Poster 35: Reexamining p16 IHC as a surrogate marker of HPV status in vulvar cancer

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Topic
Vulvar

Objectives
Accurate classification of HPV status in vulvar cancer is critical given evolving evidence of pathogenesis and prognostic differences between disease subtypes. The objective of this study was to determine the accuracy of p16 immunohistochemistry (IHC) to classify HPV-associated vulvar squamous cell carcinoma (SCC) utilizing tissue microarrays (TMA) from archival tumor tissue.

Methods
Patients with primary or recurrent vulvar SCC who had vulvar surgery or biopsy between 2000 and 2021 were identified retrospectively. Patients were excluded if prior pathology was not available for review, synchronous cancer identified, or history of pelvic radiation. TMAs were constructed from formalin-fixed paraffin-embedded (FFPE) archival tumor tissue using 2 mm cores. Slides were reviewed and annotated by a gynecologic pathology subspecialist. IHC for p16 was performed to identify tumors with block staining. RNA in situ hybridization (ISH) was utilized as the criterion standard to assess for the presence of high-risk (HR) HPV. The kappa statistic was used to evaluate agreement between p16 IHC and HR HPV ISH. To assess the performance of p16 IHC as a surrogate test for HPV association, sensitivity and specificity were calculated.

Results
TMAs were constructed from archived FFPE tumor specimens of 295 patients with primary diagnoses that occurred between 1970 and 2021. After TMA staining, 91.5% (270/295) of tumor specimens with p16 IHC and HPV RNA ISH results were evaluable. HR RNA ISH was positive in 104/270 (38.5%) tumors, and p16 was positive in 114/270 (42.2%). Of the p16-positive tumors, 91.2% (104/114) were positive for HR HPV ISH (κ= 0.9). No tumors were positive for HR HPV ISH but negative for p16. The sensitivity and specificity of p16 IHC in classification of HPV-associated vulvar SCC were 100% and 94%, respectively.

Conclusions
Our study verifies the use of p16 IHC as a surrogate marker for classifying vulvar SCC as HPV-associated or HPV-independent disease with a strong positive agreement between p16 IHC block staining and positive HR HPV RNA ISH. The use of p16 IHC appears to be a valid and practical tool for routine pathological assessment of vulvar SCC in distinguishing HPV association.