CASE REPORT

Advanced testicular cancer in a society of racial and socio-economic health disparity

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SUMMARY

This is the case of an African-American man who presented with a 6 month history of impressive unilateral testicular swelling and abdominal pain. After a thorough workup he was found to have metastatic testicular seminoma causing multiple complex sequelae. This case highlights the essential diagnostic and therapeutic features of a common malignancy seen primarily in young men. His advanced disease presentation, complex management of multiple comorbidities combined with his African-American race and lower socio-economic status (SES) highlight an unusual paradigm shift in testicular cancer epidemiology from the more typical high SES Caucasian to the lower SES, less educated male patient. Beyond the unexpected clinical presentation, this case then presents multiple avenues of discussion regarding the unfortunate effects of racial disparities on disease presentation and progression that are plaguing our healthcare system today.

BACKGROUND

Testicular cancer is the most common malignancy in 15–35-year-old men. It accounts for about 1% of all cancers and it usually has an excellent prognosis with treatment. The prevalence of testicular cancer in white men is 4.5 times that in black men. The incidence of testicular cancer is 6.3/100 000/year and rising, with a doubling every 20 years.¹ This is the case of a man with an advanced presentation of a common malignancy requiring complex management and complicated by racial and socio-economic issues. These compounding issues are prevalent in all branches of medicine and are beginning to garner a significant amount of attention as our society decides the direction it wishes to proceed with medical care.

CASE PRESENTATION

A 32-year-old African-American man, with no significant medical history, presented to the hospital with a unilateral 15 cm painless testicular mass and significant abdominal pain.

The patient was in his usual state of health until 6–8 months before admission when he began to notice a right-sided testicular swelling. He experienced no associated pain at that time and the swelling progressed over the next few months. During this time period he also noted a 40-pound unintentional weight loss from an original weight of 290 pounds to 250 pounds. At 6–8 weeks before admission the patient began to feel periumbilical cramping and right-sided flank pain which would sometimes wake him from sleep. In the month

before admission the patient felt constipated and would not have bowel movements for multiple days at a time. He also had the urge to urinate and was not always able to completely empty his bladder.

The patient had no surgical history and no chronic medical conditions that he was aware of. He was not on any prescription medications and took 1–2 acetaminophens to manage the abdominal pain periodically. He smoked one pack of cigarettes a day for 18 years and smoked marijuana for 20 years. He drinks 1–2 alcoholic beverages on weekends. His father had multiple myocardial infarctions with the first one occurring at the age of 55. The patient had not been sexually active for 3 months and had gonorrhoea a few years ago that he was treated for. At the time of presentation he had no insurance and had not seen a doctor in many years.

INVESTIGATIONS

The patient's vitals on presentation were 124/78 mm Hg, pulse 84 bpm, temperature 36.6°C and a respiratory rate of 18 with 99% saturation on room air. He was alert and oriented to time, place and person and in no acute distress. The patient had hypoactive bowel sounds in the lower right quadrant with normal bowel sounds in the other three quadrants. He had no signs of hepatosplenomegaly. There was dullness to percussion in the periumbilical region. His abdomen was soft, non-distended and tender to light and deep palpation in the periumbilical and lower right quadrant areas. He also had a palpable 8 cm mass in the same area. There was no guarding or rebound tenderness. On genital examination the patient's pubic hair distribution was classified as tanner stage 5; phallos length was 12 cm and appropriate for his age. He had a 15 cm right testicular mass with some fluid and heterogeneity in consistency. He had a negative transillumination test. The overlying scrotal skin was vascular but had no indurations or erythematous areas and looked markedly distended.

On admission day 1 we ordered a complete blood count (CBC), an electrolyte panel and a urinalysis panel. β -hCG (quantitative), α -fetoprotein (AFP) and lactate dehydrogenase (LDH) levels were also measured.

The patient was found to have a normocytic anaemia with RBC of 4.07, haemoglobin of 10.9, haematocrit of 33.4 and mean corpuscular volume of 82.1. In addition his levels of β -hCG and LDH were elevated at 75 mIU/mL and >4000 units/L, respectively. AFP levels were normal at 3.0 ng/mL.

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An ultrasound scan of the testicles showed a markedly enlarged and heterogeneous right testicle and mildly enlarged right epididymis with moderate hydrocoele. Given the history and findings of scrotal mass, there was a recommendation for further imaging to evaluate for malignancy.

We obtained a chest X-ray which showed an abnormal density to the left of the descending aorta with a differential of oesophageal diverticulum, mediastinal mass or lymphadenopathy. A CT of the thorax, abdomen and pelvis was performed and revealed a large heterogeneous right testicular mass, with extensive pelvic, retroperitoneal and mediastinal lymphadenopathy, suggestive of testicular neoplasm with metastatic disease. Choriocarcinoma was of primary consideration. The extensive retroperitoneal adenopathy was contributing to severe right and moderate left hydronephrosis due to compression of the right renal artery and vein causing hypoperfusion of the right kidney. A 9 mm pleural-based nodule in the right lower lobe and a 10 mm pleural-based nodule in the left lower lobe were also discovered. An incidental pulmonary embolism was shown with deep vein thrombosis involving the femoral and external iliac veins bilaterally, extending to the inferior vena cava (IVC). The metastatic spread also involved the left iliac bone, demonstrated by a 9 mm sclerotic lesion.

