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Cytohistological Correlation of ASC-H and HSIL in Samples Submitted During a Five-Year Period

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ABSTRACT

The classification of cytological abnormalities has been based on the Bethesda system. Since its implementation in 1988, several revisions have been made to incorporate new technical and scientific findings.

The objective of this study was to evaluate the clinical importance and the histological result of cervical cytologies reported as HSIL, in addition to those classified as ASC-H, determining their prediction of histological lesions, mainly high-grade, in subsequent biopsies.

During the period from January 2015 to December 2019, 36,984 cervical-vaginal cytology studies were performed, referred to our department. Of these, 43 (0.12%) were classified as ASC-H and 76 as HSIL (0.20%). Nine cases were excluded because they did not have a histopathological study within the period of one year after the cytopathological study and 2 cases in which the sample for the histopathological study was insufficient. Finally, 38 cases of ASC-H and 70 cases of HSIL met the inclusion criteria and constituted the total study population, a total of 108 cases.

In our study 55.3% of cases of ASC-H corresponded to a final diagnosis of a high-grade lesion and 84.3% for cases diagnosed with HSIL cytology, in which a histological diagnosis of a high-grade lesion has been demonstrated. The concordance values for the HSIL and ASC-H diagnoses demonstrated in this work correspond to those cited in previous studies and recommendation guidelines, and these data justify the study of these patients. This demonstrates the fundamental importance of diagnostic cytology in the population screening of cervical cancer.

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Introduction

Gynecological cytology has managed to reduce the incidence of cervical cancer globally. In Spain, this type of cancer has ceased to be the first in incidence to give way to other neoplasms such as breast, colon or lung in recent years [1].

The screening of healthy women using cervical cytology has clearly demonstrated its effectiveness, since its proper and systematic application in certain countries has managed to reduce the incidence and mortality from cervical cancer by 70-80%. The benefit is due to the detection of asymptomatic premalignant lesions whose diagnosis and treatment prevent their progression to invasive carcinoma [2].

In the last three decades, the classification of cytological abnormalities has been based on the Bethesda system. Since its implementation in 1988, several revisions have been made to incorporate new technical and scientific findings [3].

In this system, in addition to the HSIL (high-grade squamous epithelial lesions) category that designates high-grade squamous intraepithelial lesions, the ASC-H (atypical squamous cells - cannot exclude HSIL-high-grade squamous epithelial lesions) category is named. Designates those cases with the presence of atypical squamous cells in which the changes are suggestive of a high-grade squamous intraepithelial lesion, but insufficient for a definitive cytopathological interpretation [4].

Although cytomorphological criteria have been described for this category, it is still considered an interpretive challenge for both cytotechnologists and cytopathologists, and the prevalence of cases interpreted as ASC-H varies significantly between laboratories.

Despite its low prevalence, the clinical importance of ASC-H is based on the fact that it is frequently associated with high-grade histological lesions of the cervix. In fact, since its introduction into the Bethesda system, several studies have shown that ASC-H is frequently associated with high-grade histological lesions. Different studies evaluating the prevalence of high-grade lesions among patients with ASC-H have found values between 13% and

66% [5, 6]. This also reflects the great subjectivity and interpretive variability in the evaluation of this cytological category, resulting in poor interobserver agreement.

The objective of this study was to evaluate the clinical importance and the histological result of cervical cytologies reported as HSIL, in addition to those classified as ASC-H, determining their prediction of histological lesions, mainly high-grade, in subsequent biopsies.

Materials and Methods

Descriptive, cross-sectional and retrospective study of patients with HSIL and ASC-H results in the cervicovaginal cytology study, during the period from January 2015 to December 2019. Subsequently, the results of the histopathological study were collected, excluding those cases with an inadequate sample diagnosis, with a diagnosis date greater than one year from the cytopathological study and / or patients with a history of cervical carcinoma.

Descriptive statistics were used to report demographic data and detailed histological results. Statistical analysis was performed with the SPSS statistical package for Windows.

Results

During the period from January 2015 to December 2019, 36,984 cervical-vaginal cytology studies were performed. Of these, 43 (0.12%) were classified as ASC-H and 76 as HSIL (0.20%). Nine cases were excluded because they did not have a histopathological study within the period of one year after the cytopathological study and 2 cases in which the sample for the histopathological study was insufficient.

Finally, 38 cases of ASC-H and 70 cases of HSIL met the inclusion criteria and constituted the total study population, a total of 108 cases.

The age range of all the patients was from 20 to 64 years, with a mean of 39.2 ± 9.4 years. In the group diagnosed with ASC-H, the mean age was 37.9 ± 8.8 (26-64) years, while in the group with HSIL it was 39.9 ± 9.7 (20-61) years, without observing significant differences between both groups (p = 0.30; Student's t test).

The findings of the histopathological study after the screening cytology are reported for the ASC-H group (Table 1) and for the HSIL group (Table 2).

Table 1: Histopathological findings in patients with a cytological diagnosis of ASC-H. ASC-H: lesion with atypical squamous cells without being able to exclude high-grade lesion. HSIL: high-grade squamous intraepithelial lesion. LSIL: low-grade squamous intraepithelial lesion.

