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Case Report

Rapid Regression of Rare Sub-Cutaneous Metastasis in Urothelial Carcinoma Patient Treated with Enfortumab Vedotin Plus Pembrolizumab: A Case Report

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ABSTRACT

Bladder cancer is a common urological malignancy, predominantly affecting older adults, and metastatic disease is associated with poor prognosis. We present the case of a 70-year-old woman with metastatic urothelial carcinoma presenting as a right subcutaneous axillary mass. First-line treatment with enfortumab vedotin, an anti–Nectin-4 antibody–drug conjugate, combined with the PD-1 inhibitor pembrolizumab resulted in a rapid and clinically significant regression of the lesion. This case illustrates a rare presentation of subcutaneous metastasis in urothelial carcinoma, suggestive of aggressive tumor biology. The dramatic response to enfortumab vedotin plus pembrolizumab underscores the potential efficacy of this combination in patient's ineligible for cisplatin-based chemotherapy. Early systemic therapy proved effective in controlling metastatic progression, even in the set setting of renal impairment and advanced age.

Keywords: Metastatic urothelial carcinoma, Sub-cutaneous metastasis, Enfortumab vedotin, Pembrolizumab, Case report

INTRODUCTION

Bladder cancer (BC) is one of the most relevant neoplasms in the field of urology. It predominantly affects males and is primarily diagnosed in older adults: worldwide, it ranks as the ninth most frequently diagnosed cancer across both sexes and is the thirteenth leading cause of cancer-related mortality [1]. Recently, the combination of enfortumab vedotin, an antibody–drug conjugate targeting nectin-4, and pembrolizumab, a PD-1 immune checkpoint inhibitor, has emerged as a groundbreaking first-line therapeutic option. The Phase III EV-302/KEYNOTE-A39 trial, involving

886 previously untreated patients with locally advanced or metastatic urothelial carcinoma, demonstrated a significant clinical benefit of the enfortumab vedotin plus pembrolizumab combination over standard platinum-based chemotherapy [2,3].

Herein, we report the case of a patient with metastatic BC involving lymph nodes, who received first-line treatment with the combination of enfortumab vedotin and pembrolizumab.

CASE PRESENTATION

The patient is a 70-year-old woman with a significant history of tobacco use, currently smoking approximately 20 cigarettes per day for over five decades. Aside from untreated glaucoma, she has no major comorbidities at the time of evaluation.

Clinical Presentation and Diagnostic Work-Up

The patient first came to medical attention in December 2024 due to an episode of gross hematuria, prompting further diagnostic evaluation. Abdominal ultrasound revealed a sizable intravesical mass measuring approximately 6 cm, along with grade II hydronephrosis of the left kidney, suggestive of urinary tract obstruction.

To further characterize the lesion, a rigid urethrocystoscopy was performed on January 8, 2025. The procedure revealed a solid, vascularized mass involving the trigone, bladder neck, and proximal urethra, raising concern for a malignant neoplasm.

On February 5, 2025, the patient underwent transurethral resection of the bladder tumor (TURB). Histopathological analysis confirmed the diagnosis of a high-grade (HG) invasive urothelial carcinoma, with evidence of muscularis propria infiltration, consisting with locally advanced disease.

Laboratory investigations at the time revealed impaired renal function, with elevated serum creatinine (2.69 mg/dL) and blood urea nitrogen (85 mg/dL). A follow-up abdominal ultrasound on February 23, 2025, demonstrated progression of hydronephrosis-grade II on the right and grade III on the left-necessitating bilateral percutaneous nephrostomies placement on February 25, 2025.

Subsequent staging with contrast-enhanced thoraco-abdominal computed tomography (CT), performed on March 8, 2025, revealed thickening of both ureters in their pre-vesical segments. The bladder appeared poorly distended, with thickened and heterogeneous walls, and its floor was adherent to the cervix and vagina, suggesting possible local invasion. No clinically significant lymphadenopathy was observed.

