CASE REPORT

Metastatic Leydig cell tumor of the testicle in a young African American male

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Malignant Leydig cell tumor (LCT) of the testis are extremely rare and account for less than 0.2% of all testicular cancers. Testicular tumors of all histological types rarely occur in African American men. The authors describe a rare case of an advanced stage malignant LCT arising from the testicle of an African American man at the young age of 35, who presented with hemoptysis and a productive cough. Clinical features and treatment of Leydig cell tumor of the testis are discussed.

Key Words: Leydig cell tumor, testis, malignant

Introduction

Most tumors of the testis involve germ cells with only 3% to 4% affecting stromal cells. Leydig cell tumors (LCTs) are generally benign, however 7% to 10% of cases have a malignant course, with the metastatic variety occurring in older adults.[1,7] Testicular tumors of all histological types are less common in African American than in Caucasian men. We report a rare case of a malignant LCT arising from the testicle of an African American man at the young age of 35 presenting with hemoptysis and a productive cough, resulting from extensive pulmonary metastases. Tumor behavior and various treatment modalities are discussed.

Case report

A 35-year-old African American man with a history of schizophrenia was admitted for a work-up of hemoptysis and a productive cough of one week's duration. The patient denied fever, chills, nausea, vomiting, or weight. The patient had a right inguinal hernia repair performed 10 years ago. On physical examination, a large, painless, right scrotal mass was discovered, which was stated to have been progressively enlarging over the past 3 years. The patient denied testicular or groin pain, and had no ejaculatory, erectile, or voiding difficulties. Gynecomastia was not present and breath sounds were clear to auscultation. There were no palpable abdominal masses or lymphadenopathy. A markedly enlarged right hemiscrotum containing a hard mass with extension up the spermatic cord was present with no normal right testicle palpated. The left testicle was descended and normal upon palpation. Laboratory analysis revealed a hematocrit of 33 mL/dL (normal 40 to 54), and normal serum chemistries, liver function tests, α-fetoprotein (AFP), β-human chorionic gonadotropin (β-HCG), lactic acid dehydrogenase, testosterone, androstenedione, estradiol, luteinizing hormone, and follicle-stimulating hormone. In addition, sputum for acid-fast bacilli and antibodies for blastomycosis, histoplasmosis and human immunodeficiency virus were negative.

Scrotal sonogram revealed a large heterogeneous partially necrotic mass within the right hemiscrotum

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measuring 14.6 cm x 10.9 cm x 10.9 cm Figure 1. Bilateral scattered lung lesions were present on initial chest radiograph and computerized tomography (CT) of the chest revealed enumerable nodules scattered throughout both lungs and mediastinal lymphadenopathy at the right paratracheal, retrocaval, anterior carinal and subcarinal regions, as well as both hilar Figure 2. CT of the abdomen and pelvis revealed a heterogeneous lesion in the region of the right groin, with an ovoid soft-tissue density posterior to this lesion. Liver, spleen, pancreas, gallbladder, and adrenal glands appeared normal and evaluation of the kidneys demonstrated no evidence of hydronephrosis. No enlarged nodes were present in the abdomen or pelvis, and there was no evidence of free pelvic fluid Figure 3.

A right inguinal exploration and subsequent radical orchiectomy was performed. Grossly, the right testicle measured 14 cm x 12 cm x 10 cm extensively replaced by tumor. Tumor was present in the veins and lymphatics with invasion through the tunica albuginea. Surgical margins were negative. Tumor stage was classified as pT3NxM1. Microscopically, this was a cellular tumor with central hyalinization. Cells were arranged in a solid sheet-like pattern, and fields showed a nested arrangement, as well as a trabecular arrangement. Cells were notable for abundant eosinophilic cytoplasm, and large round and irregular nuclei Figure 4. In some fields, prominent nucleoli were noted. Atypical mitoses were seen, and mitotic activity reached four per 10 high-power fields. While lipofuscin and Reinke crystals were not seen, the cytoplasm was vacuolated. Oil Red O stain was positive for lipid in these small vacuoles. Ossification and calcification were

