Comparative study of p16ink4a expression in cytology and biopsy samples of cervical lesions

Servicio de Anatomia Patológica e *Ginecología, Hospital Fernando Fonseca-Amadora, Portugal

Introduction

It is a well-known association between human papillomavirus (HPV) and cervical pre-neoplastic and neoplastic lesions. Several studies report that certain viral types can cause genetic alterations in E6 and E7 oncogenes, leading to overexpression of p16 protein. This study demonstrated immunohistochemically using the monoclonal antibody p16INK4A (p16) the p16 reaction in all cervical cytological smear samples from the year 2000 which were matched with a conventional biopsy and compared with the p16 reaction in the histological slides.

Material and Methods

A total of 1,200 cases of cervical smears over the years 1999-2000 were analyzed. Most cases were excluded for the study because the smears did not include representative material for the cervical epithelium. Women ages ranged from 15 to 75 years old. The histological diagnoses were selected according to the Bethesda System (1991) and included all cases of HPV infection and cervical neoplasia. For the p16 reaction, a monoclonal antibody against p16INK4A (Abcam, UK) and the EnVision (Dako) detection system were used.

Results

The 63 cases that were selected for study (those that had biopsies with representative cervical epithelium) were divided as follows: using the Bethesda System (1991) classification: HSIL 30%, LSIL 26%, ASCUS 3.

The agreement between the p16 immunohistochemical expression and the histological grading (CIN) is presented in Table I. In Table I, p16 reactions in the cervical and biopsy samples of p16 were compared. HSIL and CIN II/III were present in 39% and 33% respectively, LSIL and CIN I were present in 33% and 10%, ASCUS and CIN 1 were both present in 39%, and 40% respectively, and 20% and 40% respectively. Only 6% of CIN III cases were positive for p16, whereas 6% and 10% of CIN I and II respectively were negative for p16. Overall, the results indicate a high degree of agreement between the p16 immunoexpression and the histological grading.

Table I: Total cases studied for p16 expression

Conclusions

1. There were 95% agreement, in the high grade group, between the cytology grading and the matched CIN lesion in histology.
2. In the low grade and ASCUS groups, the agreement with histology was 85% and 60% respectively.
3. There was a high level of agreement and positivity for the p16 reaction in the high grade group, and a low level of positivity in the low grade group.
4. In the low grade group and ASCUS there were higher levels of positivity for p16 reactions in cytology, although the small number of cases in these groups is considered a limitation.
5. The results are similar to those reported in the literature with the use of the EnVision detection system.