

A Case of HPV-Negative Undifferentiated Carcinoma of the Cervix

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BACKGROUND

Cervical cancer is the 4th most common cancer type in women¹. HPV-negative cervical cancers account for a minority of cases, however present more advanced and with poorer prognosis². Although mechanisms of tumorigenesis are still being studied, HPV-negative cervical cancers have distinctive molecular profiles and immunohistochemistry is essential for diagnosis. Nevertheless, treatment is based on staging, and not on subtype.

AIM

To present a rare case of HPV-negative undifferentiated carcinoma of the cervix.

CASE REPORT

A 53-year-old P2 woman presented with a several month history of malodorous vaginal discharge, postmenopausal bleeding and pain. Medical history includes hypertension, dyslipidaemia, gastric banding, appendectomy and laparoscopic right oophorectomy. She was a non-smoker with a BMI of 50. Her prior cervical screening tests were up to date and always normal. Speculum examination revealed a bulky and friable cervix completely covered by an exophytic mass.

RESULTS

A co-test was negative for HPV and cytology was consistent with squamous cell carcinoma. Histopathology demonstrated an invasive undifferentiated carcinoma, and immunohistochemistry was performed (Figure 1 and 2). Particularly, immunohistochemistry was positive for p16, CK 5/6 and Ki 67, and negative for p40, chromogranin, synaptophysin, CD56 and CEA. Endometrial biopsy was also performed, which ruled out a primary endometrial malignancy with extension to the cervix. Staging PET-CT and MRI (Figure 3) showed involvement of bilateral pelvic lymph nodes without parametrial or vaginal extension. This was consistent with FIGO Stage 3C1, grade 4 cervical carcinoma. The patient completed chemoradiotherapy with 25 fractions (totalling 55Gy) and weekly cisplatin. This was followed by definitive vault brachytherapy in 3 fractions.

CONCLUSION/DISCUSSION

This case highlights the presentation of HPV-negative undifferentiated carcinoma of the cervix in an older patient and more advanced at time of diagnosis. It is important to acknowledge that HPV-negative cancers can be falsely negative due to factors such as sampling, storing or even HPV-testing errors³. This patient's specimen was re-examined and retested in a second tertiary pathology unit. Immunohistochemistry, in particular p16, is also important in the detection and diagnosis of cervical cancers. Although p16 was traditionally thought to be associated only with HPV-dependent cervical cancers, up to 57% of HPV negative cancers may be positive for p16⁴. In fact, HPV-negative cancers with p16 expression have a higher rate of aberrant p53 staining⁵ which is linked with a poorer prognosis due to its higher mutation capacity. Additionally, several studies have also demonstrated the utility of p16 staining to aid diagnosis of HSIL or above in HPV-negative patients⁶. Nevertheless, public health efforts to detect and prevent cervical cancers focus on HPV-positive cases, and barriers still exist that result in delayed presentation, diagnosis, and management of cervical cancer. Therefore early clinical examination with co-test +/- colposcopy is paramount in any woman presenting with dyspareunia, abnormal discharge or bleeding.

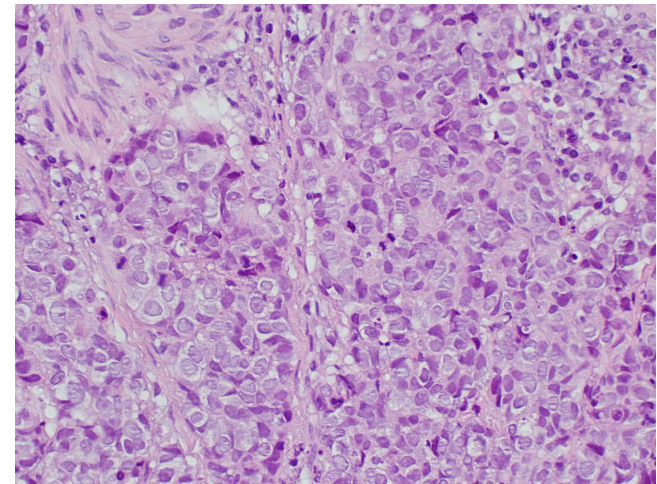


Figure 1: H&E stain - sheets and nests of tumour cells with pleomorphic nuclei and little cytoplasm

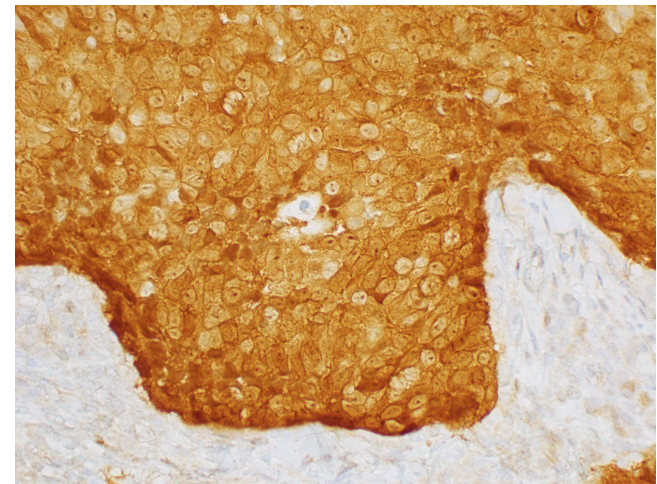


Figure 2: p16 stain - diffusely positive (brown cytoplasm)

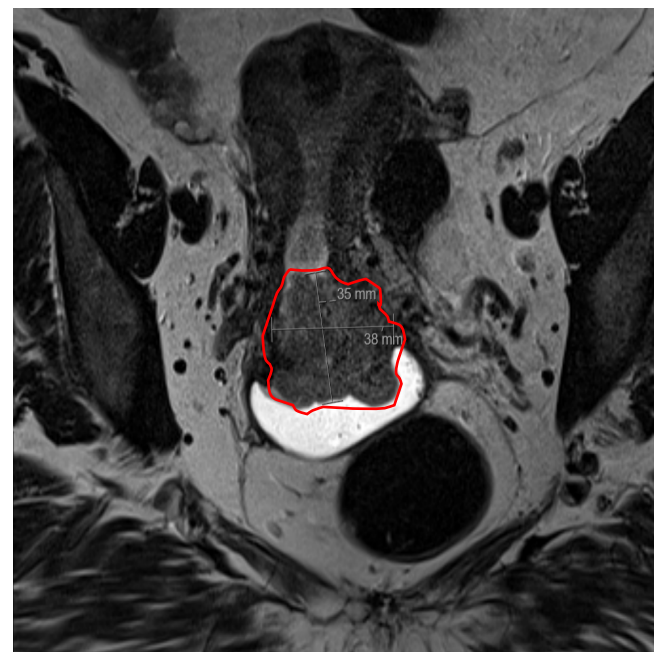


Figure 3: MRI pelvis - exophytic mass arising from cervix

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