Surgical Intervention

As there was no clear evidence of metastatic disease, and renal function contraindicated neoadjuvant chemotherapy, the patient underwent left nephroureterectomy and radical cystectomy with ileal neobladder reconstruction on March 17, 2025. Histopathological examination confirmed a HG papillary invasive urothelial carcinoma infiltrating the muscularis propria, perivesical fat, and vaginal wall. Ureteral margins were negative, and 10 resected lymph nodes were free of metastasis. Additional findings included tubular atrophy, interstitial renal fibrosis, chronic ureteral inflammation, and cervical squamous metaplasia. According to the 8th Edition (2017) of the American Joint Committee on Cancer (AJCC) staging system, the pathological stage was pT4aN0.

Metastatic Progression

On May 23, 2025, the patient was presented with a newly developed, enlarging mass in the right arm. An incisional biopsy was performed, and histological analysis confirmed the presence of metastatic urothelial carcinoma. Immunohistochemical profiling supported the diagnosis, revealing an immunophenotype consistent with urothelial origin (Cytokeratin B+, p63+, CK7-/+, GATA3+/-, CK20).

To assess the extent of disease, a whole-body CT scan was performed on June 27, 2025. Imaging revealed a 5.5 cm subcutaneous mass in the right axillary region, accompanied by a deep axillary lymphadenopathy. No additional metastatic lesions were identified at that time (Figure 1).

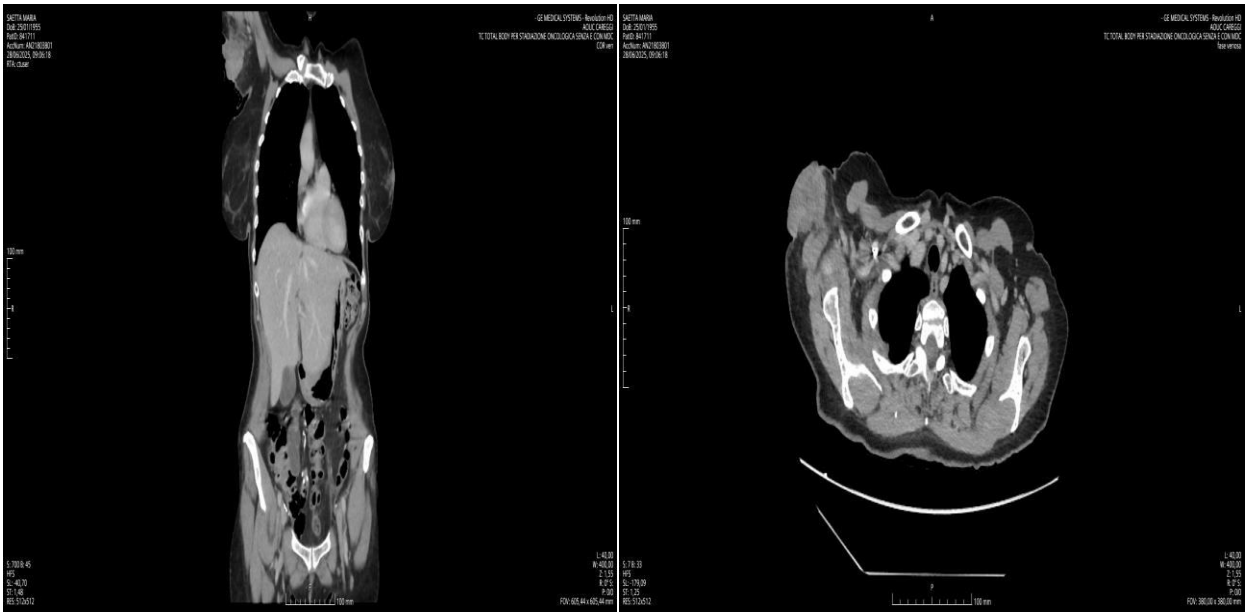

Figure 1: Baseline whole-body CT scan showing a subcutaneous mass in the right axilla.

