Case Report

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Pathology Section

Diagnosis of Cardiac Metastasis on Pericardial Fluid Cytology in a Patient of Urothelial Carcinoma of Bladder: A Case Report

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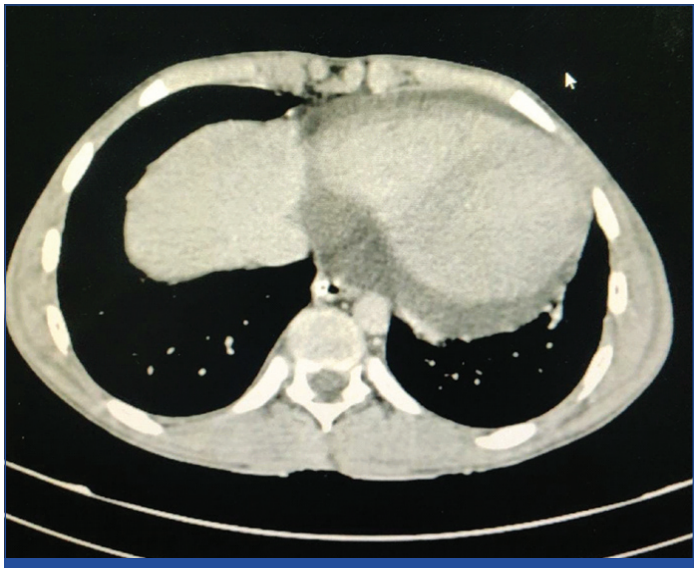
ABSTRACT

Bladder cancer ranks as the 9th most common malignancy worldwide within the urinary system. Urothelial carcinoma stands as the predominant histologic type in the United States and Western Europe, constituting approximately 90% of bladder cancer cases. While common sites of metastasis for urothelial carcinoma typically involve regional and distinct lymph nodes, the liver, lungs, and bones, instances of metastasis to the pericardium are rare. Roughly 10% of urothelial carcinoma cases exhibit cardiac metastasis, often remaining clinically asymptomatic. Hereby, the authors present a rare case of symptomatic pericardial infiltration originating from urothelial carcinoma in a 32-year-old male. The patient initially presented with a two-week history of progressive dyspnoea on exertion and had been previously diagnosed with high-grade transitional cell carcinoma with squamous differentiation upon histopathological examination and urothelial carcinoma on a Positron Emission Tomography (PET) scan 12 months earlier. Following neoadjuvant chemotherapy and radiotherapy, the patient exhibited a partial response to the treatment. However, despite the effectiveness of the therapies, he developed dyspnoea and pericardial effusion. Although pericardial involvement in advanced malignancies is not uncommon, symptomatic cardiac metastasis from urothelial carcinoma remains rare. Radiographic studies revealed right-sided pleural effusion, while a Computed Tomography (CT) scan of the thorax and upper abdomen (plain and contrast) displayed severe bilateral pleural effusion, pericardial effusion, and metastatic deposits in the mediastinal lymph nodes. Electrocardiography indicated sinus tachycardia, inverted T-waves in leads V1 to V5, and flattening of the T-wave in V6. The patient underwent pericardial tapping, yielding approximately 50 cc of pericardial fluid. A 10 cc of the pericardial fluid was subsequently sent for examination in the Pathology Department, with fluid cytology results indicating the presence of malignant cells.

