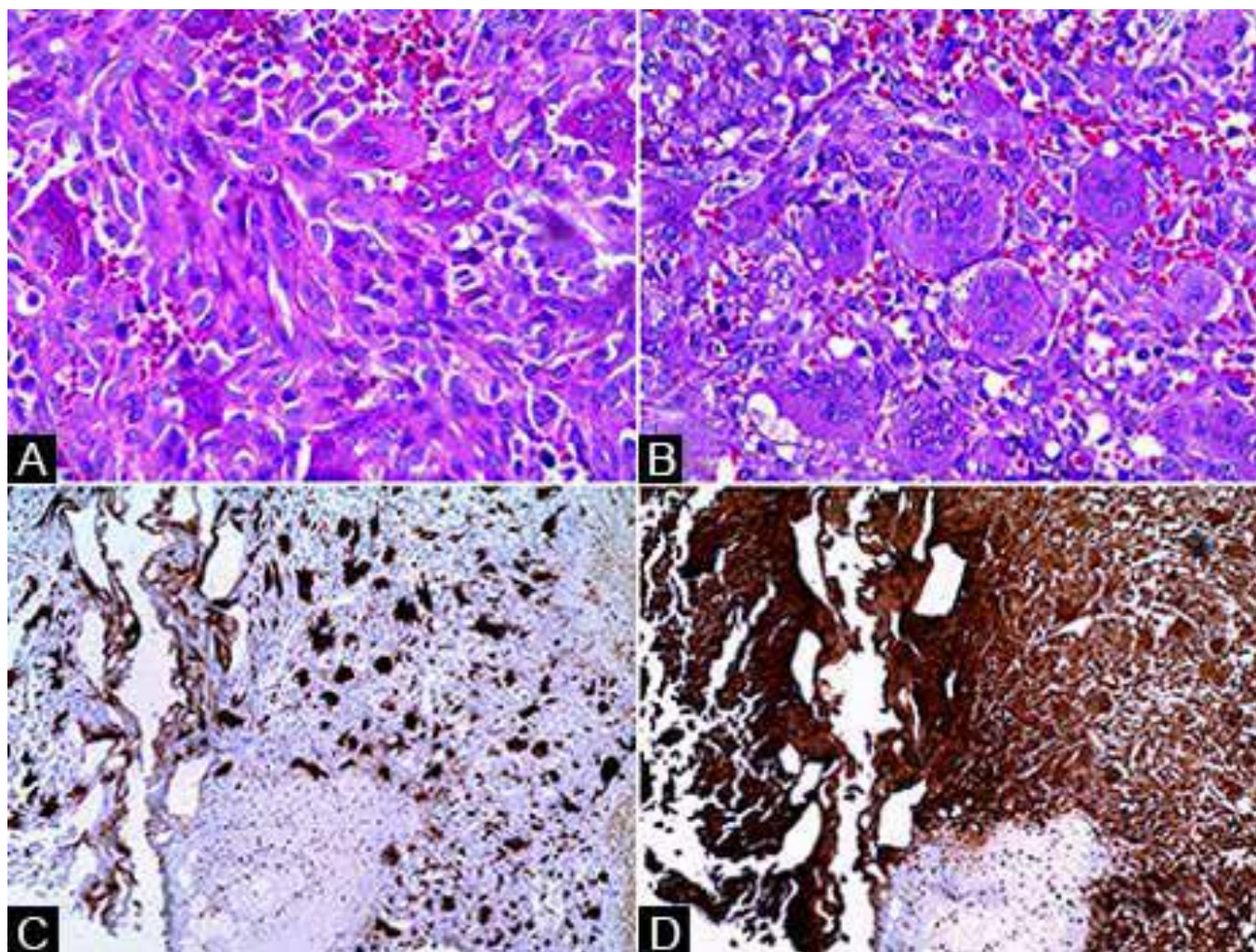


Figure 3. Osteoclast-like giant cell carcinoma identified through H & E staining and immunohistochemical analysis. Panel A (H&E, 40x): proliferation of mononuclear cells with scant eosinophilic cytoplasm, spindle morphology and presence of mitoses. Panel B (H&E, 40x): osteoclast-like giant cells without obvious atypia. Panel C (immunohistochemistry, 10x): osteoclast-like giant cells with CD68 expression. Panel D (immunohistochemistry, 10x): both cell populations with vimentin expression.