Therapeutic Strategy

The patient was initially evaluated for eligibility in the KEYNOTE-D74 clinical trial—an open- label, randomized, controlled Phase 3 study investigating Disitamab Vedotin in combination with Pembrolizumab versus chemotherapy in patients with previously untreated, locally advanced or metastatic HER2-positive urothelial carcinoma. However, she was deemed ineligible due to a negative result on centralized HER2 testing. In light of these findings, a therapeutic strategy involving Enfortumab Vedotin (Astellas) in combination with Pembrolizumab (MSD) was proposed under an open-label Early Access Program. This approach received approval from the local Ethics Committee on July 10, 2025.

Treatment was initiated on July 25, 2025, consisting of Enfortumab Vedotin at a dose of 1.25 mg/kg administered on days 1 and 8 of a 21-day cycle, alongside Pembrolizumab 200 mg every 21 days. Baseline laboratory investigations prior to treatment initiation were within normal limits.

Nursing Management

Physical examination revealed an exophytic mass in the right axillary region, measuring 7x4cm with an approximate depth of 2 cm. The lesion had irregular margins, a bright red appearance, and was markedly exudative, producing serum-hematic secretions with occasional purulent discharge at the central area (Figure 2).

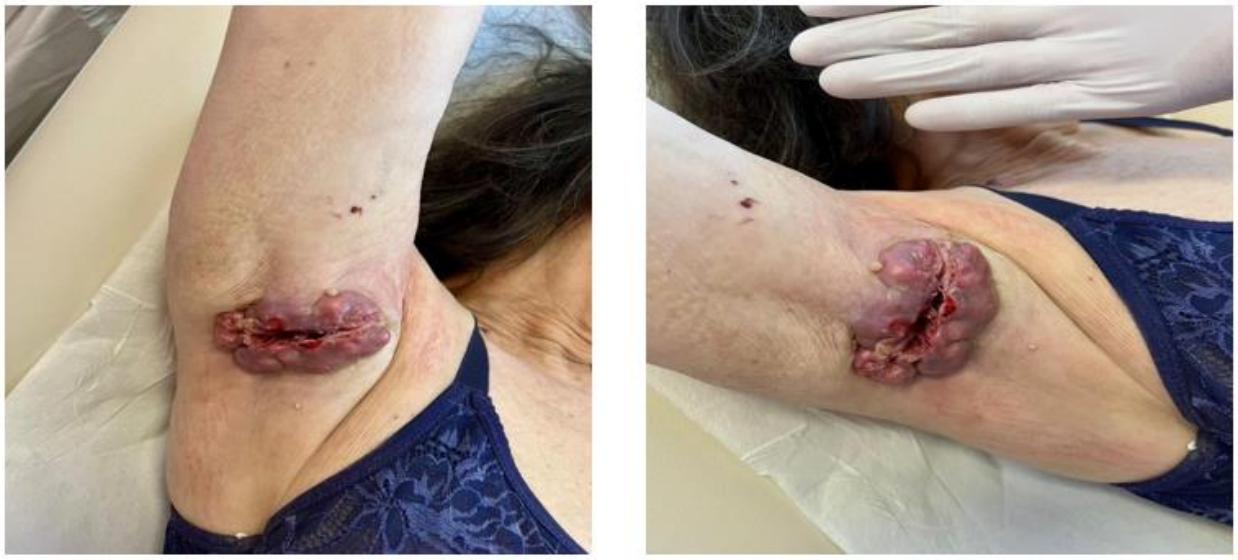

Figure 2: Cycle 1 day 1: right axillary exophytic mass measuring 7x4cm and approximately 2 cm in depth, with irregular margins and bright red color.

The patient reported movement-related pain, with a score of 5 at the numeric rating scale (NRS) along with partial functional impairment in both arm abduction and adduction.

