



Correlation of P16 Expression and Clinicopathologic Outcome of Anal Squamous Cell Carcinoma

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Background

Anal squamous cell carcinoma (ASCC) is uncommon, and accounts for 4% of carcinomas involving the gastrointestinal tract. The pathogenesis of ASCC is still unknown. Many studies have shown a strong association of anal squamous cell carcinoma with human papilloma virus (HPV). In multiple studies, over expression of P16(INK4a) by immunohistochemistry (IHC) was noted in HPV-related anal, cervical and upper aerodigestive squamous cell carcinoma. These studies showed that IHC for P16 has a high sensitivity and specificity for HPV and suggested that it is a good surrogate marker for identification of HPV-driven tumors. In this study we will identify patients with likely HPV-related ASCC using IHC for P16. We will then compare the clinicopathological and histomorphological features of P16 positive and negative ASCC.

Methods

Miraca Life Sciences (MLS) data warehouse was searched between 1/1/2009 and 6/1/2011 using diagnosis codes squamous cell carcinoma (SCC0), squamous cell carcinoma-well differentiated (SCC1), squamous cell carcinoma-moderately differentiated (SCC2) and squamous cell carcinoma-poorly differentiated (SCC3) yielded 50 anal squamous cell carcinoma biopsies. Original H&E stained slides were retrieved from storage at MLS. The slides were reviewed by 2 pathologists and a representative block was selected for P16 immunohistochemical analysis. Pertinent clinical and pathologic details were gathered.

Results

Anal biopsies from 50 patients, including 14 males and 36 females, were included in the study.

| | P16 positive ASCC | P16 negative ASCC |
|---------------------------|-------------------|-------------------|
| Number of patients | 43 (86%) | 7 (14%) |
| Gender | | |
| Male | 11 | 3 |
| Female | 32 | 4 |
| Female: Male | 2.9:1 | 1.3:1 |
| Age | | |
| Range | 47-84 | 54-91 |
| Mean | 63.6 | 74.8 |
| Grade | | |
| Moderately diff | 22 (47%) | 8 (100%) |
| Poorly differentiated | 17 (40%) | 0 |
| Basaloid | 6 (13%) | 0 |

