Metastatic Penile Squamous Cell Carcinoma to the Retroperitoneum in a Man With Human Papillomavirus Type 45

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Squamous cell carcinoma of the penis is a rare cancer associated with smoking, genital warts, lack of neonatal circumcision, and human papillomavirus types 16 and 18. Metastasis of this condition is even rarer, occurring primarily in the lungs or liver. The current report describes a case of penile squamous cell carcinoma in an uncircumcised 63-year-old man who smoked cigarettes and who had genital warts and human papillomavirus type 45. Metastasis occurred in the abdominal cavity.

Penile squamous cell carcinoma—or penile cancer—is a rare condition. Although more than 1,400,000 total new cancer diagnoses are projected in the United States in 2008, only 1,250 of those diagnoses are estimated to be penile cancer.1 Metastasis of penile cancer is even rarer. The National Cancer Institute's Surveillance, Epidemiology, and End Results program database reports that distant metastasis occurs annually at a rate of 0.034 new cases per 100,000 men.2 When metastasis does occur, it is usually to the lungs or liver.3

Most cases of penile squamous cell carcinoma are associated with human papillomavirus (HPV) types 16 and 18.4,5 Cigarette smoking, genital warts, and lack of neonatal circumcision are also associated with penile cancer.3,4 We report a rare case of penile squamous cell carcinoma occurring in a man with HPV type 45. Metastasis occurred to the abdominal cavity, causing partial small bowel obstruction that required surgical intervention after conservative therapy failed.

Report of Case

A 63-year-old man presented to an Ohio suburban community emergency department complaining of scrotal swelling. The patient was prescribed imiquimod cream, 5%, to be applied 3 times per week (Monday, Wednesday, and Friday) to lesions on the penis. Because the lesions were suspicious for squamous cell carcinoma, the patient was referred to a primary care physician for further medical attention.

Six months later, the patient presented to the internal medicine teaching clinic at the University Hospitals Richmond Medical Center in Richmond Heights, Ohio, for a refill of imiquimod cream. The patient reported that he had genital warts for approximately 10 years but never sought treatment. He further stated that, other than the previously described emergency department visit, the last time he sought any medical treatment was more than 10 years ago for upper gastrointestinal bleeding caused by peptic ulcer disease.

On presentation, the patient’s blood pressure was 140/82 mm Hg; heart rate, 117 beats per minute; and respiratory rate, 16 breaths per minute. He was obese (231 lb) and appeared in no acute distress.

The patient stated that he was a veteran of the Vietnam War. His medical history included abdominal surgery in 1969 after a stab wound, peptic ulcer disease, and genital warts. The patient had no known drug allergies but avoided aspirin because of his history of peptic ulcer disease. He reported that he smoked one pack of cigarettes per day for more than 50 years, rarely consumed alcohol, and occasionally used marijuana. Current medications included imiquimod cream for the penile lesions as previously described and lansoprazole for peptic ulcer disease, as needed.

The patient completed a review of systems, which was significant for penile lesions, drenching night sweats, and mild scrotal swelling. The patient denied weight loss, dysuria, hematuria, hesitancy, incontinence, penile discharge, frequent urination, or other problems urinating. On physical examination, palpation of the neck and supraclavicular regions revealed no bilateral lymphadenopathy. His heart beat was regular without murmur, and his lungs were clear to auscultation bilaterally. As previously noted, the patient was obese but his abdomen was soft, nontender, nondistended, without bruities, and without visceromegaly. A nontender lymph node was palpated in the right axilla and large nontender inguinal lymph nodes were palpated bilaterally. Physical examination of the scrotum revealed multiple warts, hypopigmentation of the scrotal skin, swelling, mild tenderness with palpation of the spermatic cords, and no masses. Physical examination of the penis, which was uncircumcised, revealed multiple warts, hypopigmentation, scarring, and lichenification.

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Laboratory tests and computed tomographic (CT) scans were ordered. Laboratory tests revealed 0.40 ng/mL of the prostate-specific antigen and an erythrocyte sedimentation rate of 114 mm/h. Results also indicated normocytic anemia (hemoglobin, 13.2 g/dL; hematocrit, 39.3%). All other laboratory values were within normal range. The CT scans of the chest, abdomen, and pelvis revealed significant pelvic andinguinal adenopathy (Figure 1) and a solid region of unknown etiology within the left kidney. Mild to moderate hydronephrosis of the left kidney was present with dilatation of the ureter. Two small hypodense masses were also visible within the liver.

