

Case Report

A Dual Primary Malignancy – Ewing Sarcoma and Prostate Adenocarcinoma in A Single Patient

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Abstract. Introduction: A dual malignancy with both Ewing Sarcoma and Prostate Adenocarcinoma has not been reported in the English literature. We report a case of simultaneous diagnosis of Ewing sarcoma and prostate adenocarcinoma with profound clinical manifestation. Case presentation: A 53-year-old male with advanced metastatic prostate cancer (Gleason-9) admitted with classical presentation of cauda equina syndrome including incontinence, back pain, and paresis following bilateral nephrostomy insertion for the treatment of bilateral renal hydronephrosis. The patient was diagnosed with an epidural abscess at the level of L5-S1 and an emergency surgical spine decompression was performed. No abscess was found, and pathology results showed a concomitant primary Ewing sarcoma in the spine. Conclusions: Very rare occurrences of a dual primary malignancy, in this case, Ewing sarcoma and prostate adenocarcinoma, should be kept in mind in patients suffering from complex clinical course of malignancies.

Keywords: Ewing sarcoma; Prostate adenocarcinoma; Cauda equina syndrome; Dual primary malignancy

1. Introduction

Ewing sarcoma (ES) belongs to a spectrum of neoplastic diseases known as the EFT family of tumors (EFT); They are considered to be derived from a common cell of origin. They include extraosseous ES (EES), peripheral primitive neuroectodermal tumor (PNET), malignant small-cell tumors of the thoracopulmonary region (Askin tumor), and atypical ES [1]. ES is typically occurring in patients from 5-25 years of age and is the second most common malignant bone tumor in children [2]. 85 to 90 percent of Ewing sarcomas (EWS) and peripheral primitive neuroectodermal tumors (PNETs) display a reciprocal exchange $t(11;22)(q24;q12)$ [3]. The EFT most often arises in the long bones, the femur, and the bones of the pelvis. Spine, hands, and feet are far less common sites [2]. About eight percent are found in the spine and a minority of ES arise in soft tissue [2]. Clinical presentation is usually a localized pain or swelling of a few weeks or months duration [4], which may intensify quickly. When ES affects the spine or sacrum, nerve compression can cause back pain, radiculopathy, paresis, or loss of sphincter control compatible with spinal cord compression. 10 to 20 percent of patients present with Constitutional symptoms such as fever, fatigue, or weight loss [4]. There is usually about a nine-month delay between the onset of symptoms and diagnosis [4].

The rate of metastatic disease at presentation is up to 44 percent, with lung and bone metastases being equally the two predominate sites, the spine being the most frequently involved osseous site [2]. Treatment leans towards surgical resection without radiation therapy, when possible, because of morbidity associated with radiation and the risk of secondary malignancies. chemotherapy with limb salvage resection with or without adjuvant radiation is the standard of care in most patients, where the primary tumor can be completely removed chemotherapy with radiation therapy are indicated for unresectable tumors (e.g., large spinal tumors) [5,6].

Prognosis depends on several factors such as tumor site, size, and response to therapy [5,6], the key to which being the presence or absence of metastases. Approximate five-year survival rates for patients with localized disease are 70 percent, while the average is 33 percent for those who have overt metastases at diagnosis. Thirty percent of patients with lung metastasis alone will survive five years, as compared with only 10 percent of those with bone metastasis [5,6].

Prostate cancer is the second most frequent malignancy (after lung cancer) in men worldwide, with an estimated 1,600,000 cases and 366,000 deaths annually [7]. Eleven percent of American men will be diagnosed with prostate cancer over their lifetime [7]. The clinical behavior of prostate cancer varies widely and is often asymptomatic. Seventy-eight percent of patients have localized cancer when diagnosed. Regional lymph node involvement is present in 12 percent, and 6 percent have distant metastases [8]. The disease is diagnosed with PSA testing, Digital rectal examination, imaging, urologic evaluation, and biopsy [8]. For treatment, combinations of both surgical and non-surgical methods are used. Methods such as external beam and prostatectomy are usually offered to men with localized prostate disease. Metastatic disease is typically treated with hormonal and chemotherapy. [8]

We report a case of simultaneous diagnosis of Ewing sarcoma and prostate adenocarcinoma with profound clinical manifestation.