The patient was assessed by an oncologist, who stated that the patient was not suitable for cisplatin-based chemotherapy due to his poor functional status (Eastern Cooperative Oncology Group, ECOG 2). For the same reason, the Urology department decided not to perform a radical cystectomy but instead to keep him under close surveillance, and further trans urethral resection of bladder tumor (TURBT) was performed if needed as palliative treatment. Two months after surgery, our patient was hospitalized due to a COVID-19 infection. The chest CT scan performed at that time revealed bilateral pleural effusion, interstitial pattern, and rapid progression of the metastatic disease (**Figure 1B**). Unfortunately, he died due to complications related to COVID-19 infection and metastatic disease two months after diagnosis.

3. Discussion

According to the World Health Organization's classification of urinary tract and male genitalia trans urethral resection of bladder tumors in 2016, the urinary tract tumors are divided into urothelial and non-urothelial variants ^[1]. The latter accounts for about 25% of the total and their incidence has been increasing in recent years, mainly due to a better knowledge of them by urologists and pathologists ^[2,3].

Histological subdivisions of non-urothelial carcinomas are predominantly based on their morphology observed with H & E staining ^[4], with squamous, adenocarcinoma, and neuroendocrine features, either one or mixed ^[2,5].

Among bladder tumors, non-urothelial carcinomas are rare and present a real diagnostic challenge because only 1-5% are of primary origin ^[2,6], and initial TURBT has a low sensitivity ^[7], detecting only 53% of cases ^[8], and some histological subtypes may appear to be benign lesions ^[9].

Non-urothelial carcinomas generally occur in older patients and at later stages compared to their urothelial counterparts ^[10-12]. Their prognosis is poor, regardless of clinical stage ^[13,14], with a 2- and 5-year recurrence-free survival rate of 62.0% ± 3.0% and 57.0% ± 3.0%, respectively; and a 2- and 5-year cancer-specific survival rate of 68.0% ± 2.0% and 58.0% ± 3.0%, respectively ^[15]. The effect of neoadjuvant therapies varies in their impact on patient survival, depending largely on histological subtype ^[16,17], so radical cystectomy remains the gold standard for treatment to date ^[4,18], and it should be performed within eight weeks of diagnosis to avoid compromising patient survival ^[19].

Among the non-urothelial histological variants, osteoclast-like giant cell carcinomas of the urinary tract are extremely rare, with only 30 cases reported worldwide ^[20,21]. They are predominant in male patients and has non-specific symptoms, with hematuria being the most common ^[20,22]. They are characterized by two types of cell populations: mononuclear cells with mild to moderate atypicality and expression of epithelial markers cytokeratins AE1/AE3, CAM 5.2, CK7, and EMA, and osteoclast-like giant cells with expression of CD68, LCA, CD51, and CD54 markers ^[21,22]. Both populations are positive for vimentin and acid phosphatase ^[23].

Their pathogenesis is still unknown, but one theory suggests that these are not true bone cells because there are key differences in their immunohistochemical profile, such as the expression of paraurothelial epithelial markers. It is thought that they may actually be an unusual and aggressive variant of urothelial carcinomas that subsequently differentiate into a giant bone cell morphology ^[22].

Their appearance on cystoscopy is the same as that of a urothelial carcinoma. Thus, the only way to make a diagnosis is through pathological analysis along with immunohistochemistry ^[24].

Osteoclast-like giant cell carcinomas of the urinary tract have an overall poor prognosis, with a reported median survival of less than 15 months (**Table 1**) ^[25]. Radical surgical treatment is therefore recommended because of the aggressive nature of these tumors and because there is no proven effective adjuvant treatment so far ^[20].

