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Early Vertebral Metastases in Non-Muscle-Invasive Bladder Cancer: A Case Report

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Abstract **Case Report**

Most urinary tract tumors are bladder cancers, whereas NMIBCs are the most common. In NMIBC, distant metastases are extremely rare, and imaging for staging is rarely requested without warning signs, nor recommended. Nonetheless, non-muscle invasive bladder cancers can develop distant metastases without regional progression. We present a case of NMIBC with vertebral metastasis in a young man with no risk factors for bladder tumors who responded well to systemic therapy. We also discuss possible explanations for this rare occurrence**.**

Keywords: Urothelial carcinoma; Non-muscle invasive bladder cancer; Vertebral metastases; Early metastasis.

INTRODUCTION

Bladder cancer is the most common urinary tract tumors. Nevertheless, it is relatively rare among young people. Around 70% of bladder tumors are superficial, and the occurrence of early distant metastases is rare. We report a case of a young man who developed vertebral metastases from a non-muscle-infiltrating bladder tumor. We discuss hypotheses that may explain distant metastases in this type of cancer.

CASE PRESENTATION

A 31-year-old man, with no notable medical history or smoking history, presented to our center with a 15-day history of lumbosciatica deficiency. There was no fever, tuberculosis infection, or recent trauma in the patient.

In contrast, 6 months ago, the patient presented with macroscopic hematuria, for which a reno-vesical ultrasound revealed thickening of the bladder wall. A trans-urethral resection of the bladder was performed with complete and deep lesion resection. Histological examination revealed a papillary urothelial carcinoma infiltrating the chorion. There was no muscle infiltration (PT1). There was no evidence of vascular or perineural invasion. Unfortunately, the patient did not receive any further treatment after he was lost to follow-up.

Upon admission, the patient presented with lumbar spinal syndrome and radicular syndrome type L4 and L5, without genital-sphincter disorders.

Lumbar MRI revealed a tumoral process of L4 vertebral body, infiltrating the right iliopsoas muscle. It was associated with an infiltrating mass in the posterior arch of L2 and the homolateral paravertebral and psoas muscles. There were also lytic lesions in L5 (**Figure 1**).

In light of the antecedent bladder cancer, a Uroscanner was performed, and no recurrence of the tumor was found.

In view of the rarity of vertebral metastases of non-muscle-invasive bladder cancer (NMIBC), a biopsy of the mass in the 4th lumbar vertebra was performed. Histological analysis showed poorly differentiated carcinomatous proliferation, with immunohistochemical staining positive for Ac Anti-CK7, GATA 3, and Ac Anti-P63, consistent with a urothelial origin.

As a result of the diagnosis of metastatic urothelial carcinoma, the patient was referred to medical oncology for further treatment. The patient received cisplatin-based systemic chemotherapy with good results.

