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Jurič, D., Ovanin-Rakić, A., Audy-Jurković, S., Kani, D., Ilić-Forko, J., Buković, D. (2007) *Abnormal glandular cells in a cervical smear.* Cytopathology, 17 (5). pp. 299-300.

EDUCATIONAL CASE REPORT

Abnormal Glandular Cells in Pap Smear

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Introduction

Minimal deviation adenocarcinoma (MDA), previously known as adenoma malignum (1), is a fully malignant invasive adenocarcinoma of the cervix in which neoplastic cells have a deceptively benign cytologic appearance. The tumor is often diagnosed at an advanced stage because initial superficial biopsies may be misinterpreted as benign. The diagnosis of carcinoma is often established only after the patients have undergone deep conization or hysterectomy because the depth of penetration of the glands is the key histologic feature of MDA. Although all these tumors in the original description were extremely well differentiated endocervical adenocarcinoma, MDA has been expanded to include the endometrioid and clear-cell variants

(2,3). MDA accounts for 1% to 3% of all cervical adenocarcinoma cases (2).

Case Report

In a 47-year-old female, adenocarcinoma was suspected due to cytologic detection of abnormal columnar epithelial cells and she was admitted to the Department of Obstetrics and Gynecology, University Hospital Center Zagreb for additional examination. She complained of irregular vaginal bleeding for about one year. All clinical, colposcopic and ultrasound examinations were normal. The initial Pap smear taken at the Department, showing folded branching sheets of bland appearing glandular cells in honeycomb arrangement, without significant signs of malignancy except for prominent red nucleoli, was diagnosed as adenocarcinoma (Fig. 1. Papanicolaou x100 and x 400), however, histology of endocervical curretage was interpreted as benign glandular intestinal metaplasia. One month later, Pap smear was again interpreted as adenocarcinoma, yet this time histology of punch biopsy suggested the possibility of MDA. On intraoperative examination, the cervix looked normal albeit somewhat firmer. The specimen of radical hysterectomy showed a predominance of irregularly shaped malignant glands throughout the cervical wall lined by a single layer of mucin-producing epithelial cells that appeared normal, the nuclei were basally located and showed only subtle atypia. However, significant atypia was present in a minor focus, and a metastasis was confirmed in the left ovary. The

operation was followed by pelvic irradiation. Fourteen months later, Pap smear showed neoplastic cells again, with branching sheets of glandular cells with pseudostratification ,overlapping of the nuclei and slight hyperchromasia (Fig. 2 Papanicolaou x 100 and x 200). The patient underwent reoperation, which revealed multiple metastases and she died several months later.

Discussion

Because of its rarity and subtle cytologic changes, there are only a few reports that illustrate the cytologic findings in patients with MDA, most of them confirming low sensitivity of cervical cytology in the detection of MDA (4).

Although several reports indicate MDA to express gastric phenotype and immunostaining with HIK-1084, antimucin monoclonal antibody, to be usually positive, it is still difficult to differentiate mucinous MDA from gastric metaplasia (5). Nuclear and cytoplasmic p16INK4 positivity was identified in only 30% of MDA, suggesting that high-risk HPV does not play a crucial role in the development of MDA, in contrast to the majority of endocervical adenocarcinoma (93% positivity for p16INK4) (5).

The prognosis of MDA remains controversial. An extremely poor prognosis was often reported for this disease when it was first described, but one recent study had found interobserver disagreement and significantly different mortality rates derived mostly from the

absens of consensus criteria for diferential diagnosis among benign hyperplastic lesions, MDA and common adenocarcinoma (6).

In conclusion, according to the published reports, the cytologic and histologic recognition and diagnosis of MDA may be very difficult if not impossible. However, our findings also indicate that the finding of large branching sheets of cells with prominent nucleoli points to taking MDA in consideration on differential diagnosis, and additional examination may lead to an accurate diagnosis.

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