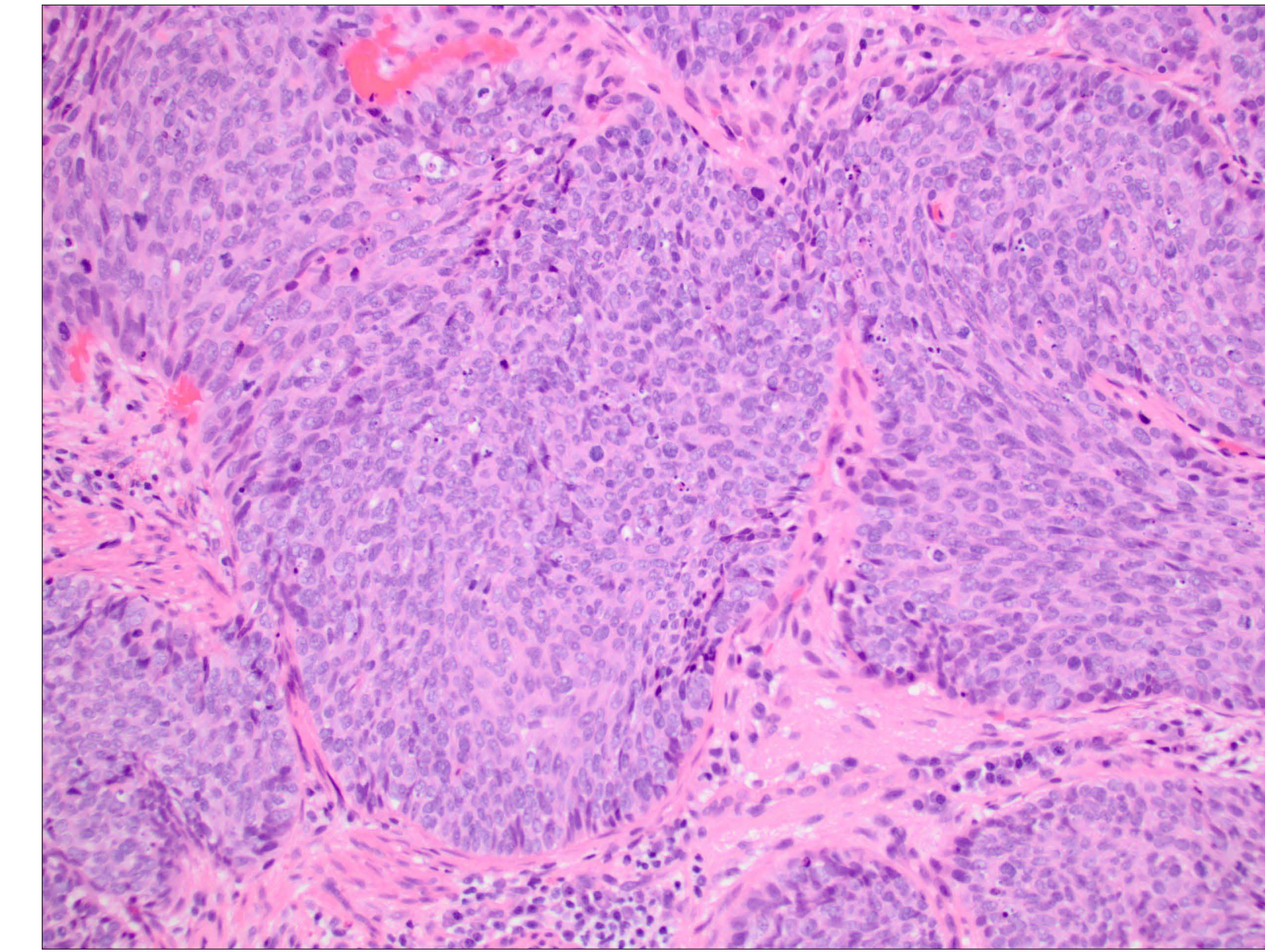


Figure 1. Basaloid Anal Squamous Cell Carcinoma (ASCC)