Pathological examination of the orchiectomy specimen (figure 1) revealed a 16 cm×10 cm×8.5 cm pure seminoma with focal necrosis. It was noted that the tumour was infiltrating the epididymis and spermatic cord. Microscopic examination revealed the classic appearance of fibrovascular septa rich in lymphocytes (figure 2). Cytological examination of the specimen revealed tumour cells that were cytokeratin, α -fetoprotein and CD-30 negative with strongly positive results for placental alkaline phosphatase, periodic-acid Schiff and CD-117 (figure 3) all of which supported the pathological diagnosis of seminoma.

Figure 1 Gross specimen.

Figure 2 Fibrovascular septa rich in lymphocytes.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis was testicular seminoma versus choriocarcinoma.

TREATMENT

The CT scan findings indicate that the cancer had spread extensively throughout the body at the time of presentation. Urology department performed a diagnostic and therapeutic orchiectomy which led to the definitive pathological diagnosis. Oncology department requested repeat measurements of β -hCG, α -fetoprotein and LDH levels to monitor response to the orchiectomy and give baseline levels for future chemotherapy treatment.

Once the patient had a definitive diagnosis, he was referred to oncology department to begin four cycles of chemotherapy with cisplatin, bleomycin and etoposide (BEP regimen) immediately. The patient's chemotherapy course was complicated by multiple episodes of febrile neutropenia. During his neutropenic episodes the patient developed multiple infections including a right facial abscess from pricking a pimple, and a surgical site infection in his right inguinal area. He also developed acute bronchitis that was managed by intravenous antibiotics. On initial discharge the patient was bridged to warfarin; however, it was later determined that the patient would gain more benefit from placement of an IVC filter. The patient has undergone two rounds of chemotherapy and has had moderate decrease in the size of his retroperitoneal and pelvic lymphadenopathy.

Figure 3 CD-117 cells.

OUTCOME AND FOLLOW-UP

In a follow-up conversation with the patient, the author elicited that fear, embarrassment, financial burden and distrust of physicians had motivated the patient's decision to delay treatment. He acknowledged that his lack of insurance kept him from seeking help in a primary care setting, a key factor in the time to his diagnosis. He never felt discriminated against, although his family was vocal when cost prohibited the hospital from discharging him on optimal anticoagulation therapy.² He has struggled to cope with his mounting financial burden but was recently granted insurance through the state and remains committed to fighting his cancer. At the time of publication he has received two doses of chemotherapy.

DISCUSSION

Testicular cancer is commonly designated into seminomatous and non-seminomatous tumours, with the former accounting for 40% and the latter accounting for 60%. This distinction guides the clinician in both prognosis and treatment. The differential diagnosis in this case was either seminoma or choriocarcinoma, with the initial highest likelihood being choriocarcinoma due to the widespread metastases at the time of presentation. Choriocarcinoma can metastasize to any part of the human body including the lungs and brain and has even been found in unusual places such as the jejunum, stomach and nasal skin.^{3–5}

In 10–25% of patients, seminomas are associated with an elevated β -HCG level, which is produced by syncytiotrophoblasts, as in our patient, who had a β -HCG level of 75 mIU/mL. However, β -HCG levels also may be elevated in patients with non-seminomatous germ cell tumours (NSGCT), such as choriocarcinomas, which are characterised by the presence of both syncytiotrophoblasts and cytotrophoblasts.⁶ Recent studies by Stenman and coworkers⁷ show that the hyperglycosylated form of β -hCG is the predominant form of hCG found preoperatively and after relapse and may be a predictor of progression free survival. The α -fetoprotein level is almost never elevated in pure seminomas, but it is elevated in 50–60% of NSGCT.⁸ An elevation of α -fetoprotein with a pathological diagnosis of pure seminoma may indicate a high likelihood of additional NSGCT in the retroperitoneum.⁹ Even an elevation of hCG with a diagnosis of pure seminoma should lead the pathologist to serially section the tumour to rule out other elements of non-seminomatous testicular tumour such as teratoma or embryonal carcinoma.^{10–11} Clinicians can use these measurements to help distinguish between pure seminomas and NSGCT.

Staging in seminomatous cancers uses comprehensive tumor/node/metastasis staging system developed by the American Joint Committee on Cancer and the International Union Against Cancer.¹² Under this staging system our patient would be classified as follows:

- ▶ pT3—Tumour invades the spermatic cord with or without vascular/lymphatic invasion.
- ▶ N3—Metastasis with a lymph node mass more than 5 cm in greatest dimension.
- ▶ M1a—Non-regional nodal or pulmonary metastasis.
- ▶ S3—LDH $>10 \times \text{NI}$ or hCG (mIU/mL) $>50\,000$ or AFP (ng/mL) $>10\,000$.