Keywords: Fluid cytology, Pericardial effusion, Transitional cell carcinoma

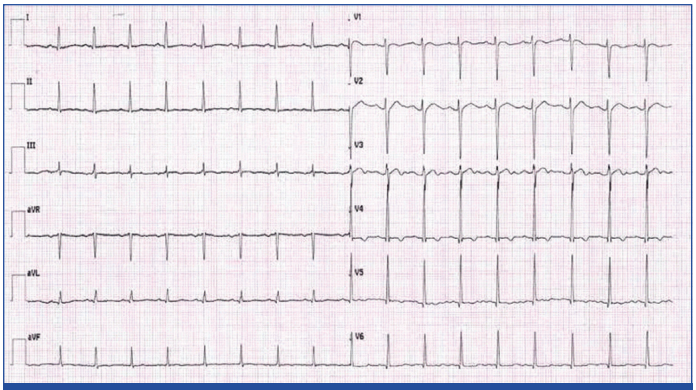
CASE REPORT

A 32-year-old male presented with two weeks of progressive dyspnoea on exertion. He had previously been diagnosed with high-grade urothelial carcinoma with squamous differentiation based on histopathological examination and a PET scan conducted 12 months ago. Immunohistochemistry (IHC) markers showed positivity for P63, P40, CK-7, CK-40, P16, and GATA-3. The patient underwent three cycles of neoadjuvant chemotherapy (5-FU, CISPLATIN) and ten cycles of radiotherapy, demonstrating a partial response to the treatment. His last chemotherapy session was administered on March 23, 2022. On February 1, 2023, the patient was brought to the casualty Department with complaints of dyspnoea, loss of appetite, and nausea persisting for two weeks. Upon examination, the patient was afebrile, with a heart rate of 120 beats/min, blood pressure of 120/70 mmHg, and respiratory rate of 16 breaths/min. Normal heart sounds were observed, with bibasilar crackles present upon lung auscultation. A chest radiograph revealed right-sided pleural effusion. Results from complete blood count, liver function tests, renal function tests, and electrolyte tests were within normal limits, except for an elevated serum alkaline phosphatase level of 362 U/L (normal range: 53-128 U/L). A CT scan of the thorax (plain and contrast) indicated pericardial effusion with metastatic deposits in mediastinal lymph nodes [Table/Fig-1].



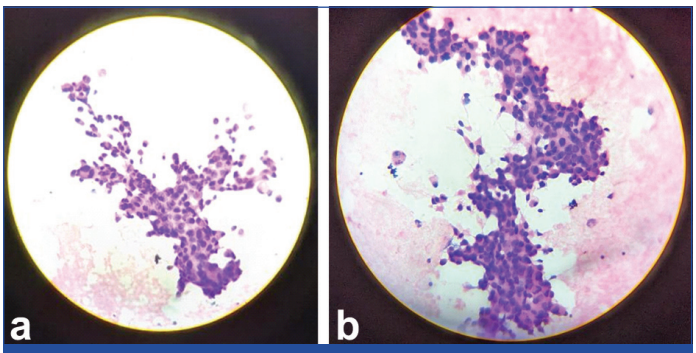
[Table/Fig-1]: CT thorax and upper abdomen (plain and contrast) revealed pericardial effusion.

Electrocardiography revealed sinus tachycardia, T-wave inversion in leads V1 to V5, and flattening of the T-wave in V6 [Table/Fig-2]. The patient's Lactate Dehydrogenase (LDH) level was elevated 502 IU/L (normal range: 140-280 IU/L). Following pericardial tapping, approximately 50 cc of pericardial fluid was extracted. A 10 cc sample of the fluid was sent for examination to the Pathology Department on February 3, 2023. The fluid, which was haemorrhagic without any clot, was centrifuged, and slides were stained with Haematoxylin and Eosin (H&E stain). Microscopic analysis of the smear revealed neoplastic cells arranged in sheets, clusters, and a few 3D balls. Individual neoplastic cells appeared round with mildly pleomorphic hyperchromatic nuclei, indistinct nucleoli, and scant cytoplasm. The background displayed reactive and degenerated mesothelial cells, inflammatory cells, and Red Blood Cells (RBCs). The pericardial fluid tested positive for carcinoma cells [Table/Fig-3,4]. A biopsy was

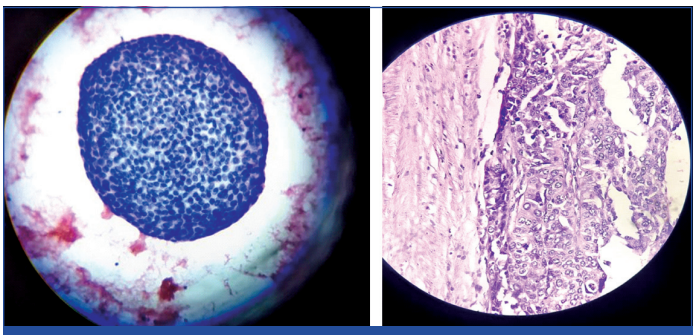


[Table/Fig-2]: Electrocardiography showed sinus tachycardia and inverted T-wave in leads V1 to V5 and flattening of T-wave in V6.

performed, confirming the presence of urothelial carcinoma [Table/Fig-5]. Immunohistochemistry markers GATA3 and CK-7 exhibited marked positivity. Therefore, the final diagnosis was metastatic urothelial carcinoma to the pericardium. Unfortunately, follow-up was not possible as the patient passed away during admission.