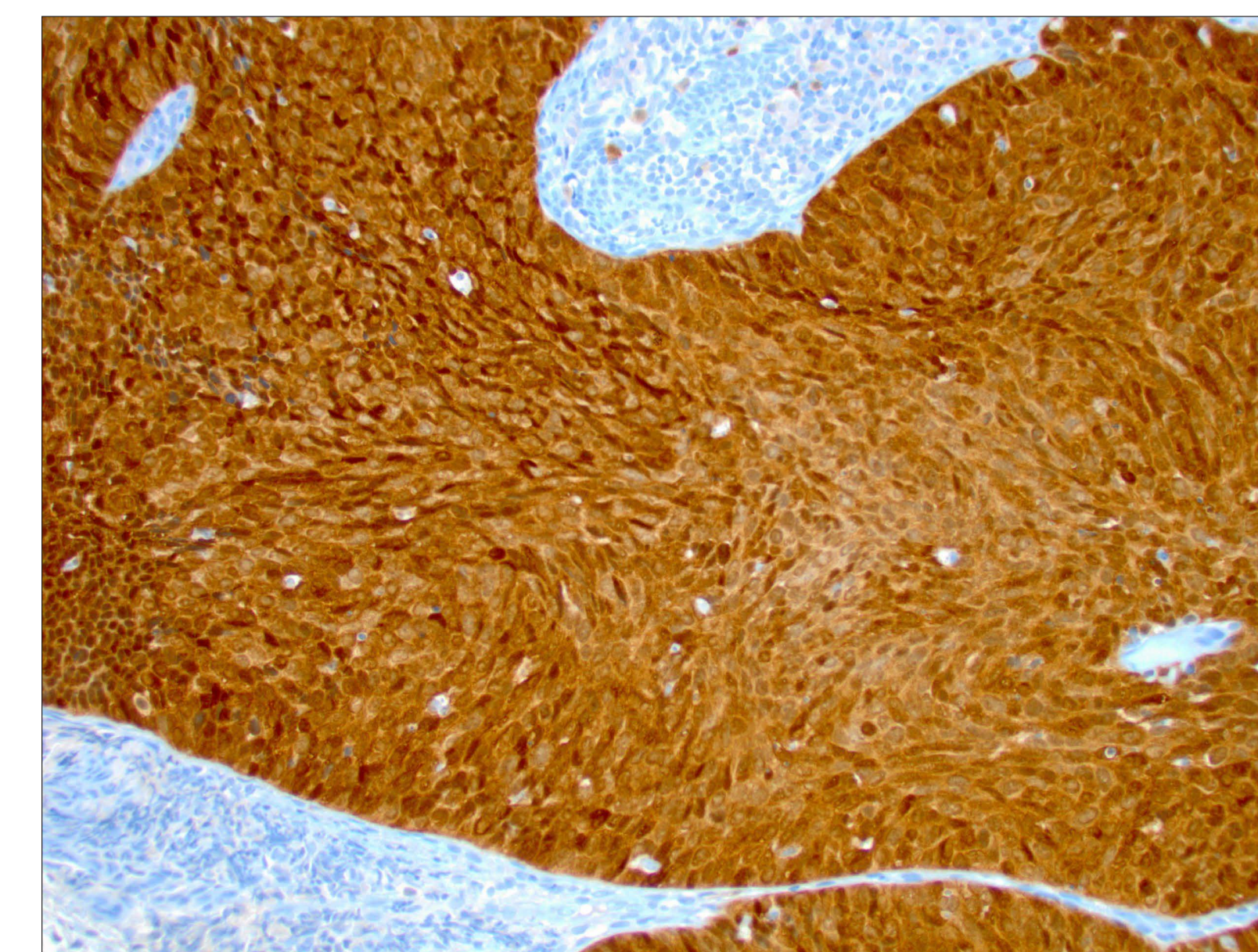


Figure 2. P16 Immunopositivity in Basaloid ASCC

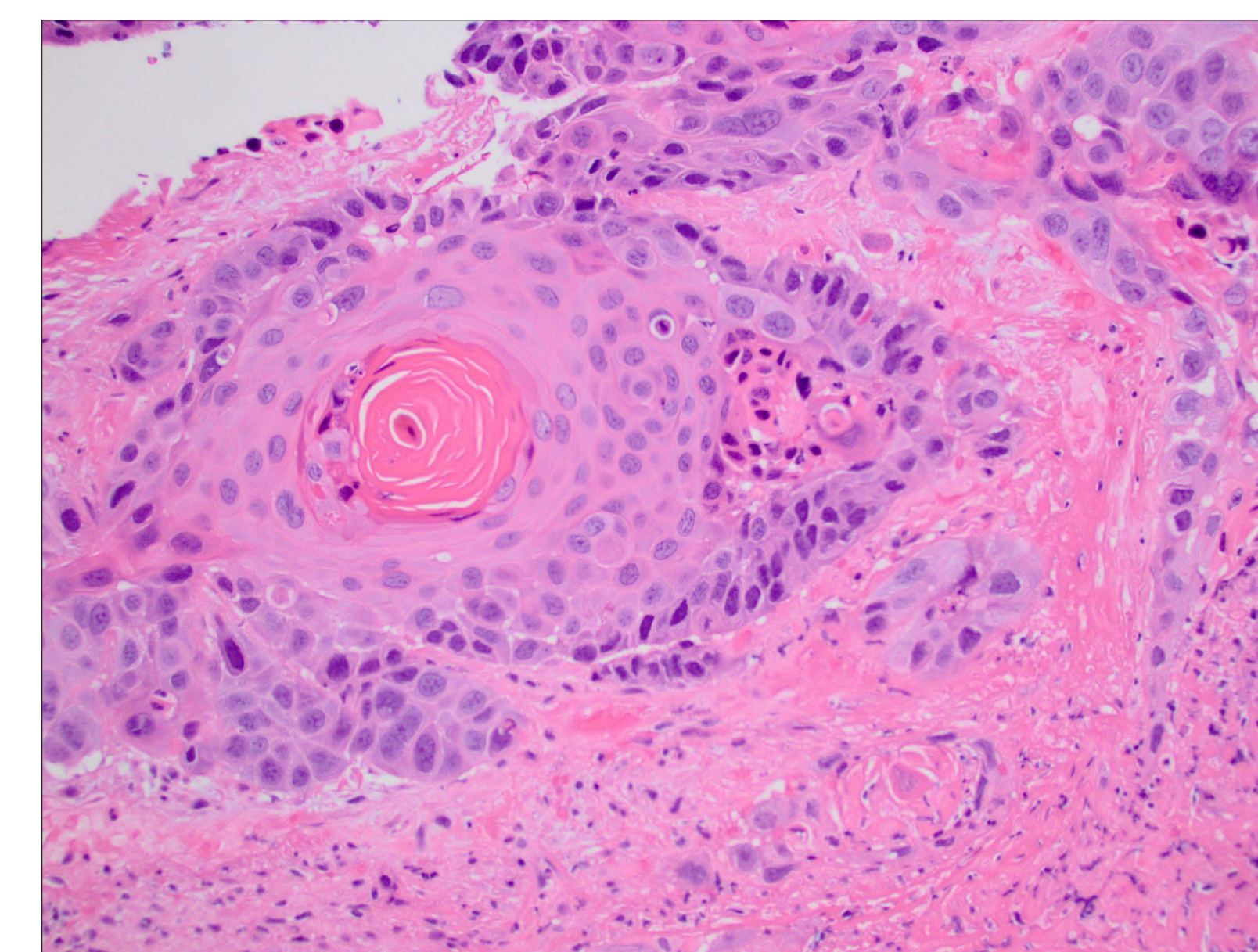


Figure 3. Keratinizing Anal Squamous Cell Carcinoma (ASCC), Moderately Differentiated