This classifies the patient into the intermediate prognostic category giving him a 5-year survival rate of around 72%.¹² Testicular seminoma is highly chemo-sensitive and radio-sensitive with excellent cure rates, even in patients with extensive metastatic disease.^{13–14}

Of note, most patients, about 85%, with seminoma present with stage I disease, which is defined as local disease with no lymph node or distant metastases.¹⁵ The patient was a unique case due to his extremely large tumour, advanced disease and multiple comorbidities on presentation. Probing further into why the patient presented so late in his disease course is a tricky subject. The patient is an African-American from a lower socioeconomic status (SES) with a high school education and the author wondered if this was a contributory factor in his late presentation. Owing to lack of insurance his follow-up with any doctor had been non-existent for many years.

Current literature has a great number of case reports regarding testicular seminoma, but few delve into the issue of race and SES. Bridges *et al* conducted a 14-year review examining the disease-specific mortality associated with ethnicity in testicular carcinoma. Their data showed that while there was no difference in stage at presentation, African-Americans had a 17% decrease in 5-year disease specific survival compared with their Caucasian counterparts.¹⁶

In comparison with Caucasians, African-Americans 5 year survival rates are substantially lower for the six most common cancer sites: prostate, breast, lung, colon, bladder and uterine corpus.¹⁷ Numerous older studies have reported a higher risk of testicular cancer in men of high SES compared with men of lower SES;^{18–20} however, more recent reports suggest this trend is reversing.^{21–22} In a 2011 meta-analysis looking at racial disparities and SES in testicular carcinoma it was shown that overall 5-year mortality rate for African-Americans was 10.7% versus 4.9% for Caucasians and 7.6% for all other race. The same study showed a 1.3-fold greater risk of overall mortality in low SES counties compared with men residing in high SES counties, and low SES men were 1.4-fold more likely to die of cancer-specific mortality.²³ Hussain *et al*²⁴ reported on 1094 cases of testicular cancer diagnosed between 1990 and 2006 and found men with 12–13 years of education had significantly lower cancer-specific mortality than those with <9 years. Not only are African-Americans more likely to die from their cancer but a review of Surveillance Epidemiology and End Results (SEER) data from 1973 to 1999 found that they are also more likely to be diagnosed with late stage disease.²⁵ Nur *et al*^{26–27} showed that in one large randomised clinical trial comparing treatment efficacy there was no difference in survival between higher and lower SES, a trend that makes logical sense and has been shown in other trials. These studies indicate that the treatments offered to patients are equally effective among socioeconomic classes but mortality rates still differ due to a number of complex factors including race, education level and SES.

The patient's case presents an opportunity to review a common malignancy in a patient who has very few epidemiological risk factors for developing a seminoma. His advanced disease presentation and complex management with multiple comorbidities and sequelae could only be handled by an interdisciplinary team of physicians. Aggressive treatment in these young patients and vigilant follow-up is necessary to prevent recurrence or development of a new cancer.

Most cases of seminomatous testicular cancer present at an early stage and are readily treatable. The patient's African-American race and SES put him at the epicentre of a typical urban population that is in desperate need of more accessible healthcare. His case also highlights an unusual paradigm shift in testicular cancer epidemiology from the high SES Caucasian to the lower SES, less educated man. The racial and socio-economic disparities in healthcare and the overall stigma of a cancer 'below the belt' have led to different mortality

statistics for different groups of men. In comparison with Caucasians, African-Americans' 5-year survival rates are substantially lower for nearly all the major cancers, including testicular cancer.¹⁷

His advanced stage was not as surprising given his lack of insurance and personal fear of healthcare providers. His late presentation also underscores the importance of regular access to primary care services, a step that may have spared him considerable morbidity and financial burden. However, while it is impossible to speculate whether regular follow-ups with a primary care doctor or a different racial/socioeconomic upbringing may have changed our patient's prognosis, it certainly highlights the disparity that faces patients on a daily basis. The patient continues to fight his cancer with considerable success. His case allowed the author to not only review the complex medical management associated with testicular cancer, but also reflect on the social and economic issues that are intertwined with everyday practice.

Learning points

- ▶ Testicular seminoma is a common malignancy of youth and is readily treatable by modern chemotherapy, even with advanced metastatic disease.
- ▶ Lack of primary care access, distrust of physicians and lower socio-economic upbringing are common themes in the urban community setting and contributed to this patient's advanced presentation.
- ▶ Lower socioeconomic status is associated with an increase in mortality and a later stage of presentation in testicular carcinoma.
- ▶ Racial disparities account for an increase in overall mortality and decrease in disease-specific survival for African-Americans compared with Caucasians in testicular carcinoma.

Competing interests None.

Patient consent Obtained.

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