[Table/Fig-3]: a) Neoplastic cells in sheets with hyperchromaticnuclei and eosinophilic cytoplasm (H&E, 10X); b) Neoplastic cells arranged in sheets with hyperchromatic nuclei and eosinophilic cytoplasm in high power magnification (H&E, 40X).



[Table/Fig-4]: Neoplastic cells arranged in 3D balls (H&E, 40X).
[Table/Fig-5]: Nests of neoplastic cells with high grade nuclear features and invading into the lamina propria (H&E, 40x). (Images from left to right)

DISCUSSION

Bladder carcinoma ranks as the 9th most common cancer globally and the 4th most common cancer among men [1]. It typically spreads via the lymphatic system, with common metastatic sites including the bones, lungs, liver, and peritoneum [2]. Cardiac metastases are often asymptomatic and are typically discovered incidentally during postmortem examinations or imaging studies. Research by Bussani R et al., found that among cases of bladder carcinoma, 9.1% had cardiac metastasis out of the 38.8% of cases examined postmortem [3,4]. Urothelial carcinoma accounts for only 1.8% of primary malignancies with cardiac metastasis, making it an exceptionally rare cause of cardiac metastasis.

Urothelial carcinoma commonly presents with painless haematuria and urinary symptoms like dysuria, frequency, and incontinence [5]. It may also manifest with pain if there is local invasion. Risk factors for urothelial carcinoma include older age, smoking, and industrial exposure.

Malignancy accounts for 13-23% of pericardial effusions. Common investigations in cases of urothelial carcinoma include cystoscopy, urine analysis, and imaging studies like CT urograms or intravenous pyelograms. Prognosis is dependent on the stage at presentation, with an 85% survival rate for stage 1 and less than 15% for advanced stages of carcinoma [6].

In cases of cardiac metastasis, the myocardium is usually the most affected layer, followed by the pericardium and endocardium. Patients with cardiac metastasis may present with symptoms such as respiratory failure, changes in cardiac auscultation, tachycardia, asthenia, weight loss, and haematuria [7].

Histopathologically, urothelial carcinoma displays discohesive cells with eccentric nuclei. The immunohistochemical staining pattern for urothelial carcinomas can vary. Cytokeratin (CK) 7 staining is common in these tumours, while CK20 expression ranges from 15% to 97% depending on the study. The cells often stain positive for CK, epithelial membrane antigen, GATA binding protein 3 (endothelial transcription factor 3), Cluster of Differentiation (CD) 15, CD138, protein 53 (p53), and protein 16 (p16) [7-9].

Similar findings in terms of symptoms, electrocardiogram results, CT scans, and IHC markers were observed in a study by de Araujo Souza LC et al., [10]. Additionally, a case report by Hattori S et al., on metastatic urothelial carcinoma to the pericardium presenting with dyspnoea showed tumour spread from the renal pelvis to the pericardium, aligning with the present study findings [11]. Another case report by Yeaman CT et al., on a rare presentation of urothelial bladder carcinoma as cardiac tamponade demonstrated exophytic bladder growth metastasising to the pericardium, with results similar to the present study [12].

CONCLUSION(S)

The present case highlights a rare occurrence of cardiac metastasis from urothelial carcinoma, confirmed through pericardial effusion cytology showing neoplastic cells. In patients with a prior history of urothelial carcinoma and presenting with signs and symptoms of cardiac or pulmonary complications, echocardiography should be considered for early detection. Supportive investigations like pericardial effusion cytodiagnostics and radioimaging are crucial, given the very poor prognosis associated with cardiac metastasis from urothelial carcinoma.

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