A multidisciplinary discussion was held to determine the most appropriate management approach for the lesion, both in outpatient setting and at home. The primary objectives were exudate control and reduction of patient discomfort. The selected wound care protocol included cleansing with 0.9% normal saline, disinfection with 0.05% chlorine derivative solution, and application of a dressing covering the entire wound bed. The primary dressing consisted of a bacterial-binding gauze pack, followed by a highly absorbent and hemostatic calcium alginate layer. A neutral paraffin gauze was applied to the wound margins to provide symptomatic relief, and the procedure was completed with a flat secondary dressing. The dressing was maintained in place for 5-7 days or until the maximum absorption capacity of the alginate layer was reached. Written recommendations were therefore provided to ensure continuity of care, enabling the local community nursing service closest to the patient's residence to replicate the same wound management protocol.

Follow-Up and Response To Therapy

At the beginning of the second treatment cycle (August 14, 2025), the right axillary lesion had significantly regressed, measuring 3x2 cm. It was minimally exudative and no longer ulcerated (Figure 3). Wound management continued as previously described, with cleansing and disinfection followed by neutral the application of neutral paraffin gauze and

flat dressing. The treatment was well tolerated, and the patient did not experience significant adverse events or hematologic toxicity.

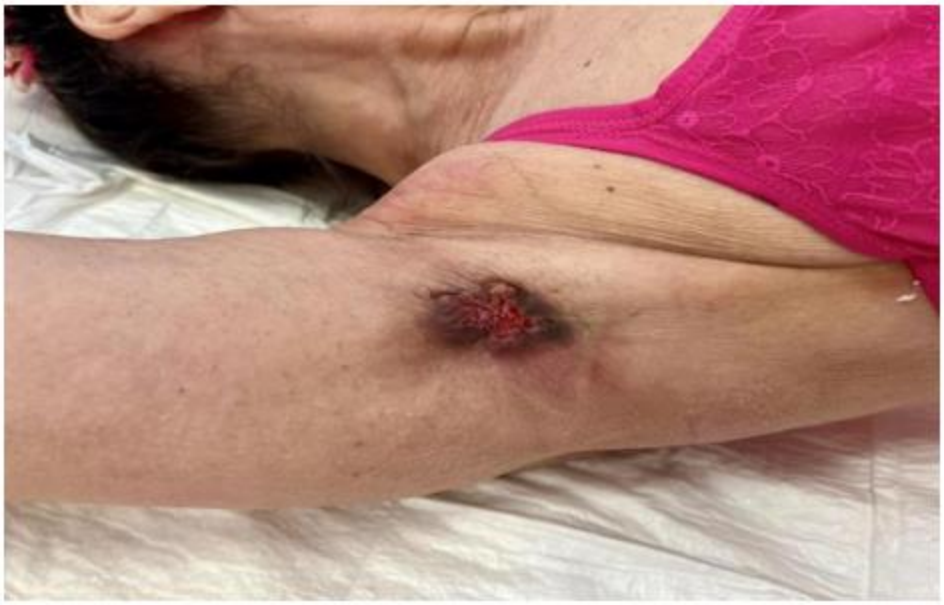

Figure 3: Cycle 2 day 1: right axillary lesion measuring 3x2 cm, no longer ulcerated.

By the beginning of the third cycle (September 3, 2025), further improvement of the lesion was observed, with dimensions reduced to 2x1 cm (Figure 4). The exophytic and exudative components had completely resolved, leaving only residual marginal discoloration. The patient was pain-free (NRS 0) with full recovery of limb function.