Table 1. Summary of similar cases reported in literature: age at presentation, gender, site, treatment, and reported survival data

Authors	Gender	Age	Site	Treatment	Survival
Park ^[20]	Male	76 years old	Distal ureter	Radical nephroureterectomy	Alive at five months post-diagnosis. No evidence of recurrence
Palazzetti et al. ^[21]	Female	54 years old	Bladder	Radical cystectomy	Alive one year after diagnosis, no evidence of recurrence.
Baydar et al. ^[22]	Male	65 years old	Pelvis renal	Radical nephroureterectomy	Died 15 months after diagnosis. Pulmonary metastases
Baydar et al. ^[22]	Male	39 years old	Pelvis renal	Radical nephroureterectomy	Died 10 months after diagnosis. Recurrence of liver and lung metastases.
Baydar et al. ^[22]	Male	82 years old	Pelvis renal	TURBT	Died 5 months after diagnosis. Pulmonary metastases
Baydar et al. ^[22]	Male	81 years old	Bladder	TURBT	No follow-up or survival is reported.
Baydar et al. ^[22]	Male	81 years old	Bladder	Radical cystectomy	Alive four months after diagnosis, with local recurrence.
Baydar et al. ^[22]	Male	67 years old	Bladder	Radical cystectomy	Died 12 months after surgery.
Wu et al. ^[24]	Male	62 years old	Bladder	Radical cystectomy and partial ureterectomy	Alive five months after diagnosis. No evidence of recurrence
Osman et al. ^[25]	Male	55 years old	Bladder	Radical cystectomy	Died 10 months after diagnosis due to a lung infection. Received four sessions of gemcitabine along with cisplatin chemotherapy.

4. Conclusion

4.1. Limitations

The main limitation of this case report is the short follow-up period given to our patient, besides the late presentation of his disease. His poor condition also precluded him from being a candidate for systemic chemotherapy as adjuvant treatment, which would have potentially extended his survival.

4.2. Summary of scientific evidence and further recommendations

After a systematic search of indexed journals, no reports of similar cases were found locally or in Latin America with which to contrast immunohistopathology findings, treatment, and patient follow-up.

The cases published in international indexed journals, which are the treatments and follow-up are summarized in **Table 1**. It is noteworthy that only two patients received a treatment similar to our case (TURBT) instead of radical surgery, one of them presenting early recurrence at four months; and the follow-up and survival are unknown. The gold standard of treatment for these patients remains early radical surgery, within eight weeks of initial diagnosis.

4.3. Strengths

The greatest strength of this article is the microphotographs of pathology and immunohistopathology presented, which, to our knowledge, are the highest quality found in literature. As this is a highly unusual pathology, we believe that these information may help in the identification of future cases.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Moch H, Humphrey PA, Ulbright TM, et al., 2016, WHO Classification of Tumors of the Urinary System and Male Genital Organs, International Agency for Research on Cancer, Lyon.
- [2] Park S, Reuter V, Hansel D, 2018, Non-Urothelial Carcinomas of the Bladder. *Histopathology*, 74(1): 97–111.
- [3] Matulay J, Narayan V, Kamat A, 2019, Clinical and Genomic Considerations for Variant Histology in Bladder Cancer. *Curr Oncol Rep*, 21(3): 23.
- [4] Lobo N, Shariat S, Guo C, et al., 2020, What Is the Significance of Variant Histology in Urothelial Carcinoma?. *Eur Urol Focus*, 6(4): 653–663.
- [5] Grilo I, Rodrigues C, Soares A, et al., 2020, Facing Treatment of Non-Urothelial Bladder Cancers in the Immunotherapy Era. *Crit Rev in Oncol Hematol*, 153: 103034.
- [6] Aron M, 2019, Variant Histology in Bladder Cancer — Current Understanding of Pathologic Subtypes. *Curr Urol Rep*, 20(12): 80.
- [7] Hansel D, Amin M, Comperat E, et al., 2013, A Contemporary Update on Pathology Standards for Bladder Cancer: Transurethral Resection and Radical Cystectomy Specimens. *Eur Urol*, 63(2): 321–332.
- [8] Abd el-Latif A, Watts K, Elson P, et al., 2013, The Sensitivity of Initial Transurethral Resection or Biopsy of Bladder Tumor(s) for Detecting Bladder Cancer Variants on Radical Cystectomy. *J Urol*, 189(4): 1263–1267.
- [9] Lopez A, Cheng L, 2006, Histologic Variants of Urothelial Carcinoma: Differential Diagnosis and Clinical Implications. *Hum Pathol*, 37(11): 1371–1388.
- [10] Zaffuto E, Gazdovich S, Leyh-Bannurah S, et al., 2016, Contemporary Rates of Pathological Features and Mortality for Adenocarcinoma of the Urinary Bladder in the USA. *Int J Urol*, 24(2): 117–123.
- [11] Hayashi T, Tanigawa G, Fujita K, et al., 2011, Two Cases of Plasmacytoid Variant of Urothelial Carcinoma of Urinary Bladder: Systemic Chemotherapy Might be of Benefit. *Int J Clin Oncol*, 16(6): 759–762.
- [12] Tiwari R, Ngo N, Lee L, 2020, The Optimal Management of Variant Histology in Muscle Invasive Bladder Cancer. *Transl Androl Urol*, 9(6): 2965–2975.
- [13] Deuker M, Martin T, Stolzenbach F, et al., 2021, Bladder Cancer: A Comparison Between Non-Urothelial Variant Histology and Urothelial Carcinoma Across All Stages and Treatment Modalities. *Clin Genitourin Cancer*, 19(1): 60–68.
- [14] Mori K, Abufaraj M, Mostafaei H, et al., 2020, A Systematic Review and Meta-Analysis of Variant Histology in Urothelial Carcinoma of the Bladder Treated with Radical Cystectomy. *J Urol*, 204(6): 1129–1140.

