



## Case Report

# Non-seminomatous germ cell tumor with bone metastasis only at diagnosis: A rare clinical presentation



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## KEYWORDS

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**Abstract** Bone metastasis of non-seminomatous germ cell tumors (NSGCT) of the testes is a rare event and even more uncommon at initial presentation. Generally, bone lesions are discovered in the presence of concurrent retroperitoneal lymph node or visceral disease. However, in this case, a 37 years old male complaining of a growing testicular mass was found to have isolated bone metastasis with associated caudaequina syndrome without apparent abnormal findings on initial computed tomography (CT) scans. Continued neurologic symptoms prompted further evaluation with magnetic resonance imaging (MRI), which demonstrated multiple sites of bone metastasis without evidence of retroperitoneal lymph node or visceral organ involvement. This case represents a rare clinical presentation and disease manifestation of NSGCT.

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## 1. Introduction

Bone metastasis at initial presentation of non-seminomatous germ cell tumor (NSGCT) of the testes is an uncommon

event, as it is usually associated with concurrent retroperitoneal lymph node or visceral disease. We present a case of NSGCT with an isolated bone metastasis that was not documented on initial staging computed tomography (CT)

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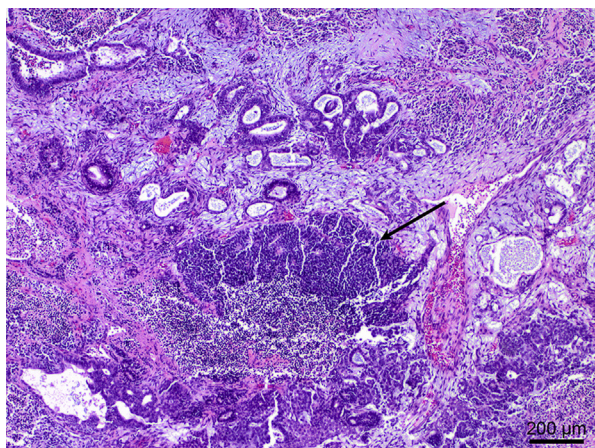
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that caused caudaequina syndrome, without any lymph node or visceral involvement and only discovered after additional imaging with magnetic resonance imaging (MRI).

## 2. Case report

A 37-year-old man presented to our center with a 6-month history of a growing right testicular mass. One week prior to presentation at our center the mass had become acutely painful prompting the patient to seek treatment at an outside emergency center. A right-sided mass concerning for malignancy was found on testicular ultrasound and the patient was referred to our center for further evaluation. He reported right testicular pain, left buttock pain radiating to his left lateral thigh, constipation, and difficulty urinating. He denied nausea, vomiting, fever, personal history of cryptorchidism, trauma, sexually transmitted infections, or urinary tract infections. His past surgical history was unremarkable. He denied family history of testicular cancer. Physical exam revealed a well-circumscribed, hard mass involving the right testicle, without tenderness to palpation or evidence of tracking along the spermatic cord. The left testicle was palpably normal. Serum  $\alpha$ -fetoprotein (AFP),  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) and lactic dehydrogenase (LDH) levels were elevated at 2613 ng/mL, 7.1 mIU/mL, and 1130 IU/L, respectively. All other routine laboratories were normal. A CT of the abdomen and pelvis with and without contrast showed a mass in the right testicle consistent with NSGCT, without evidence of retroperitoneal lymphadenopathy or metastatic disease. He was prescribed a bowel regimen and hydrocodone for pain management, and was scheduled for orchiectomy.

He returned 3 days later with worsening testicular pain, urinary retention and constipation, which the patient attributed to pain medications. At that time he underwent emergent radical right inguinal orchiectomy. Pathology demonstrated a 12 cm  $\times$  9 cm  $\times$  6 cm NSGCT with extensive necrosis, composed of 85% immature teratoma, 10% yolk sac tumor, and 5% embryonal carcinoma, with invasion of the tunica vaginalis (pT2 cN0 cM0 SX; Stage IB) (Fig. 1). There was no evidence of lymphovascular infiltration and