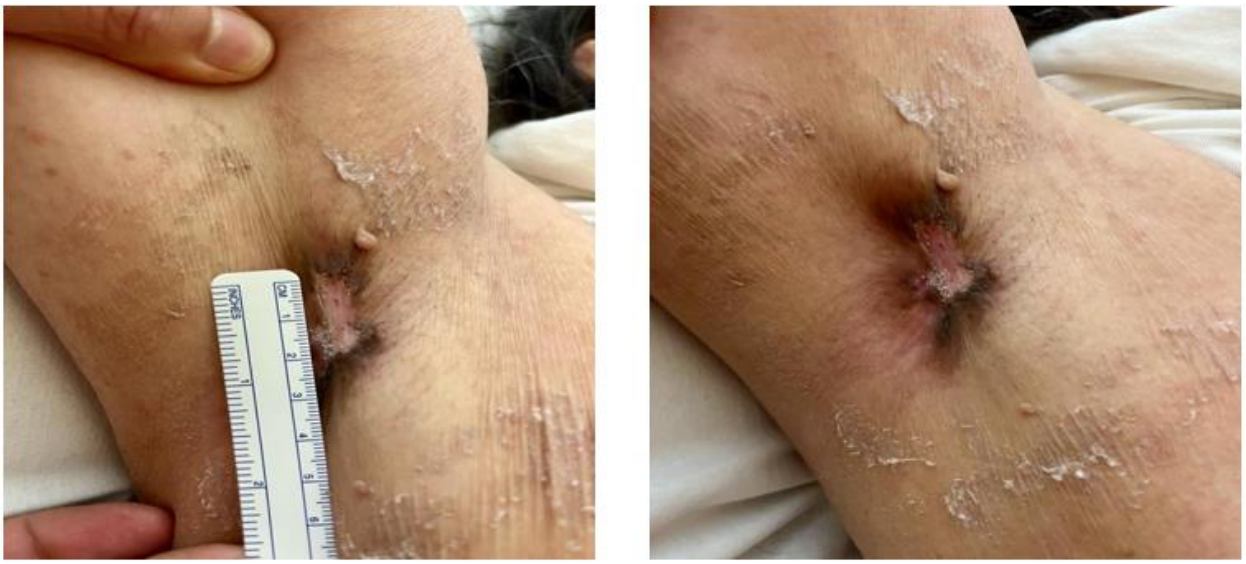

Figure 4: Cycle 3 day 1: right axillary lesion measuring 2x1 cm with only residual marginal discoloration remaining.

The patient adhered to the prescribed standard treatment regimen without encountering any significant adverse events throughout the course of therapy.

A CT scan conducted on October 13, 2025, demonstrated complete resolution of the previously identified right axillary lesion, with no new lesions detected (Figure 5).

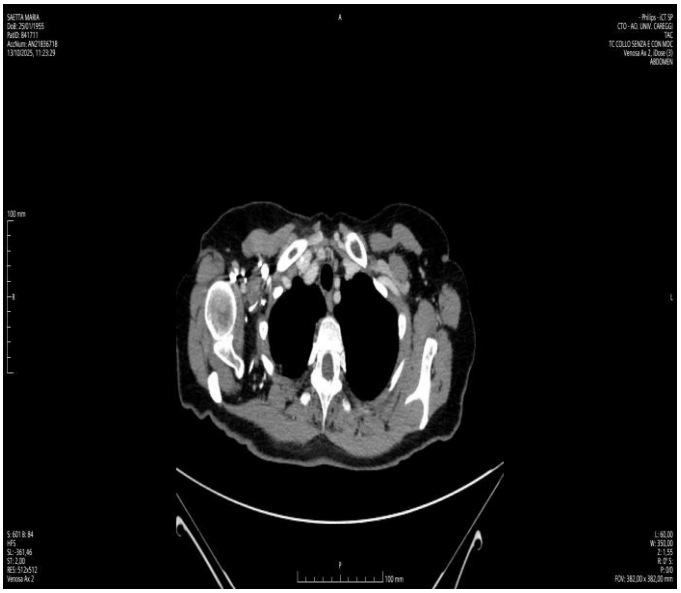

Figure 5: Whole body CT scan revealed the complete resolution of the previously identified right axillary lesion.

Upon completion of the fifth treatment cycle, on October 22, 2025, clinical evaluation revealed no detectable evidence of disease (Figure 6).

