Background

Cervical smears may exhibit unequivocal 'low grade squamous intraepithelial lesion' (LSIL) in association with atypical cells cytomorphologically suspicious for, but not sufficient to be interpreted as, 'high grade squamous intraepithelial lesion' (HSIL) [1,2]. This concurrence has been identified recently by many laboratories, but its reporting is not addressed in the 2001 Bethesda System terminology (Bethesda 2001) [3-5]. Lack of a standardized method of reporting, however, may affect proper application of American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines based on Bethesda 2001 [6,7]. Although 'atypical squamous cells, cannot exclude HSIL' (ASC-H) is not a definitive interpretation, it is related to an increased risk of higher-grade lesions on biopsy [3]. On the contrary, LSIL is a definitive interpretation with relatively lower prevalence of high-grade lesion on subsequent biopsy.

Currently, the reporting pattern to communicate this concurrence varies amongst different cytopathology laboratories. In our institution, for statistical and quality assurance reasons, we report this concurrence under definitive interpretation as LSIL with a comment that ASC-H cells are also present. Others essentially follow a reverse approach and report it as ASC-H with LSIL in the comment. Some interpreters may choose to combine the associated ASC-H component with LSIL and report the combination as HSIL, which may lead to a potentially high false positivity rate. Rarely, the ASC-H component may be downgraded to 'atypical squamous cells of undetermined significance' (ASCUS) with the final interpretation as LSIL, with potentially false negative results for high-grade lesions.

In the current study, we evaluated cervical biopsies in cases of "LSIL with ASC-H" (LSIL-H) (Figure 2 &3) in comparison to other categories in Bethesda 2001, to see if this designation as a distinct category is justified.

pv dna testing

Materials and methods

We studied SurePath™ [TriPath Imaging Inc, Burlington, NC] preparations of cervical specimens over a one year period (Figure 1). Initial cytopathologic interpretations were performed by more than five different cytopathologists, based on Bethesda 2001 criteria and were representative of general cytology reporting patterns [4].

LSIL-H was defined as cases with unequivocal LSIL, in concurrence with ASC-H (Figure 2 and 3). ASC-H cells showed cytomorphologic features reported previously [8]. As observed in a subset of ASC-H, some of these cases showed small atypical parakeratotic (SAPK) cells (Figure 3), which may demonstrate superficial resemblance to high grade cells in liquid based cytology [9,10].

The cytology results were correlated with concurrent biopsies (both colposcopically-guided and LEEP biopsies) performed at the time of, or within 3 months of cytologic interpretation. Many institutions, in addition to our primary hospital, submitted cervical cytology specimens. Cervical biopsies from some outside institutions were not sent to our institution for surgical pathology and the cyto-histo correlation was available in only a fraction of cases. The cervical biopsy results for cases with cytologic interpretation as LSIL, LSIL-H, and ASC-H were compared using the Chi-square test for statistical analysis.

In addition, the status of HPV DNA testing (Hybrid Capture (HC) II, Digene, Silver Spring, MD, USA) performed within a year of biopsy was noted in LSIL-H cases with biopsy results.

Results

We studied 77,979 cases over a one year period (Figure 1). Out of these 1,970 cases (ages 16 to 65 years) were interpreted as abnormal (1,523 LSIL, 146 LSIL-H (Figure 2 &3), 109 ASC-H, and 192 HSIL). The cyto-histo correlation was available in 40% (792 of 1,970) cases. These included 557 LSIL, 88 LSIL-H, 38 ASC-H, and 109 HSIL (Figure 1).

The biopsy results were grouped into: A. negative for dysplasia (ND), B. low grade (HPV, CIN1, or CIN1 with HPV), and C. high grade (CIN 2 and above) (Table 1). Positive predictive value (PPV) for each category of biopsy result was calculated for LSIL, LSIL-H, ASC-H, and HSIL interpretations (Table 1).

LSIL-H (Figure 2 &3) had a lower prevalence of negative biopsy results, compared to ASC-H and LSIL (24% negative results with LSIL-H versus 32% with ASC-H and 32% with LSIL) (Table 1). LSIL-H had a higher chance of association with high grade dysplasia on biopsy, comparable to that for ASC-H (Positive predictive value [PPV] of 33% with LSIL-H and 31% with ASC-H). LSIL alone was associated with a significantly lower risk (PPV 10%) for high grade dysplasia as compared to LSIL-H (PPV 33%). PPV of LSIL-H (33%) was lower for high grade lesions as compared to HSIL (69%). LSIL-H was associated with higher number of negative biopsy results (24%) as compared to HSIL (5%). However, as compared to ASC-H (32%), the prevalence of negative biopsy results with LSIL-H was relatively lower (24%) (Table 1, Figure 4).

PPVs between different groups were compared by performing two separate 2 × 3 Chi-square tests for LSIL versus LSIL-H and LSIL-H versus ASC-H (Table 1). Applying the Bonferroni correction for multiple testing, the significance level was adjusted to 0.025. The differences between LSIL and LSIL-H were statistically significant (Chi-square value