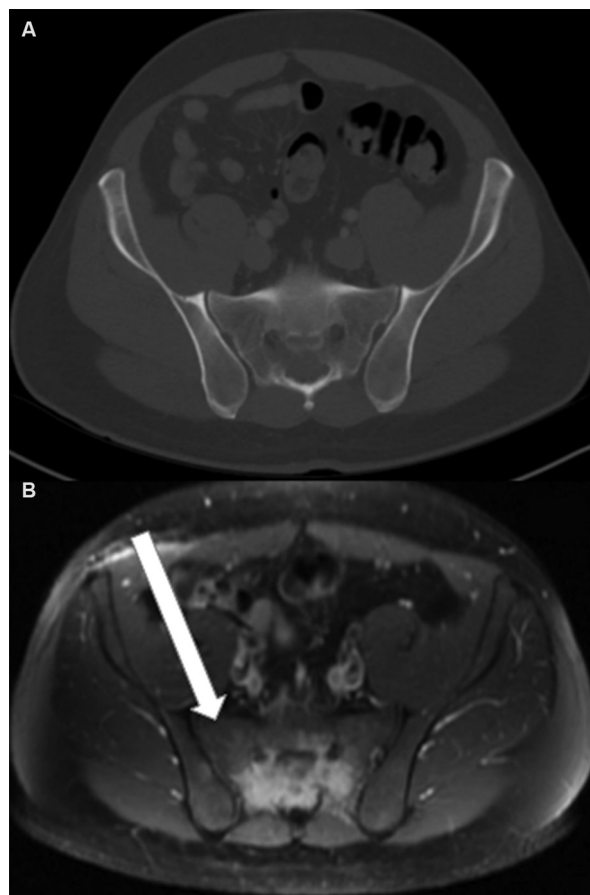


**Figure 1** Histologic section of testicular mass. Teratomatous component (arrow) with areas reminiscent of immature neural tissue.

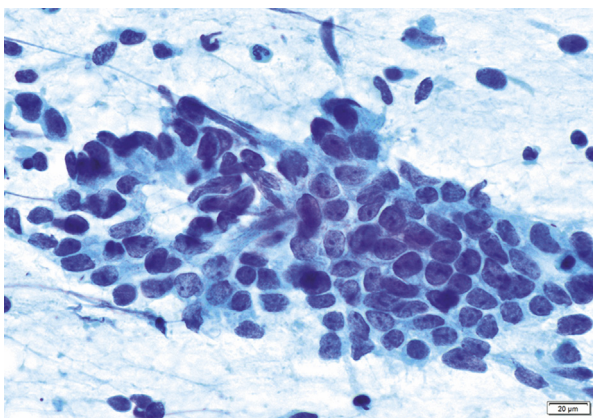
all margins were negative. He was discharged on postoperative day 1 with routine follow-up.

The patient returned on postoperative day 2, with continued constipation, urinary retention and severe rectal pain. He also continued to have left buttock pain radiating down the left thigh. He had no focal deficits on neurologic exam. Abdominal X-ray showed no evidence of ileus or obstruction. MRI of the pelvis with and without contrast was obtained and showed a large infiltrative mass concerning for metastasis in the sacrum as well as the left acetabulum (Fig. 2). Scattered foci of metastatic disease were prominent in the ilea, bilateral proximal femora, and lumbar vertebrae. There was no evidence of retroperitoneal lymphadenopathy or visceral organ metastasis. A percutaneous sacral biopsy was obtained that confirmed metastatic NSGCT (Fig. 3).

The patient was reclassified as stage IIIC with poor risk and immediately started on etoposide, cisplatin, and bleomycin (BEP), with dexamethasone. He had significant improvement of constipation, urinary retention and pain after initiation of chemotherapy. Due to the rapid tissue response to chemotherapy, radiation therapy to the spinal lesion was withheld and planned only in the event that chemoreduction did not provide an adequate symptomatic response. After two cycles of BEP the patient developed characteristic post-inflammatory pulmonary changes on chest CT likely secondary to bleomycin. He was switched to taxol, ifosfamide, and cisplatin (TIP), receiving three cycles. The patient responded well to chemotherapy initially, but became resistant by the



**Figure 2** CT (A) and MRI (B) of the pelvis without visible sacral lesion (arrow).



**Figure 3** Sacral biopsy. Histologic section demonstrating cells consistent with metastasis of non-seminomatous germ cell tumors. Scale bar = 20  $\mu$ m.

third cycle of TIP per measurement of tumor markers. His LDH and  $\beta$ -hCG normalized, but his AFP remained elevated at 16.6 ng/mL 8 months after initial diagnosis. Although there is no evidence of additional metastases, his bone disease remains present and he is currently undergoing high dose chemotherapy and stem cell rescue.

### 3. Discussion

The most common malignancy in men aging 15–40 years is germ cell tumor of the testes [1]. Metastatic bone disease is relatively uncommon, and is usually found in the setting of retroperitoneal lymph node and/or visceral metastases [2]. Isolated bone metastases, such as this case, is an exceptionally rare presentation.