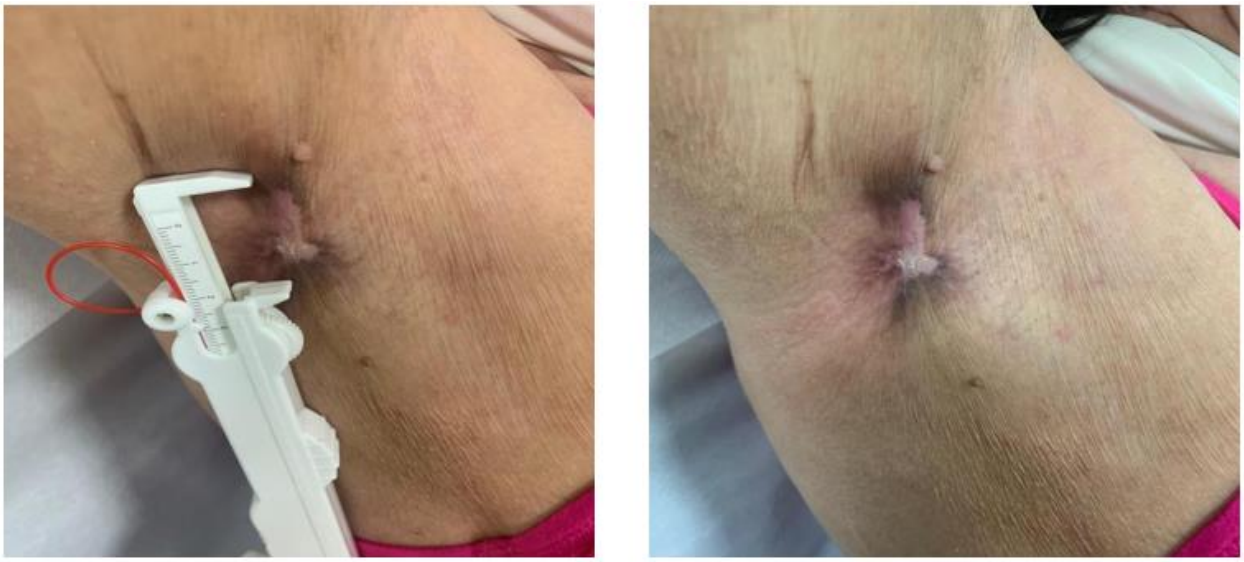

Figure 6: Cycle 5 day 8: No clinical evidence of the right axillary lesion.

DISCUSSION

The emergence of subcutaneous axillary metastasis in this patient represents a notably rare manifestation of urothelial carcinoma. Cutaneous metastases from bladder cancer are infrequent, with an estimated incidence of less than 1%. When present, they typically indicate aggressive tumor biology and are associated with a poor prognosis [4]. The

combination of enfortumab vedotin (an anti-Nectin-4 ADC) and pembrolizumab (a PD-1 inhibitor) was selected for this patient. The early treatment response was remarkable: the axillary lesion decreased from 7x4 cm to 3x2 cm within three weeks. Such rapid and clinically evident tumor regression underscores the potential efficacy of this combination in patients with metastatic BC, highlighting the importance of early systemic therapy. The patient's dramatic response is consistent with previously published reports 2, 3 suggesting that tumors expressing Nectin- 4 may be particularly sensitive to Enfortumab Vedotin. Our experience reinforces the potential benefit of this regimen in real-world settings, particularly in elderly patients with impaired renal function who are ineligible for cisplatin based chemotherapy.

CONCLUSION

This case illustrates an aggressive, high-grade urothelial carcinoma in an elderly patient with compromised renal function, successfully managed through a combination of surgical intervention and novel systemic therapy. The atypical metastatic presentation, along with the remarkable early response to enfortumab vedotin plus pembrolizumab highlight the importance of individualized treatment strategies, early recognition of uncommon metastatic patterns, and the emerging role of ADC- immunotherapy combinations in cisplatin-ineligible patients. This report contributes to the growing body of evidence supporting personalized treatment approaches in advanced urothelial carcinoma and underscores the need for clinical vigilance in identifying rare metastatic sites.

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