Definitive histopathological diagnosis	Number of cases with ASC-H	Percentage of all cases with ASC-H
Cervical biopsy without dysplasia	8	21%
Cervical biopsy with squamous metaplasia	1	2,6%
Second negative cytology for malignant cells	2	5,3%
Second cytology with HSIL and conization with HSIL	6	15,8%
Biopsy of the cervix with dysplasia of an undetermined grade and conization with HSIL	1	2,6%
Cervical biopsy with LSIL	6	15,8%
Cervical biopsy with HSIL and conization with LSIL	1	2,6%
Cervical biopsy with HSIL	2	5,3%
Cervical biopsy with HSIL and conization with HSIL	10	26,4%
Cervical biopsy with HSIL and conization with microinvasive carcinoma	1	2,6%
Total diagnosed cases	38	100%

Table 2: Histopathological findings in patients with a cytological diagnosis of HSIL. HSIL: high-grade squamous intraepithelial lesion. LSIL: low-grade squamous intraepithelial lesion. VAIN1: vaginal intraephitelial neoplasia type 1

Definitive histopathological diagnosis	Number of cases with HSIL	Percentage of total cases with HSIL
Cervical biopsy with follicular cervicitisTotal diagnosed cases	1	1,4%
Cervical biopsy with squamous metaplasia	1	1,4%
Cervical biopsy without dysplasia	1	1,4%
Cervical biopsy without dysplasia and conization with HSIL	4	5,8%
Cervical biopsy without dysplasia and conization with LSIL	1	1,4%
Cervical biopsy with LSIL	4	5,8%
Cervical biopsy with LSIL and conization with HSIL	2	2,8%
Cervical biopsy with HSIL	2	2,8%
Cervical biopsy with HSIL and conization with HSIL	47	67,2%

Cervical biopsy with HSIL and conization without dysplastic remains	2	2,8%
Cervical biopsy with squamous cell carcinoma	2	2,8%
Biopsy with diagnosis of VAIN1	3	4,4%
Total diagnosed cases	70	100%

The definitive histopathological diagnosis is the highest grade lesion determined during follow-up, the absence of dysplasia or any non-neoplastic lesion identified. This diagnosis could be obtained by repeating the vaginal cytology, incisional biopsy of the cervix or cervical conization.

For both groups, we sought to determine the concordance of the diagnoses of ASC-H and HSIL with high-grade lesions. Those a case in which dysplasia was not subsequently detected, a low-grade lesion or lesions with pathology other than the one studied were classified as discordant.

For the cases of ASC-H, the following findings were identified as concordant:

- Second cytology with HSIL and conization with HSIL
- Biopsy of the cervix with dysplasia of an undetermined grade and conization with HSIL
- Cervical biopsy with HSIL and conization with LSIL
- Cervical biopsy with HSIL
- Cervical biopsy with HSIL and conization with HSIL
- Cervical biopsy with HSIL and conization with microinvasive carcinoma On the other hand, the following were classified as discordant:
- Cervical biopsy without dysplasia
- Cervical biopsy with squamous metaplasia
- Second negative cytology for malignant cells
- Cervical biopsy with LSIL

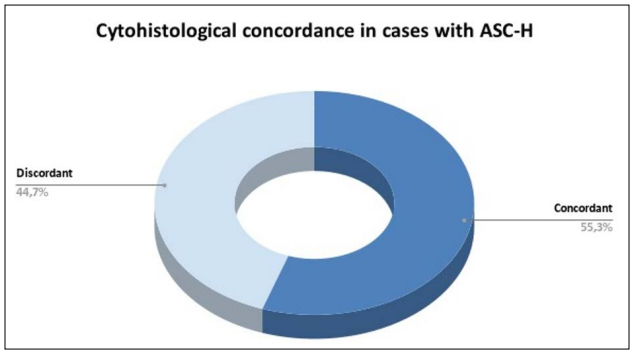

Figure 1: Cytohistological Concordance pie Chart in Cases with Cytological Diagnosis of ASC-H. ASC-H: lesion with a typical squamous cell without being able to exclude high-grade lesion.

For the group of cases with HSIL, the following diagnoses were identified as concordant:

- Cervical biopsy without dysplasia and conization with HSIL
- Cervical biopsy with LSIL and conization with HSIL
- Cervical biopsy with HSIL
- Cervical biopsy with HSIL and conization with HSIL
- Cervical biopsy with HSIL and conization without dysplastic remains
- Cervical biopsy with squamous cell carcinoma While the following were determined as discordant:
- Cervical biopsy with follicular cervicitisTotal diagnosed cases
- Cervical biopsy with squamous metaplasia
- Cervical biopsy without dysplasia
- Cervical biopsy without dysplasia and conization with LSIL
- Cervical biopsy with LSIL
- Biopsy with diagnosis of VAIN1 Figure 2 shows the distribution of cases.