- [15] Soave A, Schmidt S, Dahlem R, et al., 2015, Does the Extent of Variant Histology Affect Oncological Outcomes in Patients with Urothelial Carcinoma of the Bladder Treated with Radical Cystectomy?. *Urol Oncol*, 33(1): 21.e1–21.e9.
- [16] Daneshmand S, Nazemi A, 2020, Neoadjuvant Chemotherapy in Variant Histology Bladder Cancer: Current Evidence. *EurUrol Focus*, 6(4): 639–641.
- [17] Vetterlein M, Wankowicz S, Seisen T, et al., 2017, Neoadjuvant Chemotherapy Prior to Radical Cystectomy for Muscle-Invasive Bladder Cancer with Variant Histology. *Cancer*, 123(22): 4346–4355.
- [18] Porten S, Willis D, Kamat A, 2014, Variant Histology: Role in Management and Prognosis of Non Muscle Invasive Bladder Cancer. *Curr Opin Urol*, 24(5): 517–523.
- [19] Lin-Brandt M, Pearce S, Ashrafi A, et al., 2019, Assessing the Impact of Time to Cystectomy for Variant Histology of Urothelial Bladder Cancer. *Urology*, 133: 157–163.
- [20] Park H, 2011, Osteoclast-Like Giant Cell Carcinoma of the Distal Ureter. *Korean J of Urol*, 52(1): 68.
- [21] Palazzetti A, Oderda M, Falcone M, et al., 2016, Osteoclast-Like Giant Cell Carcinoma Hidden by a Bladder Stone in a Patient with Neurogenic Bladder. *Clin Genitourin Cancer*, 14(1): e127–e130.
- [22] Baydar D, Amin M, Epstein J, 2016, Osteoclast-Rich Undifferentiated Carcinomas of the Urinary Tract. *Mod Pathol*, 19(2): 161–171.
- [23] García-García F, García-Ligero J, Rico-Galiano J, et al., 2003, A Rare Case of Bladder Carcinoma with Osteoclast-Type Giant Cells: A Literature Review. *Actas Urol Esp*, 27(4): 317–320.
- [24] Wu P, Su C, Li J, et al., 2009, Osteoclast-Like Giant Cell Carcinoma of the Urinary Bladder. *J Chin Med Assoc*, 72(9): 495–497.
- [25] Osman C, Muammer B, Murat O, et al., 2018, Osteoclast-Type Giant Cell Carcinoma of the Urinary Bladder: An Unusual and Aggressive Variant of Urothelial Carcinoma. *Urol Case Rep*, 23: 50–51.

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