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Case Report

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Metastatic Cervical Carcinoma with High-Risk Human Papillomavirus (HPV) Positive and P16/Ki-67 Positive in a 28 Year-Old Female That Did Not Meet the Current Screening Guidelines

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ABSTRACT

A case presentation about an individual treated at Oklahoma State University Medical Center with high-grade metastatic squamous cell carcinoma of the cervix that was high-risk HPV and p16/Ki-67 positive. The clinical presentation, laboratory data, imaging, and subsequent therapy are reported as well as highlights of screening guidelines for cervical pathology

KEYWORDS: Cervical squamous cell carcinoma; Human papillomavirus; P16; Ki-67; Cervical screening guidelines.

INTRODUCTION

The clinical guidelines for frequency of cervical cytology testing were updated in March 2012 and have since been adopted by American Congress of Obstetricians and Gynecologists (ACOG), United States Preventive Services Task Force (USPSTF), American Cancer Society (ACS), and American Society for Colposcopy and Cervical Pathology (ASCCP). Physicians are obligated to interpret and implement these updated guidelines into their own clinical practice. Patient education, along with increased public awareness of the importance of cervical cancer screening, has resulted in a higher percentage of women being screened for cervical cancer. In 2013, the Centers for Disease Control and Prevention reported that while more women are being screened, this group includes women younger than 21 years of age, which conflicts with screening recommendations.[1] The report also revealed an increased in the percentage of women 22-30 years of age that have not been screened.[1] Another potentially concerning aspect of the updated guidelines is the recommendation for co-testing HPV screening every five years for women aged 30 or older. These findings raise the issues of reconsidering screening for high-risk HPV in a younger age group and decreasing the screening interval from three years to one or two years in women with high-risk HPV and negative cytology.

CASE PRESENTATION

A 28 year-old G3 P3003 Caucasian female presented with complaints of headaches, numbness on her left side, right shoulder pain, left hip and left knee pain. She also noted decreased energy and activity, as well as weight loss, in the past month. The patient denied any past medical history. Her Pap smear which was a satisfactory sample in 2011 was negative; however, patient did not have one performed in 2014. She did not have a history of sexually transmitted diseases or a family history of cancer. The patient did have increased risk for cervical cancer because of early onset of sexual activity, multiple sexual partners, early age at first parity, increased parity, and cigarette smoking. Upon presentation, basic labs were performed

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and abnormalities are as noted: white blood cell count of 28.2, hemoglobin of 9.0, platelets of 112,000, sodium of 121, calcium 14.0 and alkaline phosphatase was 389. Significant findings on imaging studies included erosive changes at the distal clavicle and acromion on chest x-ray, which was new from an exam 30 days prior. A head CT showed lytic lesions of the skull with overlying soft tissue swelling and dural thickening.

With the initial findings, the patient was admitted to the intensive care unit under her Family Medicine team for further care. The primary source was then found on CT of the abdomen and pelvis: a nodular mass within the uterus near the cervix measuring approximately 3.2 cm x 3 cm x 4 cm. Cervical exam performed by the gynecology service exhibited an approximately 5 cm cervical mass that was firm, irregular shape, friable and adhered to the anterior vaginal wall. Tissue sample showed high grade squamous cell carcinoma that was HPV p16 positive and Ki-67 positive. Gynecology/Oncology was consulted and their recommendations were initiated. Metastasis was noted in the skull, dura, bony spine, clavicle, scapula, ribs, pelvis, femur, adrenal glands, liver, lung, and esophagus. She was given Vitamin D, dexamethasone, controlled-release morphine, along with one dose of pamidronate. Other pathologic changes required supportive therapy, such as packed red blood cells and platelets. While the patient initially insisted she would eat more, megestrol acetate was administered to assist with appetite stimulation. The patient consistently had low blood sugar readings, and dextrose 5% with half-normal saline was required prior to steroid administration. For the concern for infection, the patient was treated with ampicillin/sulbactam. The patient was transferred to another facility for higher level of care to receive palliative radiation therapy due to an erosive lesion at T4-T5 vertebrae with significant compressive features on her spinal cord at the same level. She received two radiation treatments inpatient and was then released to continue outpatient therapy. The patient later died, within 3 weeks of initial diagnosis.

DISCUSSION

This case brings forward an important discussion about screening for cervical cancer and highlights the necessity of regular screening in this population. Current recommendations from the ACS, the USPSTF, and ACOG suggest that this patient have cytology performed every three years and that HPV co-testing should be performed in women once they become 30 years of age.[2] The current guidelines take into account increased risk of unnecessary procedures such as colposcopy, and likelihood that women under 30 years of age have the potential to clear the infection. However, in 2015, the Society of Gynecologic Oncology and the ASCCP suggested screening women for HPV starting at the age 25.[3] Also this year, the FDA approved the Cobas HPV test for the age of 25 or older. While the interim guidelines were given and testing is available, these recommendations are not consistent across all organizations and are not widely known; therefore they are not likely being used by all physicians. The patient presented had negative cytology on her last Pap smear but failed to have routine examination and did not meet criteria for HPV testing. Had guidelines recommended co-testing in a younger population, closer screening may have been warranted and early discover may have been possible.

One of the markers not currently being utilized to help screen for cervical cancer is p16/Ki-67. Protein p16 is overexpressed in cervical and/or HPV associated cancers. At the time of diagnosis of metastatic cancer, this patient was positive for HPV p16 and Ki-67. A study that looked at the dual stained cytology of p16/Ki-67 showed these markers have superior sensitivity with noninferior specificity with that of Pap cytology when screening for CIN2.[4] However, this testing currently is not FDA approved for routine screening.

CONCLUSION

It is unclear if this patient's outcome would have been different if routine screening had been performed according to the guidelines at that time. It falls upon the physician to stay current on screening recommendations to improve the chances of earlier detection of cervical cancer. Early recognition of this particular cancer is critical to institute the proper therapy and improve prognosis. In the future, the testing and guidelines may evolve to include testing for HPV at an age younger than 30 or other innovations that include screening with a precursor p16/Ki-67.

CONFLICTS OF INTEREST

Authors have no conflicts to declare.

CONSENT

No consent is required for our article publication.

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