2. Case Presentation

A 53-year-old male presented at our emergency department with urinary retention in September 2019. His past medical history consisted of dyslipidemia, treatment with aspirin and Atorvastatin as primary prevention, and smoking status. A urinary catheter was inserted, and a urinary resting volume of 1000 ml was registered. A rectal examination demonstrated a firm prostate gland. Urine cytology at that time was normal. A prostate biopsy was performed in December 2019 demonstrating prostate adenocarcinoma with a Gleason score of 9 with perineural invasion.

A PET CT performed in December 2019 showed evidence of substantial involvement of the prostate gland with lymphatic spreading both above and below the diaphragm, iliac and pararectal vessels. Metastasis was also noted in the lungs (a 1.4 cm mass at the LUL) and skeletal system, urinary bladder, and rectum. Metastasis was noted at the right scapula and proximal humerus, the sacrum and ileum bilateral, the femur, the L2 vertebrae, and the right 2nd and 6th rib. Degarelix treatment was initiated, and chemotherapy was scheduled. His blood profile showed a mild increase in hepatocellular enzyme levels and a normal coagulation panel. The patient went through a successful elective channeling Trans Urethral Resection of the Prostate on January 30th, 2020. The patient went through ten treatments of irradiation throughout August and September 2020 at a different facility. On October 28, 2020, the patient presented with urinary retention, and was treated with a urinary catheter and started treatment with Abiraterone and prednisone on October 26, 2020. In October 2020, a CT scan demonstrated an enlarged 2.4 cm LUL lung metastasis as compared with the previous CT. A hypodense cystic mass consistent with an abscess was identified at the prostate gland measuring 4.5 X 6.3 X 4.5 cm in diameter. A PSMA PET CT showed markedly decreased signals in the lungs. The patient was admitted for abscess incision and drainage on November 5th, 2020, via TURP. The abscess seemed to be self-dissolving. Transrectal sonar demonstrated minimal pus collection. The urinary culture showed growth of *Klebsiella pneumoniae* susceptible to Invanz which was then initiated for 3 weeks of 1 Gr per day parenteral treatment. The urinary catheter was then removed, and the patient was able to void spontaneously. The patient continued to take Degarelix and prednisone, along with the aspirin and Atorvastatin which he took previously to his illness. Laxadin was also added to relieve constipation. On December 16, 2020, a lung biopsy was performed which demonstrated adenocarcinoma of the prostate. The patient started treatment with Cabazitaxel. Later in December 2020, the patient was

reevaluated due to recurrent urinary retention and a permanent urinary catheter was introduced.

In December 2020, the patient was readmitted to our facility due to recurrent pain in the pelvis and perineal region. Digital rectal examination demonstrated a markedly enlarged tender prostate gland with the impression of fluid fluctuation. Laboratory studies have shown a white blood cell count of twenty thousand with a left deviation, normal renal function, an electrolyte panel, a CRP of 7 mg/L, and leukocyturia. Renal sonar performed 2-week prior demonstrated mild hydronephrosis. The patient had a CT guided drainage of the collection in the prostate, but no pus was aspirated, due to the abscess being mostly solid and embedded in dense necrotic tissue. Urine culture showed growth of *Pseudomonas aeruginosa* susceptible to Ciprodex which was initiated for ten days instead of Invanz. During hospitalization, the patient was also diagnosed with DVT involving the lower limb up to the confluence of the iliac vessels and the Inferior vena cava. Treatment with Enoxaparin was initiated and was later switched to Rivaroxaban. Nasal spray PecFent was administered for Pain management. A CT scan of the thorax abdomen and pelvis including a CTU was performed in December 2020 which demonstrated a more profound spreading of the tumor in the pelvis, with substantial pelvic lymphadenopathy and little Para sacral fluid collection.

In November 2021, the patient was readmitted to our facility complaining of nausea and vomiting. Laboratory studies showed a white blood cell count of twenty thousand with neutrophilia. His hemoglobin count was 9.9 g/dL. Electrolyte, renal function, and coagulation panel were normal. An abdominal CT scan was performed with oral and parenteral administration of contrast material which demonstrated no bowel obstruction. A moderate left and mild right hydronephrosis was detected and was assumed to be caused by his substantial paraneoplastic pelvic involvement. The patient went through a bilateral nephrostomy tube placement.