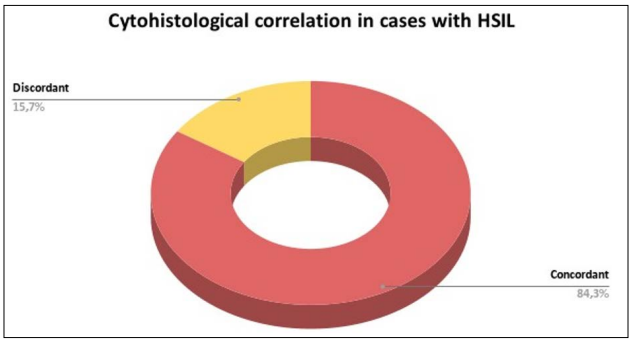

Figure 2: Pie chart of cytohistological concordance in cases with cytological diagnosis of HSIL. HSIL: high-grade squamous intraepithelial lesion.

Discussion

Most of the women diagnosed with ASC-H were in the age range of 29 to 42 years, while those with HSIL were more widely distributed in the ranges of approximately 33 to 42 years. Cervical cancer is most often diagnosed between the ages of 35 and 44. About 15% of cervical cancers are diagnosed in women who are over 65 years old and it is rare for women under 20 years old to develop it. The figures correspond to the detection of cytological lesions from screening in these age ranges, during the period studied in this work.

Given the importance of this type of cancer, an attempt has been made to standardize criteria in order to achieve a better diagnostic approach. For this reason, the Bethesda system is used to report cervical cytology, which considers the category of squamous cell atypia in which high-grade squamous intraepithelial lesion (ASC-H) cannot be excluded [7]. This category designates cases with the presence of atypical squamous cells in which cytological changes are suggestive of a high-grade squamous intraepithelial lesion, but insufficient for a definitive cytopathological interpretation [8, 9].

In our study, a frequency of ASC-H of 0.12% was found, which is consistent with the literature, which reports it between 0.12 and 1.49%. Elsheick et al. report a frequency of ASC-H of 0.15% in a total of 129,911 cytologies [10].

The American College of Pathologists (CAP) of the United States, already in 2002-2003 comments that the ASC-H category should belong to 0.2% of the total cytopathological interpretations; these same results were found in India, Brazil [11, 12] and in Venezuela, with 0.21% [8].

The age ranges in the different studies range from 19 to 71 years. In our study, the age range of the patients with ASC-H was from 26 to 64 years, the mean being

37.9 years, which is related to the reviewed literature, where the mean age is between 38.2 and 47.3 years [7, 13, 14].

The diagnostic interpretation of ASC-H has a high positive predictive value for high-grade lesions, that is, 24 to 94% of patients could have this diagnosis during follow-up, compared for example with cases of ASC-US, of the of which only 5 to 17% will present high-grade intraepithelial lesion [15].

According to the previous study by Srodon et al, in 41% of cases a high-grade lesion was detected [16]. In our study we found superior results, since 55.3% of cases of ASC-H corresponded to a final diagnosis of a high-grade lesion. Nogara et al. reported a lower prevalence than ours, 23.7% [17]. Kietpeerakool et al. found figures greater than 61.2%, as did Barreth et al. with 65.6% [18, 19].

It is considered that colposcopy and sampling may be the main factors associated with cytohistological discordance, in addition to inadequate or insufficient cervical conization samples, and of course, the erroneous interpretation of cytology [20].

The importance of knowing this diagnostic interpretation lies in the management that the gynecologist will perform. The Management Guide of the American Society of Colposcopy and Cervical Pathology (ASCCP) comments that cases with high-grade lesions are often preceded by an interpretation of ASC-H in cytopathology, which corresponds to the findings of our study. study. For this reason, the management of this result is colposcopy and biopsy as if it were a high-grade lesion, a conduct endorsed by the World Health Organization (WHO) and the American Society of Clinical Oncology (ASCO) [8, 9, 21].

In previous studies, high-grade squamous intraepithelial lesions (HSIL) usually represent between 0.5% and 1% of all screening cytologies [2]. In our study, the frequency is lower, approximately 0.20%. This may be due to early detection and definitive treatment of LSIL lesions, which prevent their progression and therefore the detection of high-grade lesions.

In addition, with an HSIL cytology, the definitive histological diagnosis shows a high-grade lesion in approximately 60% and invasive carcinoma in 2%. These data justify the study of these patients [22]. In the present study, even higher figures have been detected, of 84.3% for cases diagnosed with HSIL cytology, in which a histological diagnosis of a high-grade lesion has been demonstrated. In the case of invasive carcinoma, it corresponds to figures from previous studies mentioned above of 2%, in our case 2.8% [22].

Therefore, the concordance values for the HSIL and ASC-H diagnoses demonstrated in this work correspond to those cited in previous studies and recommendation guidelines. This demonstrates the fundamental importance of diagnostic cytology in the population screening of cervical cancer, demonstrating its ability to reduce the incidence and related mortality.

Ethical Responsibilities

Protection of people and animals. The authors declare that no human or animal experiments were performed for this study.

Confidentiality of the data. The authors declare that no patient data appears in this article.

Right to privacy and informed consent. The authors declare that no patient data appears in this article, the patients signed a consent form and the study was approved by an ethics committee.

Conflict of Interests

The authors declare that they have no conflict of interest.

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