HPV-related lesions in anal and cervix Pap-smears in HIV+ patients under anti-retroviral treatment: interest of cytology coupled to rapid HPV-PCR

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OBJECTIVE

- It is known that the prevalence of oncogenic HPVs [high risk HPV = hrHPVs] related to ano-genital lesions in immunodepressed HIV+ patients is elevated (near 90%, Walker et al. Diagn Mol Pathol 1996).
- Few data existed concerning the prevalence of low (LSIL) and high (HSIL) grade squamous intraepithelial lesions of anus and cervix in HIV+ patients under antiretroviral (ARV) treatment, with normal immunity.
- In precedent works we found the persistence of a high level of HPV lesions in that population (Walker et al. Clin cancer Res 2003 and Human Pathol 2009).
- We co-tested, in anal and/or cervical Pap-smears of consecutive HIV+ patients under ARV therapy, the cytopathological lesions and Rapid PCR technique detection of oncogenic HPVs types (hrHPVs).

METHODS

- Anal and/or cervical smears using the Rovers brush, collected in liquid medium (Queloyt) treated by lisa diagnostic system, were obtained under colposcopy and/or anoscopy in 101 subjects recruited during 2 months. If lesion existed, one biopsy was removed.
- Bethesda System classification (Negative, ASC-US: atypical squamous cells of undetermined significance, ASC-H: suspect for high-grade squamous intraepithelial lesion, LSL: Low or undetermined significance, HSIL: high-grade squamous intraepithelial lesion) was used in association with Rapid PCR (Xpert Cepheid) to detect oncogenic-HPVs: HPV 16, both HPV’s 18/45, P3 (HPV’s 31, 35, 33, 52, 58), P4 (HPV’s 51, 59), P5 (HPV’s 39, 68, 56, 66).
- They were 33 anal smears in 28 patients (5 patients had margin and canal samples) and 73 cervical smears.
- The pathological cytomorphological findings were compared to results of biopsies.
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RESULTS

- In this HIV immunocompetent population under highly active antiretroviral treatment:
  - The incidence of oncogenic HPV lesions remained at a high level.
  - This could be due to the loss of Langerhans cells in the anal or cervical mucosa (Walker et al. Clin Cancer Res 2005, Human Pathol 2009).
- Oncogenic-HPVs prevalence was higher in anus (78%) than in cervix (37%).
- In anus
  - HPV 16 predominates with multiviral lesions especially in homosexual men representing 67% of the entire population studied, with 68% of oncogenic-HPVs in the MSM cohort.
  - In two patients, standard ancytology and colposcopy were negative whereas oncogenic-HPVs were present suggesting a non-cytologic or ancytologic complex lesion or healthy carriers needing High Resolution Anoscopy and appropriate follow up.
- In cervix
  - The group P3 of HPVs predominates (HPVs type: 31, 35, 33, 52, 58) especially in African HIV-positive women representing 71% of the entire population, with 38% of oncogenic-HPVs in this african cohort.
  - Multiviral lesions were noted in 6 patients.
  - In two patients, colposcopy and cytology were obvious for a condyloma, negative for oncogenic HPVs but positive in the biopsy for HPV-11 probe (in situ hybridisation).
- Rapid PCR (1 hour) linked to colposcopy eliminated non oncogenic HPVs related ASC-US (inflammatory lesions).
- In the two locations (anus and cervix), the cytopathological and Rapid-PCR findings were confirmed by histology.

CONCLUSIONS

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- In cervix
  - The group P3 of HPVs predominates (HPVs type: 31, 35, 33, 52, 58) especially in African HIV-positive women representing 71% of the entire population, with 30% of oncogenic-HPVs in this african cohort.
  - Multiviral lesions were noted in 6 patients.
  - In two patients, colposcopy and cytology were obvious for a condyloma, negative for oncogenic HPVs but positive in the biopsy for HPV-11 probe (in situ hybridisation).
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The impact of co-testing in this immunocompetent HIV+ population

- Both Negative or ASC-US/oncogenic HPVs:
  - Routine screening.
  - POSSIBLY, to realise biopsy to eliminate condyloma with non oncogenic HPV 6/11.
- ASC-US/oncogenic HPVs:
  - Colposcopy and/or High Resolution Anoscopy and biopsies.
- LSIL/hSIL/oncogenic HPVs:
  - Colposcopy and/or ancytologic and biopsies.
- Negative cytology but oncogenic HPV+:
  - Colposcopy and/or High Resolution Anoscopy and biopsies if lesions are observed.
  - No lesion, to repeat co-test in 12 months (healthy carrier or inflammatory or complex lesion?)

Question:

Is ancytology associated to colposcopy relevant in HIV+ women?

REFERENCES

3 Laurent Abramowitz (3), Dalila Benabderrahmane (3), Fabrice Bouscarat (4), Anne Couvelard (1).