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Letter to the Editor

p16 Block Type Overexpression, p53 Wild Type Reactivity, and Cervical Involvement do not Always Exclude the Diagnosis of Primary Endometrial Squamous Cell Carcinoma (PESCC)

To the Editor:

Almost a year after we presented a rare case of primary endometrial squamous cell carcinoma (PESCC) characterized by PAX8 positivity, abnormal p53 expression, and p16 negativity (1), we saw a second case showing new peculiarities and challenging both the differential diagnosis and staging. The endometrial biopsy of a 77-year-old woman admitted to our hospital for endometrial bleeding showed diffuse necrotic material and squamous cell carcinoma, which could have been mistaken for cervical squamous cell carcinoma because the neoplastic cells displayed p16 block-type overexpression, p53 wild-type immunoreactivity, and cervical involvement (2).

Nevertheless, clinical presentation and pathological examination of the uterus and adnexa showed that a bulky tumor measuring 35 mm occupied the uterine cavity. In addition, the tumor infiltrated the deeper half of the myometrium to <1 mm from the serosa, and the left fallopian tube stroma was involved, whereas the cervical stroma was only superficially affected. Histologic examination confirmed the diag-

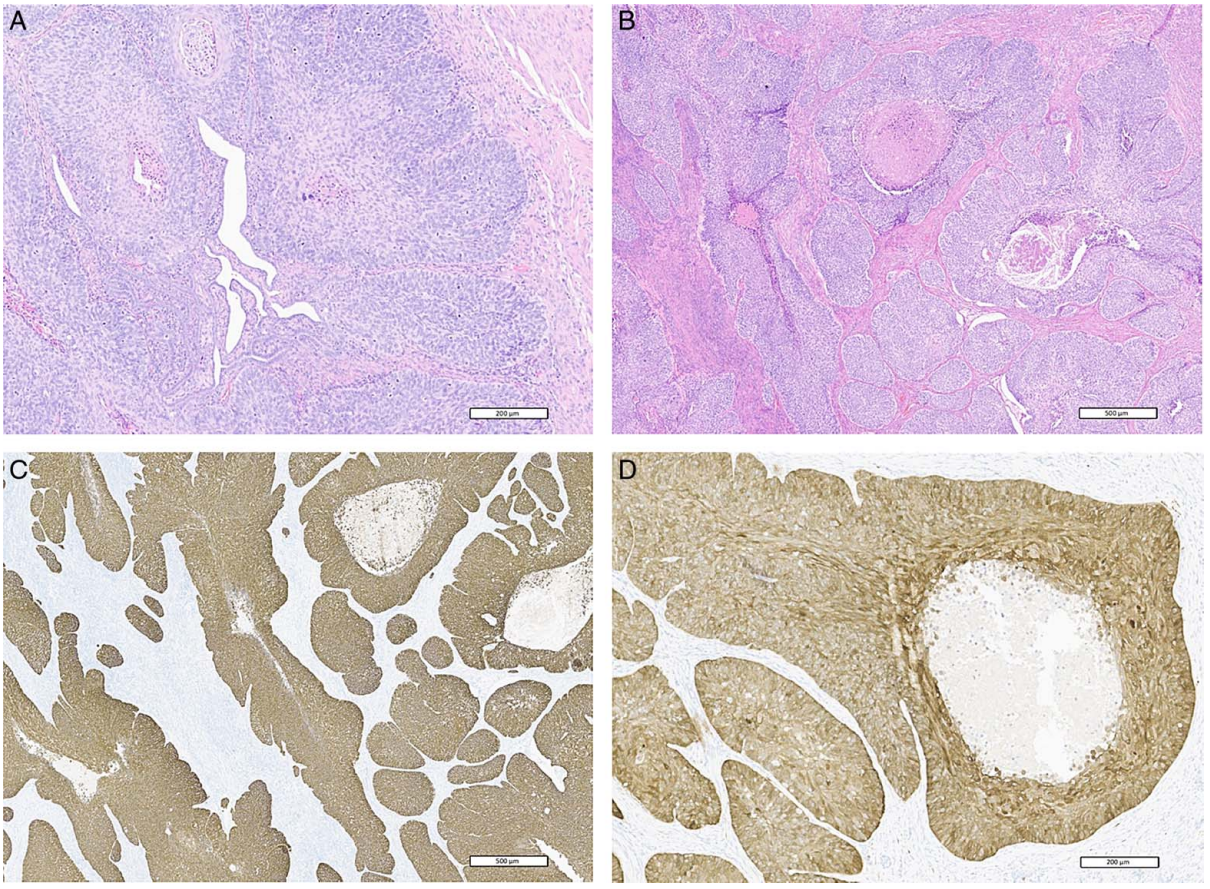

FIG. 1. (A) Left fallopian tube infiltrated by squamous cell carcinoma (hematoxylin and eosin, 40×). (B) Myometrum infiltrated by squamous cell carcinoma (hematoxylin and eosin, 40×). (C) Immunoreactivity for Cytokeratin 5 (40×). (D) p16 block type overexpression (100×).

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nosis of squamous cell carcinoma (Fig. 1) with intratumoral necrosis as neither residual endometrial nor endometrioid adenocarcinoma foci were detected. The immunophenotype of the tumor cells exhibited reactivity to cytokeratin 5, p40, cytokeratin 7, p16 (block-type), PTEN/MMAC; proficient mismatch repair proteins, wild-type p53, and Ki67 (MIB-1) comprised ~60% of the cells. Tests for PAX2, estrogen receptor, progesterone receptor, and PAX8 were negative. Thus, the final diagnosis was PESCC, FIGO (International Federation of Gynecology and Obstetrics) stage IIIA (pT3N0M0).

According to the 2020 World Health Organization (WHO) classification, the absence of an endometrioid component and the exclusion of cervical origin are essential and desirable diagnostic criteria for diagnosing this rare entity (3). In our case, there was no evidence of endometrioid carcinoma; however, p16 block-type overexpression and cervical involvement raised doubts regarding the exclusion of the cervical origin of the tumor. The cervical carcinoma staging classification includes the depth of cervical stromal invasion and the dimension of the tumor but clearly states that the extension to the corpus uteri should be disregarded (3,4). Therefore, for the diagnosis of cervical carcinoma the stage and therapeutic approach would have been underestimated. Moreover, although it has been claimed to particularly favor the diagnosis of cervical squamous cell carcinoma (2,3), p16 overexpression has also been found to be positive in PESCCs by different authors, as p16 is not always related to HPV infection (5–7).

In conclusion, our case demonstrates that p16 reactivity and cervical involvement may lead to an incorrect diagnosis. Thus, to avoid underestimating staging and treatment, PESCC should be the proper diagnosis for squamous cell carcinomas mainly localized in the corpus uteri.

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The authors declare no conflict of interest.

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