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Solitary cardiac metastasis of urothelial carcinoma of the urinary bladder with squamous cell differentiation – a rare manifestation

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ABSTRACT

We present a case of bladder cancer with a singular cardiac metastasis. A 51-year-old female patient was referred to our department for painless macrohematuria. We confirmed the diagnosis of muscle-invasive urothelial carcinoma of the urinary bladder with partial squamous cell differentiation. Computed tomography (CT) staging demonstrated a singular cardiac metastasis. Two months after receiving six cycles of chemotherapy control CT scan revealed massive tumour progression. The singular cardiac metastasis size increased to approximately two thirds of right ventricle size. Singular cardiac metastases of urothelial carcinoma are extremely rare and show rapid progression, hence introduction to therapy should not be delayed.

1. Introduction

Urothelial carcinoma (UC) of the bladder is the second most common urologic tumour associated with limited survival in metastatic stage. Primary metastatic UC is detected in approximately 25% of all patients. The cancer typically spreads through the iliac and pelvic lymph nodes, while metastases usually occur in the lung, liver or bones. Cisplatin-based chemotherapy represents standard first-line treatment of choice whereas immunotherapy can be administered in platinum-ineligible patients with positive PD-L1/PD-1 expression. Avelumab is currently the only established Federal Drug Agency (USA) approved drug for maintenance therapy.

2. Case presentation

A 51-year-old female patient in good general condition (Eastern Cooperative Oncology Group "ECOG" performance status of zero) was referred to our department for further evaluation of macrohematuria and cystoscopically confirmed mass of the urinary bladder. The only known pre-existing disease was mild manifestation of multiple sclerosis. After transurethral resection, the diagnosis of muscle-invasive UC of the urinary bladder (TNM classification: pT2, G2-3, high grade) with partly extensive squamous cell differentiation was confirmed. Our pathologists further described a moderately to poorly differentiated carcinoma with partial extensive keratinization in the sense of a squamous epithelial differentiation. Immunohistochemistry staining revealed negativity for protein p16 (cyclin-dependent kinase inhibitor 2A, CDKN2A) and partial reactivity for protein CK20 (keratin 20), while clear staining was described for transcription factor GATA3, especially in cancer tissue with urothelial differentiation. No further tests for immunohistochemical markers, such as PD-1 or PD-L1 were performed at this point.

The CT scan of the chest and abdomen showed a tumor-specific mass in the right ventricle, hence a cardiac-CT was ordered, which confirmed the diagnosis of cardiac metastasis with infiltration of the pericardium (see Fig. 1). Additionally, transthoracic echocardiography validated the rare finding with total size of 25 × 38 mm. After case presentation within our multidisciplinary cancer conference, palliative treatment with six cycles of chemotherapy with gemcitabine and cisplatin was initiated. Throughout the entire course of therapy, the cardiac metastasis was defined as inoperable by our department of cardiac surgery due to its infiltration into pericardium. In order to achieve clear margins, excision of the entire right ventricle would have been mandatory.

After the second cycle of chemotherapy follow-up CT-scan revealed a reduction of the cardiac metastasis from a maximum of 38 mm–30 mm.

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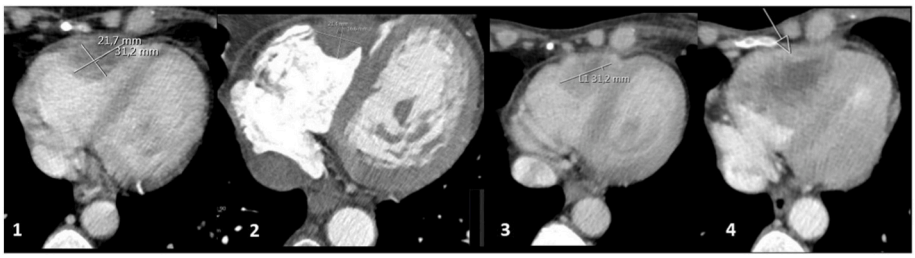

Fig. 1. CT-scans showing cardiac metastasis at different time points during treatment: 1) before starting six cycles of chemotherapy, maximum diameter of 38 mm; 2) after two cycles of chemotherapy, maximum diameter of 30 mm; 3) after six cycles of chemotherapy, constant maximum diameter 30 mm; 4) two months after six cycles of chemotherapy, tumor mass filling two third of right ventricle.