The patient was referred to the urology department, where he underwent biopsy of the penile lesion and excision of the right inguinal lymph node. The biopsy revealed invasive, moderately differentiated squamous cell carcinoma with intraepidermal squamous cell carcinoma in situ extending to the inked margins of resection. The excised inguinal lymph node was consistent with metastatic squamous cell carcinoma. The penile biopsy, which was sent to the laboratory services at Esoterix, Inc, in Austin, Tex, was positive for HPV type 45.

The patient was advised to have a total penectomy, bilateral groin dissection, and pelvic lymphadenectomy. The patient declined these procedures and opted to start weekly combination chemotherapy (paclitaxel IV) and radiation therapy. After several treatments and eventual placement of a left nephrostomy tube as a result of an obstruction in the ureter, the patient declined further chemoradiotherapy.

Three months after discontinuation of chemoradiotherapy, the patient once again presented to the emergency department complaining of midepigastric pain, nausea, and vomiting. A CT scan of the abdomen and pelvis was compared with previous CT scans and revealed a decreased size of groin lymph nodes, a new soft tissue mass in the anterior abdominal wall, a dilated stomach, and a proximal small bowel with a mass near the duodenum (Figure 2). The patient was readmitted and underwent a small bowel follow-through, which demonstrated a fungating mass and a partial obstruction of the second portion of the duodenum. Contrast was visualized within the colon 5 hours after the patient drank an oral contrast agent. An esophagogastroduodenoscopy was attempted, but the scope was unable to pass because of a fixed obstruction in the duodenum.

Several days later, the patient was transferred to a tertiary care center for further surgical evaluation. A CT scan of the chest revealed no evidence of pulmonary parenchymal metastatic disease. Magnetic resonance imaging of the abdomen revealed an annular constricting mass lesion in the pyloric canal of the stomach and stenosis of the third section of the duodenum to the superior mesenteric artery by another eccentric constricting mass lesion. An esophagogastroduodenoscopy was successfully completed the next day using a pediatric colonoscope. Findings included a normal esophagus, gastroesophageal junction, stomach, and pylorus as well as a narrow lumen in the third portion of the duodenum. Several biopsies were taken of this region, but pathology reports did not indicate cancer.

The patient consented to surgery. On opening the
abdomen, surgeons found carcinomatosis with multiple nodules and incisional hernia with cancer inside the hernial sac. Four to five samples of the nodules were tested and reported as poorly differentiated squamous cell carcinoma—evidence of metastasis from the penis. Additional findings included a large cancerous mass in the third and fourth portions of the duodenum extending to the retroperitoneum. Results from a liver biopsy demonstrated no evidence of malignancy. An antecolic gastrojejunostomy was performed to palliate the patient. Hospice care was discussed with the patient as he recovered from the surgery, but he declined further medical care. He continued to improve, tolerating a full diet, and was discharged to his home 8 days postsurgery.

Discussion
Cigarette smoking, genital warts, lack of neonatal circumcision, and HPV infection—all present in the patient described—increase patient risk of penile squamous cell carcinoma. In the presence of HPV, cigarette smoking may cause a synergistic effect that promotes malignant transformation. In one population-based case control study, smokers were three times more likely than nonsmokers to have penile cancer. In addition, the presence of genital warts is associated with a 5.9-fold increased risk of penile cancer. The prevalence of HPV infection in men with penile cancer ranges from 27% to 71%. In such patients, penile cancer is most often associated with HPV types 16 and 18. The present report describes penile squamous cell carcinoma with coinfection of HPV type 45, which is rarely reported in the literature. Likewise, distant metastasis of penile squamous cell carcinoma is rare, occurring most often in the lungs or liver. However, the present report demonstrates extensive metastasis to the abdominal cavity without evidence of metastasis to the lungs or liver.

Conclusion
The current report illustrates the importance of physicians educating their patients on the risk factors for penile squamous cell carcinoma and encouraging them to seek medical treatment at the onset of penile lesions. In addition, patients with HPV require periodic follow-up with physical examination of the genitalia. Early recognition of cancer allows physicians to initiate early management, therefore improving patient prognosis.

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References

Editor’s Note: The April 2008 supplement to JAOA—The Journal of the American Osteopathic Association focused on HPV vaccination and its potential to decrease the incidence of cancer diseases, including penile cancer. To view this supplement, visit http://www.jaoa.org/content/vol108/4_suppl_2/.