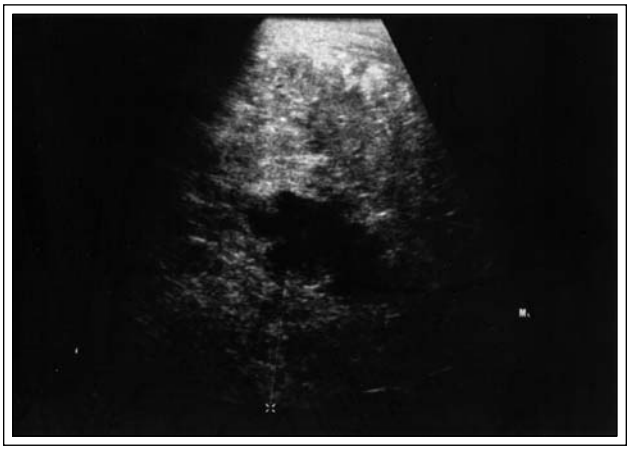

Figure 1. Sonogram demonstrates a large heterogenous partially necrotic mass within the right hemiscrotum.

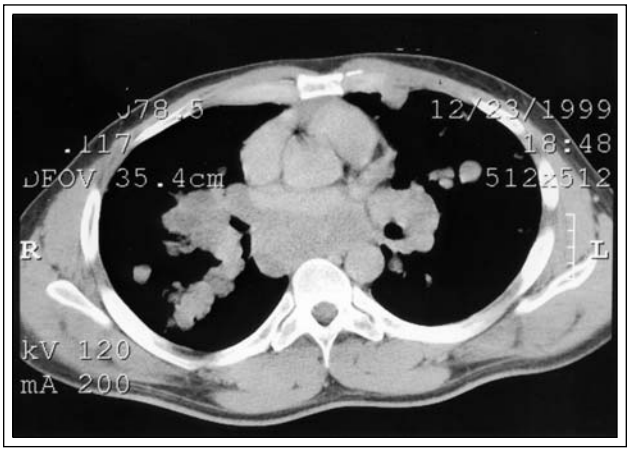

Figure 2. Chest CT demonstrates enumerable nodules scattered throughout both lungs and mediastinal lymphadenopathy.

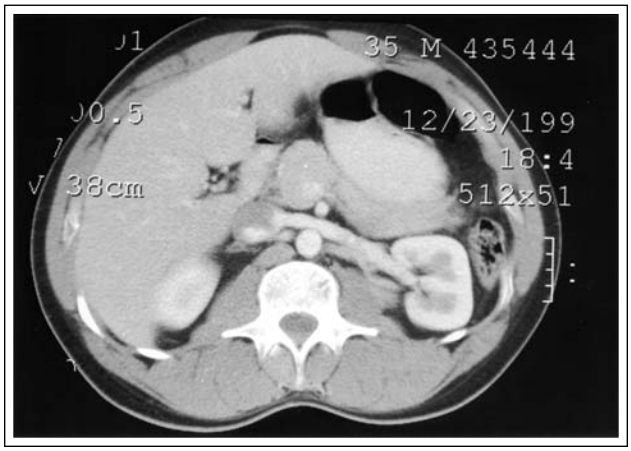

Figure 3. Abdominal and pelvic CT reveals no enlarged nodes and no evidence of free pelvic fluid.

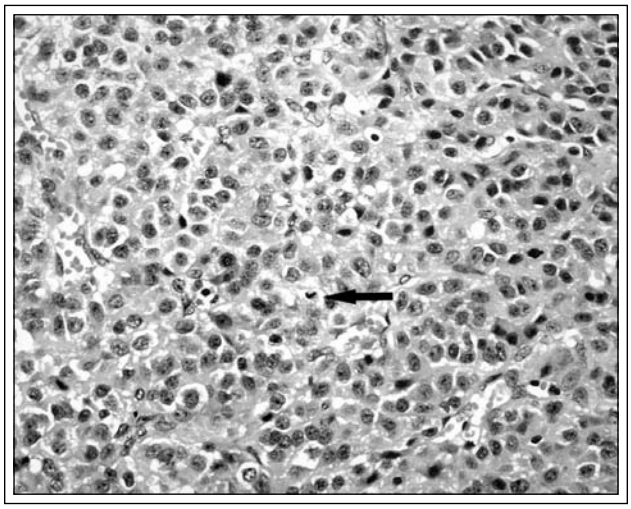

Figure 4. Tumor is composed of large cells with round nuclei, visible nucleoli, and abundant eosinophilic cytoplasm. Cytoplasmic vacuoles and multiple mitotic figures are seen (one at arrow). H & E, reduced from X100.