Immediately after the nephrostomy, the patient started complaining of severe back pain and bowel incontinence. Physical examination showed a positive left straight leg raise test at about 60 degrees, decreased motor strength of about 4/5 in the left extensor hallucis longus, saddle anesthesia, numbness along his left L4-L5 sensory distribution, and an absent rectal tone on rectal examination. An MRI was immediately performed which demonstrated a space-occupying lesion, originally thought to be an abscess on the level of L5-S1 (Figure 1).



Figure 1. Sagittal STIR (A), axial T1-weighted (B), axial T1-weighted post-contrast and sagittal fat-saturated post contrast images, demonstrate decreased T1 signal, increased T2 signal, and enhancement, the classic appearance of epidural enhancing soft tissue, causing mass effect on the thecal sac.

After obtaining the imaging results, Dexamethasone and Antiemetic treatment with Levomepromazine were given. The patient went through L5-S1 open decompression, no pus was noted during the surgery. The space-occupying lesion was noted as an extradural solid tissue that was compressing the Dural sac at the L5-S1 level, biopsy was obtained from the space-occupying lesion. On POD1 the patient reported a relative improvement in his back pain and rectal sphincter control, but still presented with saddle paresthesia. He began ambulating with a supportive lumbar brace and physiotherapy guidance. After a few weeks, the biopsy result confirmed the diagnosis of Ewing sarcoma.

3. Discussion

The first to report dual malignancy was Billroth in 1889, the first comprehensive study was done in 1921 in which from three thousand patients with malignancy 4.7% of them had multiple malignancies [9]. In recent epidemiological studies, the frequency of multiple primary malignancies is reported to be in the range of 2–17% [10-15]. Despite being rare, the incidence of double primary tumors has been rising, primarily related to a longer life span and advanced imaging techniques [16]. And yet, dual malignancy with both an Ewing sarcoma and prostate adenocarcinoma has not been reported in the English literature. Double primary tumors are either synchronous cancers (malignant tumors occurring within the first six months of the first primary cancer) or metachronous cancers

(malignant tumors occurring beyond the first six months) [17]. Thus, we should keep in mind that the presence of dual malignancy is rare but still possible.

The pathophysiology behind the occurrence of two primary malignancies in our patient is unknown. The patient has a history of smoking but there has not been any lifestyle (such as smoking) or inherited risk factors that have been directly linked to Ewing's sarcoma. Other possible causal factors include persistent carcinogen exposure from the environment or effects of ionizing radiation from irradiation therapy. Furthermore, we cannot exclude a genetic predisposition to neoplasia that is not yet known to science.

In our patient's last admission before the diagnosis of ES, he presented with a classical presentation of Cauda Equina Syndrome (CES). CES is a neurosurgical emergency warranting urgent surgical decompression [18]. Treatment delay may precipitate permanent adverse neurological sequelae [19]. A meta-analysis supports the superiority of early surgical decompression before 24 hours ($P = 0.03$) and before 48 hours ($P = 0.004$) after the onset of symptoms [20]. Thus, there is no difference in the emergent treatment of CES in the case of a primary ES tumor or metastasis from prostate adenocarcinoma. We are pleased to report that due to the emergent L5-S1 open decompression the patient reported an improvement in his back pain and rectal sphincter control, and after few days, he reported an improvement in his saddle paresthesia.

ES is typically occurring in patients from 5-25 years of age and is the second most common malignant bone tumor in children [17]. Only about 8 percent are found in the spine [17]. Our patient was presented at an age that is uncharacteristic for ES and in a relatively less common location in the body for this type of malignancy. These facts made it challenging to diagnose this disease. The combination of the uncharacteristic presentation of the disease with another known malignancy with metastases to the bones added another level of difficulty to the diagnosis of ES in our patient. This case highlights the fact that the presence of a lesion anatomically away from the primary malignancy should be labeled as a metastasis only after detailed evaluation; otherwise, there is a possibility of missing a synchronous primary malignancy.

4. Conclusions

In conclusion, dual malignancy of Ewing Sarcoma and Prostate Adenocarcinoma in a single patient is rare but possible, furthermore, this case is the only documented case in the English literature. Moreover, even in a patient with a known metastatic Prostate Adenocarcinoma including bone metastases, in case of a new space-occupying lesion in the spine, we should always bear in mind a new primary malignancy. We present this case due to the rarity in the presentation.

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