

# A rare case of minimal deviation mucinous adenocarcinoma of the uterine cervix and review of literature

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## ABSTRACT

Minimal deviation adenocarcinoma (MDA) is uncommon and accounts for only 1-3% of all cervical adenocarcinomas, and most pathologists diagnose only one or two cases during their professional life. MDA is unusually well-differentiated adenocarcinoma of the cervix formed by neoplastic cells displaying only minimal cytological atypia. Because of the high degree of differentiation, there is a high frequency of failure to diagnose this malignancy histologically. To better understand the presentation of MDA, we are reviewing the clinical, histological, and immunohistochemistry findings in one case.

**Key words:** Adenoma malignum, cervix malignancy, minimal deviation adenocarcinoma

## INTRODUCTION

Minimal deviation adenocarcinoma (MDA), also termed 'adenoma malignum', has been reported since the first review by Gusserow in 1870. Originally, the tumor was termed as adenoma malignum because of the resemblance of its glands to endocervical glands and its lack of malignant cellular features. MDA is a rare form of cervical adenocarcinoma characterized by glandular proliferation with little or no stratification and is comprised of well-differentiated columnar epithelium of an endocervical type. Because of the high degree of differentiation, there is a high frequency of failure to diagnose this malignancy histologically.<sup>[1-3]</sup> Minimal deviation adenocarcinoma is uncommon and accounts for only 1-3% of all cervical adenocarcinomas and most pathologists diagnose only one or two cases during their professional life.<sup>[4-6]</sup> The definition of MDA has been recently amended to include endometrioid and clear cell variant, and Young and Scully have suggested that the term adenoma

malignum should be restricted to mucinous endocervical type of MDA.<sup>[1,2,4]</sup> The occurrence of a recent case in our practice afforded the opportunity to review current opinions in the literature concerning this controversial topic.

## CASE REPORT

A 35-year-old woman presented with 6-month history of profuse watery vaginal discharge and irregular vaginal bleeding. Patient had no history of hormone intake and was gravida 3, para 2. On clinical examination, the cervix was normal in size and appearance but felt firm. Sagittal T2 weighted magnetic resonance image showed a multicystic lesion. On papanicolaou smear cervical intraepithelial neoplasia 2 was diagnosed. Later on, cervical cone biopsy was performed as a therapeutic procedure and sent to our department for histopathology.

Histological examination of cervical biopsy showed neoplastic glands with marked variation in shape and size and irregular branching. Each gland was lined by a single layer of tall columnar cells with mucinous apical cytoplasm, bland looking basal nuclei, and approximated the appearance of a normal endocervical gland [Figures 1 and 2]. The glands occasionally exhibited intraluminal papillary projection with cores of fine fibrous connective tissue producing characteristic bridging and branching shapes. Stromal reaction with local inflammatory infiltration and

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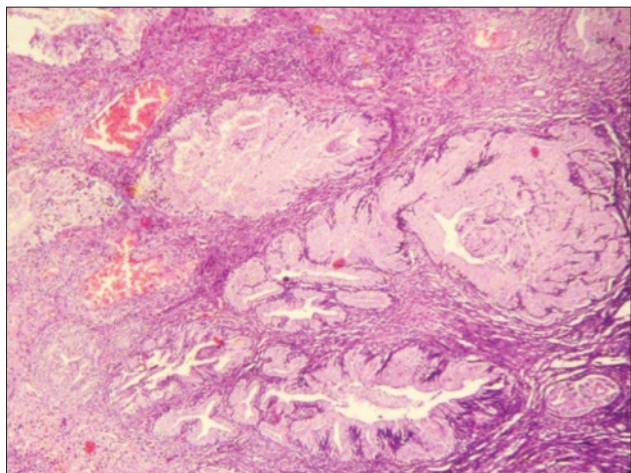
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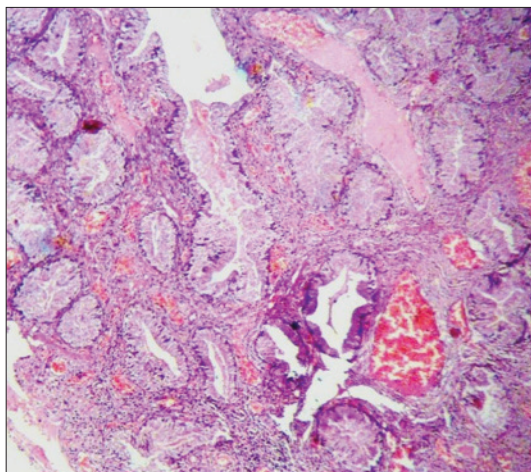
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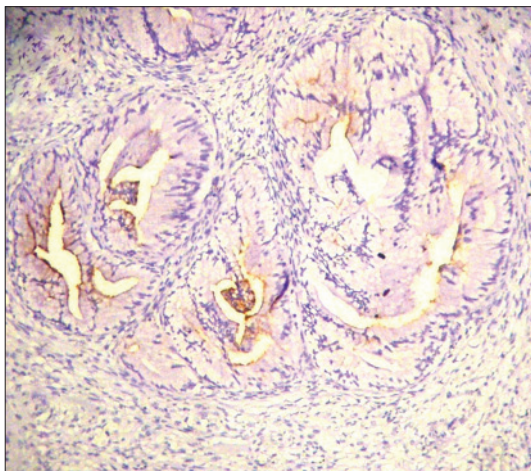
desmoplastic reaction was noted. Immunohistochemistry for carcinoembryonic antigen (CEA) showed focal