absent. Immunohistochemistry revealed a vimentin positive tumor, generally negative for cytokeratin and epithelial membrane antigen (EMA) (rare cells showed cytokeratin reactivity). In addition, placental alkaline phosphatase, β-HCG and AFP immunohistochemistry were negative. Given the morphology of the cells, relevant negative immunohistochemistry and Oil Red O positivity, it was concluded that the tumor represented a LCT. The presence of mitotic activity, size, and vascular invasion were evidence for malignancy, as was the presence of metastatic disease.

Possible chemotherapeutic regimens were discussed, however, the patient's condition continued to deteriorate. It was felt that the patient would not be able to tolerate chemotherapy and he was discharged to hospice care.

Discussion

Testicular cancer is rare in black men.[2,3] In a large series of testicular neoplasms in African American men, no significant differences in disease features were noted between African American and Caucasian men.[2] African American men were found to have a slightly higher incidence of interstitial tumors and a greater delay in diagnosis was observed in African American patients. Moul and colleagues reported the diagnosis of LCT in three African American men, however, no details were given of the stage or course of disease.[2]

LCTs are usually benign and rare accounting for 1% to 3% of testicular tumors and found to be bilateral in 3% of patients.[1] Painless testicular enlargement or a palpable mass is the most common presentation. Gynecomastia resulting from the secretion of androgens, estrogens or both occurs in approximately 15% of patients and may be the presenting symptom.[4] Impotence, loss of libido, and precocious virilization may occur in young men. They are usually small, solid and hypoechoic on ultrasound. Foci of hemorrhage and necrosis are present in 25% of tumors and may enlarge the tumor by forming cystic spaces.

LCTs are malignant in 7% to 10% of cases and occur exclusively in adults.[1] Malignant LCTs occur in older men at a median age of 60 years, however, our patient was only 35 years old.[5,7] Approximately 20% of patients have metastatic disease at the time of initial LCT diagnosis, with another 40% having metastatic disease within 2 years.[5] Metastatic disease frequently involves the lymph nodes, specifically the retroperitoneal and inguinal nodes, liver, lungs, and bones.[5] Approximately 50% of patients with malignant LCTs have increased levels of androgens and estrogens.

Several prognostic features for malignant behavior have been identified, including: diameter of 5 cm or greater; infiltrative margin; lymphatic or vascular invasion; necrosis; cells undergoing mitosis that number over 3 of 10 under high-power field; and grade 2 or 3 nuclear atypia.[6,7] Reinke's crystals (an elongated rectangular cytoplasmic eosinophilic inclusion) are present in 40% of LCTs and are pathognomonic.[6,7] Mitoses, hemorrhage, and necrosis are usually absent. However, differentiation between benign and malignant tumors on histologic criteria alone is unreliable.

The natural course of metastatic LCTs is one of progression at an unpredictable pace and durable remission rates for treatment of metastatic LCTs are dismal. These tumors are generally refractory to radiotherapy and conventional chemotherapy.[5] The initial treatment for the primary LCT is surgical removal of the tumor. A review of the literature did not provide a proven treatment choice for our patient. Surgery has been attempted for some patients with metastatic LCT. Although there are a few cases of rendering a disease-free status, surgery has generally been unsuccessful at treating metastatic LCT. Our patient's metastatic disease was unresectable. Several chemotherapeutic agents, including platinum-based regimens, have been used alone, or in combination, in the treatment of metastatic LCT with little success. Mitotane (o,p'DDD) has also been used with limited success, but was followed by reports indicating lack of response.[8] It was thought to be more promising because LCTs have hormonal activity similar to that of adrenocortical carcinomas. Doxorubicin has also been tried in a few patients without benefit.[5] In conclusion, LCT is a rare tumor and if it becomes metastatic, it is fatal because it does not respond to surgery, radiation, and chemotherapy. □

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