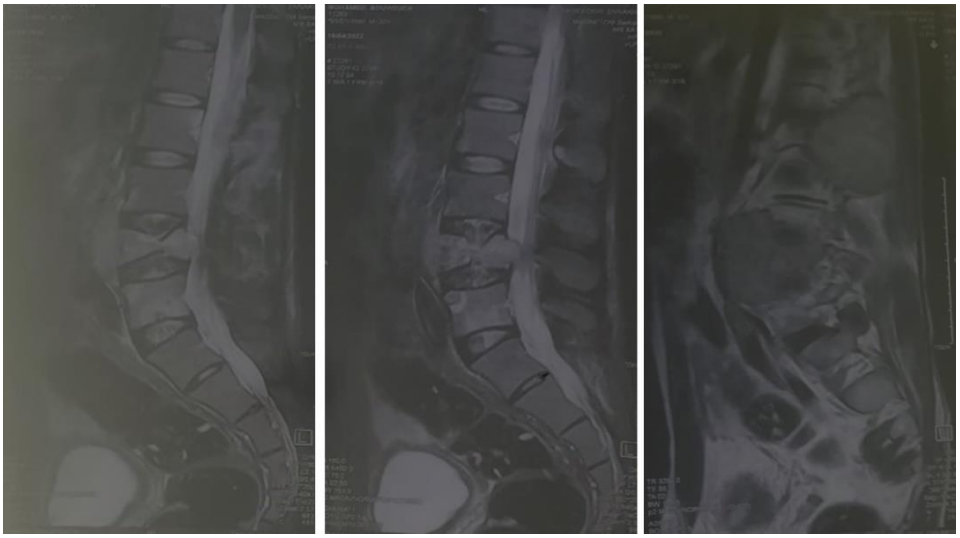

Figure 1: Sagittal lumbar MRI: Tumoral process of L4 vertebral body, the posterior arch of L2 and infiltrating the iliopsoas muscle

DISCUSSION

Bladder cancer is the 10th most common malignancy diagnosed and the 13th most deadly globally (Sung *et al*., 2021). Around 75% of patients are diagnosed with non-muscle-infiltrating cancer, while 25% are muscle-infiltrating or metastatic (Kamat *et al*., 2016). NMIBC has a high recurrence rate (50-70%), and a significant proportion (15-20%) progresses to muscle-infiltrating cancer (Witjes *et al*., 2021).

Bladder cancer is relatively rare in the young population, and several studies have shown that younger bladder cancer patients have more favorable clinical, pathological, and prognostic features (Al-Zalabani *et al*., 2016). There are several risk factors associated with bladder cancer, including smoking, male gender, age, exposure to carcinogens, chronic bladder inflammation, drugs (phenacetine and cyclophosphamide), and pelvic radiotherapy. Several genetic polymorphisms have been proposed as being associated with the development of bladder cancer (Woldu *et al*., 2017).

The patient's history does not reveal any occupational or environmental exposure, and his young age makes it difficult to implicate external factors.

Transurethral resection of the bladder is the first critical step in bladder tumor staging and management. Inadequate resection of the tumor, inadequate sampling of the muscularis propria, or missing a tumor such as CIS, can lead to poor staging and early recurrence (Matthews *et al*., 1984).

Although most NMIBC remain non-infiltrative, the risk of progression is significant. However, NMIBC rarely metastasizes directly to distant sites without progression to the bladder or regional lymph nodes (Hsieh *et al*., 2015).

Metastasis rates for bladder cancer are 10%. The most common site of metastasis was lymph nodes (69%), followed by bone (47%), lung (37%), liver (26%), and peritoneum (16%) (Shinagare *et al*., 2011). Of the bone metastases, 40% occurred in the spine (Sengeløv *et al*., 1996).

Several mechanisms may explain distant metastases in NMIBC:

- Lymphovascular invasion of tumor cells into the microcirculatory system (Sundar & Ganesan, 2007), circulating tumor cells excreted into the bloodstream from the primary tumor act as a proxy for early metastatic spread of the disease (Mathieu *et al*., 2016).
- TURBT or intravesical therapy may cause tumor cells to spread (Sylvester *et al*., 2006).
- Batson's venous plexus facilitates the attachment of tumor cells to bone tissue. As in the spine, this plexus has no valve structure (del Regato, 1977) (Sasaki *et al*., 2013).
- On the other hand, stage may be underestimated.

For NMIBC, metastases are detected between 7 and 40 months after treatment of the primary tumor (D'Souza *et al.*, 2011), while metastasis-free survival for MIBC is between 1 and 2 years (Rodríguez López *et al*., 2018). There is a shorter metastasis-free survival interval in patients with bone metastases than elsewhere (Xu *et al*., 2022).

Metastatic NMIBC is treated according to metastatic bladder tumor guidelines. Platinum-containing chemotherapy is proposed as first-line therapy.

This case highlights the possibility that distant metastases may occur even in patients without local recurrence or progression. It isn't recommended that

clinicians perform routine CT or extension tests for patients with NMIBC, but clinicians should be aware that NMIBC can cause metastases.

CONCLUSION

NMIBC rarely metastasizes to the spine. However, it should be considered as a possible diagnosis when a patient presents with neurological signs and has a history of bladder cancer.

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