A few large studies have been done to characterize patients with germ cell tumors and bone metastases. Jamal-Hanjani et al. [2] reviewed 2550 patients with germ cell tumors (GCTs), 19 of which had bone metastasis at either diagnosis (13/19) or relapse (6/19). The majority of the patients with bone metastases (11/19) were of non-seminomatous origin. Concurrent metastasis to other sites were found in 63% (12/19) of patients, while only 37% (7/19) of patients had isolated bone metastases. The most common site of bone metastasis in this group was the vertebral column, with symptomatic spinal cord compression in 4/19 patients, and caudaequina syndrome in 2/19 patients. Another study by Hitchens et al. [3] reviewed 297 patients with metastatic GCTs, of which 3% had clinically detectable bone involvement at presentation, and 9% at relapse. All of the patients with bone metastasis at presentation had concurrent metastatic disease in the lymph nodes, lungs, or mediastinum. Symptomatic spinal cord compression occurred in two patients. All affected patients exhibited localized bone pain. A third study by Oechsle et al. [4] was more selective in its patient population, but produced similar results after assessing 434 patients with poor prognosis GCTs who underwent high-dose chemotherapy. In this group, 9% (40/434) of patients presented with primary bone metastases. They noted that bone metastases were more common with primary mediastinal non-seminomatous tumors, yolk sac tumor histology, and concurrent liver

metastases. According to the international germ cell tumor consensus classification, the presence of non-pulmonary visceral metastases in NSGCT places patients into a poor prognostic category, with a 48% 5-year survival rate [5]. Well-established risk factors for metastatic disease in NSGCT include location and size of the tumor, multiplicity, tumor extension, pT category, histological type, the presence or absence of carcinoma *in situ*/testicular intra-epithelial neoplasia (CIS/TIN) and the presence or absence of lymphovascular invasion, with the latter being the most significant risk factor for advanced disease [1].

A small number of case reports have been published, demonstrating other patients with NSGCTs who presented with isolated bony metastases in the absence of other nodal or visceral involvement [6–9]. Metastasis of NSGCT usually occurs via lymphatic vessels, spreading first to retroperitoneal lymph nodes then sequentially to extranodal sites. Our patient lacked this typical metastatic pattern. This implies that the typical nodal pattern for spread of testicular NSGCT is not absolutely necessary for the disease to metastasize to bone.

Assessment of our patient's risk factors for metastatic disease also highlights some unique features of this case. Histological examination showed a large tumor size with yolk sac tumor histology, which increased his risk for metastatic disease according to the study by Oechsle et al. [4]. However, the pathology report of our patient showed no identifiable lymphovascular invasion. This demonstrates extratesticular metastases cannot be ruled out, even in the setting of seemingly confined disease.

At initial presentation the patient complained of pain in his left buttock radiating down his left thigh, and bowel and bladder dysfunction, which are consistent with caudaequina syndrome. However, he was never noted to have sensory or motor deficits throughout his course, nor did he have bony tenderness or pain on exam. At the time of diagnosis, his urinary retention and constipation were thought to be attributed to pain and narcotic use since the staging CT was normal. As mentioned above, very few cases of symptomatic spinal cord involvement at diagnosis of NSGCT have been reported. Although it is rare, symptoms of potential spinal cord compression should raise awareness and prompt evaluation for metastatic lesions given the affinity of NSGCT to the vertebrae in such cases, and its associated poor prognosis.

Additionally, bone metastasis was not detected during routine staging for our patient. The European Germ Cell Cancer Consensus group currently recommends staging of NSGCT based on serum tumor markers, orchiectomy with histopathology, and CT of the chest, abdomen, and pelvis. MRI is generally reserved for patient with contraindications to CT. Positron emission tomography (PET) scan has been shown to have low diagnostic yield over CT or MRI in the setting of NSGCT [5]. Patients are not traditionally evaluated for bone lesions during routine staging due to the rare presentation of these lesions without associated visceral metastatic disease visible on CT imaging. In this case the patient had multiple, significantly sized areas of bone metastasis. The CT scan of these areas showed no visible lesions. However, MRI visualized the sites of metastases (Fig. 2). This demonstrates that CT may not be as sensitive as MRI in detecting bone involvement in metastatic NSGCT.

In the study done by Hitchins et al. [3], the CT scans of patients with bone involvement were positive in seven out of eight patients. Although only three patients underwent MRI, bone lesions were visible in all three cases.

#### 4. Conclusion

This case had a unique presentation of a testicular NSGCT with skeletal metastases causing symptomatic caudaequina syndrome, initially undetected by routine staging. Although this is a rare finding, particularly in the absence of concurrent nodal or visceral metastases, it is important to evaluate patient with NSGCT presenting with neurologic symptoms for bony and spinal cord involvement. Additionally, it is important to acknowledge that routine staging by CT scan may not always detect skeletal metastases of this disease, and MRI should be considered as confirmative imaging when suspicion warrants further investigation for lesions of the bone.

#### Conflicts of interest

The authors declare no conflict of interest.

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