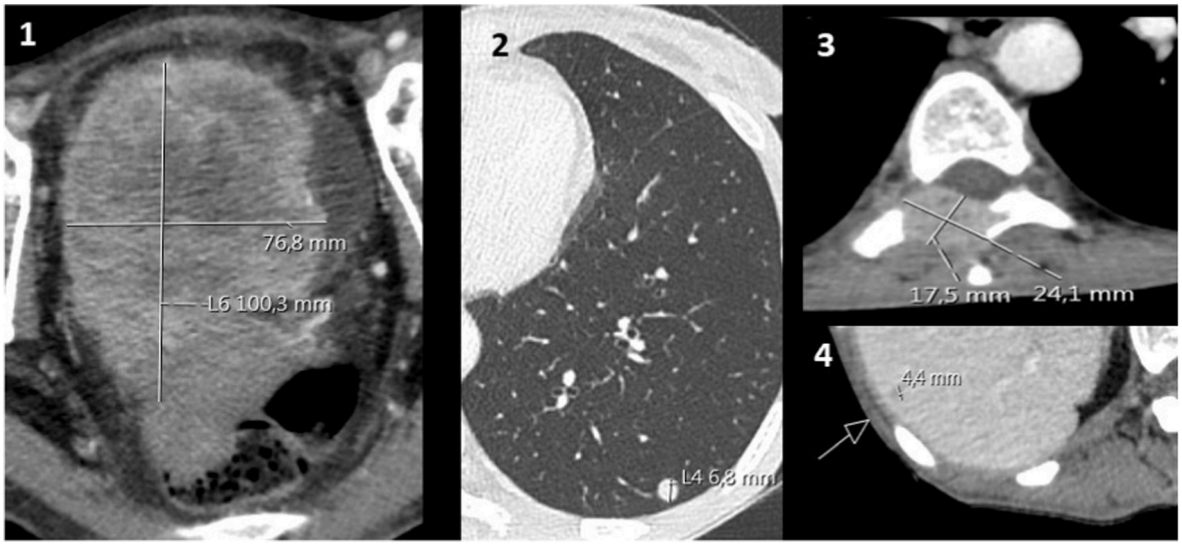

Fig. 2. CT-scan demonstrating massive progress of metastatic disease two months after six cycles of chemotherapy: 1) enlargement of local bladder cancer, size of 78 mm × 100 mm x 81 mm; 2) multiple new bilateral pulmonary metastases, maximum diameter of 7 mm at left basal lower lobe; 3) osteolysis with soft tissue component of the right dorsal vertebral arch 7 with spread to epidural, size 18 mm × 24 mm; 4) live lesion subcapsular in segment VI.

Therefore, we chose to continue with chemotherapy (see Fig. 1) and decided not to conduct endomyocardial biopsy of the cardiac mass to rule out another form of malignancy. Due to chemotherapy-associated renal insufficiency cisplatin was administered in a split dose for another two cycles and hereafter replaced by carboplatin for the fifth and sixth cycles.

During second half of chemotherapy the patient suffered several complications, beginning with hypokalemia and hypercalcemia. Additionally, due to the presence of intermittent macrohematuria, bladder irrigation and transurethral tamponade evacuation needed to be performed. By the end of the treatment the patient presented with severe pancytopenia with leading thrombocytopenia developed, which was treated with appropriate infusions of erythrocyte and platelet aggregates. Due to heavy complications, the patient's general condition decreased from an initial ECOG performance status of zero toward a score of three, including a weight loss of approximately 30 kg within the last 3–4 months.

After finishing six cycles of chemotherapy, maintenance immunotherapy with avelumab was recommended.[1] However, treatment was delayed against our medical advice by two months due to the patient's personal wishes. Before starting the delayed maintenance therapy, we performed a new CT-scan which revealed a massive overall progression of local as well as metastatic disease. In addition to the increasingly infiltrating carcinoma of the urinary bladder, new bilateral pulmonary and osseous metastases and cancerous suspicious liver lesions were described (see Fig. 2). The cardiac metastasis also grew rapidly with increase in size from 2 mm to approximately two thirds of right ventricle volume (see Fig. 1). Finally, we discussed best supportive care and palliative treatment due to deteriorating health and progressive disease with poor prognosis of overall survival.

3. Discussion

This case presents cardiac metastasis as an extraordinarily rare localization of distant metastasis in a patient with urinary bladder carcinoma with squamous cell differentiation. Over the past 35 years, only ten cases of cardiac metastases have been described in current literature. In these cases, approximately 60% of UC were with squamous cell differentiation which is known as the more aggressive subtype with lower response rates to chemotherapy resulting in worse overall survival.[2]

To our knowledge, we describe the first case with only a single cardiac metastasis at initial diagnosis without any presence of lymph node involvement or other visceral metastasis. In all other published cases, cardiac metastases were diagnosed either after surgical or systematic treatment, after autopsy or in patients with oligometastatic disease. Additionally, only two out of the ten publications have described isolated cardiac metastasis.[3,4] Interestingly, both of the reported patients suffered from UC with squamous cell carcinoma. For example, one of the two presented patients was diagnosed with cardiac metastasis of 30 mm × 40 mm mass in the right ventricle four months after transurethral resection with pathologically confirmed high-grade, stage T1 bladder cancer.[4] In that case, treatment with radiotherapy was conducted for a short time due to progressive respiratory complications and poor functional status, followed by best supportive care concept.

4. Conclusion

Even if rear, radiologic findings suspicious for cardiac metastasis should be regarded a highly serious clinical situation and rapid decision making is mandatory. We did not performed biopsy of the cardiac mass due to certainty of radiologic findings and treatment response after starting chemotherapy.[5] Therapy of metastatic disease should follow evidence-based guidelines regardless of rare localization. We assume generally poor survival based on published data.

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Author contributions

Gregor Duwe Writing - Original Draft, Visualization.
Nikita Dhruva Fischer Writing - Review & Editing.
Maximilian Haack Writing - Review & Editing.
Thomas Höfner Writing - Review & Editing.
Axel Haferkamp Writing - Review & Editing.
Maximilian Peter Brandt Writing - Review & Editing, Supervision.

Declaration of competing interest

All authors certify that they have no affiliations with, or involvement in any organization, or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript. Furthermore, the authors have no competing interests to declare that are relevant to the content of this article.

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