**Figure 1:** Cervical glands showing irregular branching and intraluminal papillary projections. Stromal reactions such as mild edema and inflammatory cell infiltration are seen (H and E,  $\times 400$ )



**Figure 2:** Cervical glands showing irregular branching and intraluminal papillary projections. Infolding and irregular branching are lined by mildly atypical cells. Mitoses are rarely found (H and E,  $\times 400$ )



**Figure 3:** Positive expression of CEA in minimal deviation adenocarcinoma of the cervix (H and E,  $\times 400$ )

reactivity [Figure 3]. Based on above histological and immunohistochemistry findings, diagnosis of minimal deviation adenocarcinoma of mucinous type was diagnosed.

The patient subsequently underwent radical hysterectomy for curative reason. No abnormality was seen in uterus, endometrium was unremarkable. No evidence of malignancy was found in endomyometrium, parametrium, and pelvic lymph nodes. Patient is alive with no evidence of disease 12 months after the hysterectomy.

## DISCUSSION

MDA is an extremely well-differentiated variant of cervical adenocarcinoma in which cells composing the tumor lack typical cytologic features of malignancy. These tumors were originally referred to as adenoma malignum because of the resemblance of its glands to endocervical glands and its lack of malignant cellular features.<sup>[5,6]</sup> The deceptively benign histologic appearance of adenoma malignum results in frequent diagnostic difficulties, particularly when only small biopsy specimens are available for examination.<sup>[7]</sup>

Depending upon the size of tumor, the presenting feature may be abnormal vaginal discharge and uterine bleeding. More often, it is an incidental finding in cone biopsy or hysterectomy specimen. Since papanicolaou smear or superficial biopsy may be unreliable in the diagnosis of adenoma malignum, deep conization, or hysterectomy may be necessary.<sup>[4]</sup>

The characteristic microscopic features of MDA are the presence of architecturally atypical glands that vary in size, shape, and location. In the mucin-producing forms, the glands are lined by a single layer of tall columnar epithelium that usually has minimal, if any nuclear atypia. The nuclei are bland, and are located at the base of epithelium. The glands have bizarre angular outpouchings, which vary greatly in size. Desmoplasia is frequently present. MDA often involves more than two-thirds of the thickness of cervical stroma and glandular tissue may infiltrate beyond 5.0 mm into the cervical wall.<sup>[5]</sup>

The most reliable criterion to assess malignant nature of MDA is the haphazard arrangement of glands that extend beyond the level of normal endocervical glands and presence of occasional mitosis in glandular cells. Deeply positioned nabothian cysts, tunnel clusters, microglandular hyperplasia, and mesonephric hyperplasia are the major considerations when making a differential diagnosis. Nabothian cysts appear grossly as cystic spaces filled with mucoid material and microscopically as cystically dilated glands lined by flattened epithelium, sometimes focally absent. In tunnel clusters there is localized proliferation of endocervical glands with side channels growing out from

them. However, they retain a lobular configuration and mitotic activity is not present.

In abnormally shaped benign endocervical glands, the typical stromal response may be a helpful indicator of infiltrative nature of the glands. In microglandular hyperplasia, the lobules are usually confined to the inner half of cervical wall with an unremarkable intervening cervical stroma. Adjacent mucinous glands are usually present and help exclude a mesonephric lesion.<sup>[5]</sup>

MDA often involves more than two-thirds of the thickness of cervical stroma and should be regarded as invasive because the normal endocervical crypts and tunnel clusters do not extend beyond 5 mm. Hence, in most cases diagnosis is missed on superficial cervical biopsy, and requires either a cone biopsy or a hysterectomy specimen.<sup>[5]</sup>

MDA is highly variable in its staining for CEA. It is usually positive in focal areas, whereas well differentiated cervical adenocarcinoma is usually more diffusely positive. All benign lesions, except for microglandular hyperplasia are negative for CEA. Microglandular hyperplasia differs from MDA in that it is more everting, polypoid, and superficial; and does not extend below the level of endocervical glands. Microglandular hyperplasia also has greater crowding of glands, squamous metaplasia is usually present and enlarged branching glands are absent.<sup>[2,8]</sup>

## CONCLUSION

An accurate diagnosis of MDA relies upon pathological examinations; therefore, cases with abnormal findings on clinical manifestation, CT and MRI, but with negative results on cytology, should undergo deep cervical tissue biopsy or cervical conization. As glandular tissues may infiltrate

more than 5.0 mm into the cervical wall, general cervical biopsies are not able to put forward an accurate diagnosis. Cervical conization, however, may determine the depth of interstitial infiltration.

Hence, the correct path to diagnosis of MDA is based on specimen tests obtained from cervical conization or hysterectomy.

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