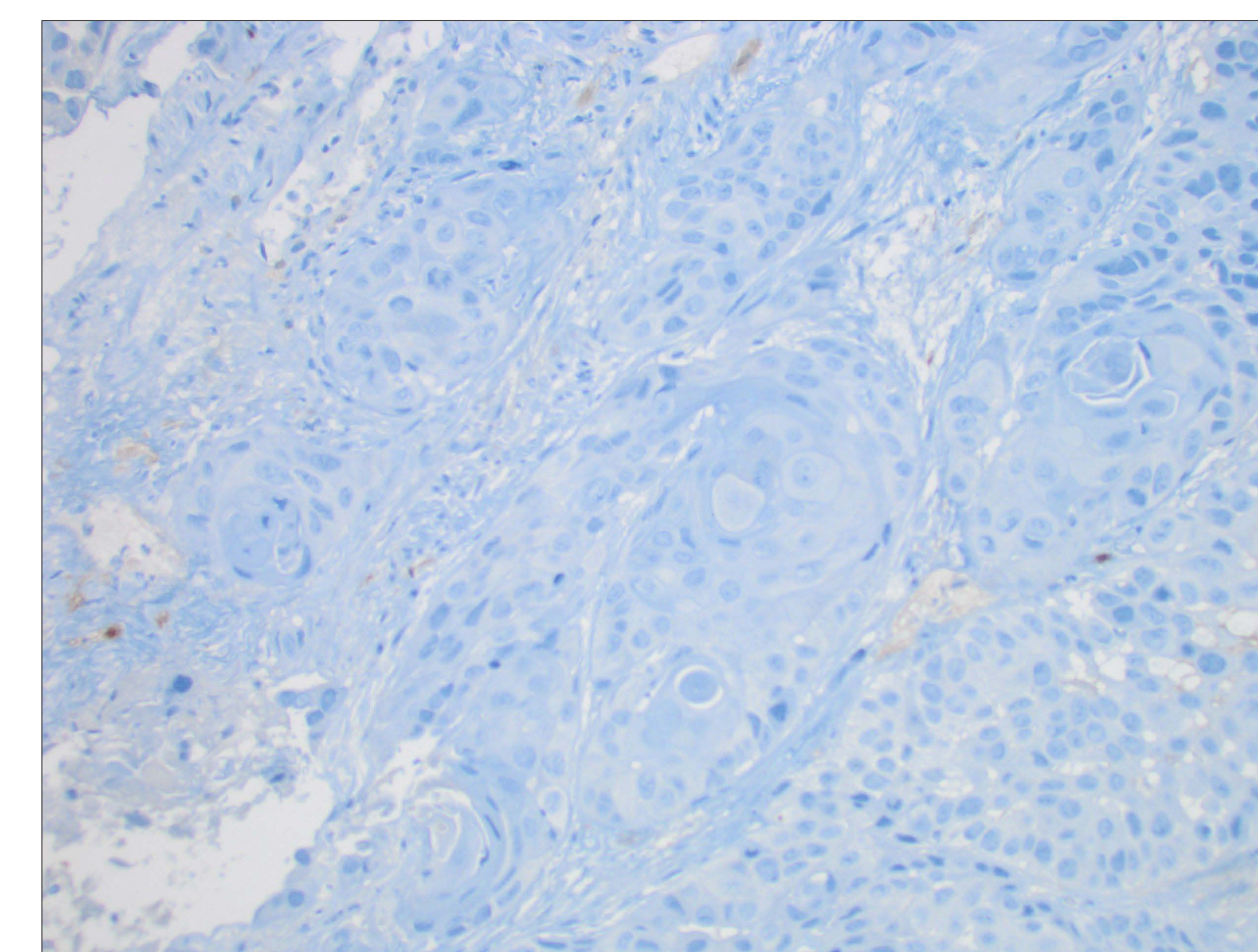


Figure 4. P16 Immunonegativity in Keratinizing ASCC, Moderately Differentiated

Study Highlights

- Two subgroups of ASCC are identified with P16 immunohistochemistry in our study.
- The first subset of P16 positive ASCC (HPV related) has a female predominance and carcinomas exhibiting varying degree of differentiation (moderate-poor basaloid).
- The second subset of P16 negative ASCC (non-HPV) has equal male-to-female ratio, occurs in older patients with no basaloid features.
- This study indicates most likely two or more separate molecular genetic alterations are involved in development of ASCC, depending on the HPV status..

References

1. Yutaka et al. Two distinct Pathways to Development of Squamous Cell Carcinoma of the Vulva. *Journal of Skin Cancer*. Volume 2011.
2. Lu DW et al. Expression of p16, Rb, and p53 proteins in squamous cell carcinomas of the anorectal region harboring human papillomavirus DNA. *Mod Pathol*. 2003 Jul;16(7):692-9