Adenocarcinoma with Minimal Deviation of the Cervix: What Management?

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Summary
The cervix adenocarcinoma results in an average 15% of cervical carcinomas. It is most often associated with infection with HPV type 16 or 18. Screening has its particularities compared to squamous cell carcinoma.

The minimal deviation adenocarcinoma is a rare histological entity of cervix adenocarcinoma. Cervical cytology provides an imperfect diagnosis of glandular cells compared to squamous lesions, although the 2001 Bethesda system still allows a better management of patients with abnormal glandular cells; the diagnosis is based on histological study. We report a case of 46 years-old woman that was treated for minimal deviation adenocarcinoma of the cervix.

It is likely that in future, the screening either cytological or viral must be completed by a specific molecular marker of these lesions.

Keywords: Adenocarcinoma in minimal deviation; Cervix

Introduction
The minimal deviation adenocarcinoma was described in 1975 by a gynecologist as "malignant adenoma".

In 2003, the WHO has defined it as endocervical adenocarcinoma mucinous, well differentiated, consisting of an endocervical glandular hyperplasia of lobular architecture resembling glands but with the characteristics of adenocarcinoma [1].

It is associated in 10 to 15% with Peutz-Jeghers syndrome, but also frequently Lobular Endocervical Glandular Hyperplasia (LEGH). A mutation in the gene STK11 was also found in half of the sporadic cases [1].

Observation
A 46 years old woman, followed for fibrocystic dystrophy breasts for 1 year, G5P3, who consulted for peri-menopausal metrorrhagia. The endometrial atrophy is revealed on a curettage endometrial biopsy. Surgical treatment was offered to the patient who received a total hysterectomy adnexal inter-vaginally, the pathological results returned for minimal deviation adenocarcinoma of the cervix with simple hyperplasia of the endometrium without atypia.

A staging was done without abnormalities, especially a pelvic MRI that objectified pelvic hematoma lateralized to the right of 45/35 mm without invasion of parameters.

The patient was treated with bilateral pelvic lymph node dissection and bilateral parametrectomy and oophorectomy bilateral.

Monitoring post-operative clinical and biological was without particularities and showed no recurrence. Macroscopically, the collar measures 3 cm wide and 3 cm high and shows no visible abnormality. The endometrial cavity shows no abnormality.

Histological examination shows on the ectocervix squamous epithelium of normal morphology based on a chorion seat of an inflammatory infiltrate. The surface epithelium of the endocervix showed no abnormality. There is, on the other hand, a hyperplasia of the endocervical glands. Some of these glands contain no cytological atypia. Others have a unistratified core with slightly increased volume with few mitotic figures. The cytoplasm is clear or has a low secretion of mucin. These abnormal glands penetrate deeply into the stroma of the endocervix. Endocervical glands in tubal metaplasia are associated with it. The endometrium is the seat of a simple and non atypical hyperplasia (Figures 1 and 2). The abnormal endocervical glands showed positive staining with CD 10 and P16 INK 4a is negative.

The patient received no adjuvant therapy. She was still alive, without local or distant metastases after 2 years.

Discussion
Well-differentiated mucinous endocervix adenocarcinomas correspond to 70% of endocervix adenocarcinomas [2].

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Adenocarcinoma with minimal deviation or “adenoma malignum” is a very rare well-differentiated form of endocervical adenocarcinoma.

Clinic: Bleeding with an aqueous especially abundant vaginal discharge, mucinous Clinical examination, the cervix is usually firm and indurated barrel.

Histology, the lesion consists of glands cylindrical coating with apical secretory vacuoles and some atypical nuclei with irregular contours angular, of varying size and shape and desmoplastic stroma, especially located deep in the neck more than 5 mm from the surface.

The presence of vascular emboli or neoplastic engainements confirmed malignancy. The prognosis is similar in all respects to that of other well-differentiated invasive adenocarcinoma Positivity: PAS-Alician Blue 2.5 + periglandular actin and negativity: acid mucin, p53, CD10, calretinin. Anti-CEA antibody appears focally positive, with cytoplasmic staining in tumor glands, and negative in normal glands. The ACE was initially considered a good tumor marker for the diagnosis of minimal deviation adenocarcinoma, but other immunohistochemical studies have challenged this point involved. By cons, RE / RP - on tumor glands, while a nuclear staining is observed in normal glands.

It is noted in the literature an expression of CA 125 in the normal endocervical glands unlike tumor glands, and the more abundant presence of sialomucins over sulfomucins. In addition, gastric mucin type have been identified in tumor glands. HPV most often negative.

Most glands are bordered by columnar cells which have the nucleus in basal position and with a cytoplasm which retains mucosecretion. Some glands contain nuclear atypia and mitotic (Figure 2). An important point to make the diagnosis is the penetration glands in the stroma deeper than normal endocervical glands. The perineural and vascular invasion is common. This entity must be differentiated from endocervical glandular hyperplasia where the glands in the stroma remain superficial and where there is no vascular or perineural emboli. Adenocarcinoma which develops from the mesonephric remnants is another differential diagnosis [3]. Abnormal glands do not contain mucin; the light on the other hand contains an eosinophilic secretion or hyaline. Abnormal glands, in addition to the marking with the epithelial markers cytokeratin and EMA-type, are often marked by the CD 10 antigen. Labeling with CD10 antigen is more variable in adenocarcinomas with minimal deviation.

Adenocarcinoma with minimal deviation may be associated with an ovarian tumor. Ovarian tumor is in this case a mucinous adenocarcinoma or a sex cord tumor with annular tubules [4,5]. There is also a Peutz–Jeghers syndrome in 15% of cases. Somatic mutation of the STK11 gene, which is the gene responsible for Peutz–Jeghers syndrome, is found in half of the cases of minimal deviation adenocarcinoma.

The development of minimal deviation adenocarcinoma is generally pejorative because of late diagnosis and the presence of perineural and vascular emboli.

The presence of endocervical glands located deep in the endocervical stroma should encourage the search for the presence of atypia and vascular emboli.

Several benign lesions, cytologically and histologically, may simulate adenocarcinoma: tubal metaplasia, glandular atypies related with inflammations or radical changes, microglandular hyperplasia.

The atypia is not marked differential diagnosis arises with benign glandular lesions tunnel clusters, the mesonephric hyperplasia, cysts deep Naboth the microglandular hyperplasia, glandular hyperplasia and diffuse hyperplasia deep strip of endocervical glands.

The criteria that help in the diagnosis of malignancy is the presence of variable glands in size and shape, a fibrous stroma reaction, desmoplastic, glands with irregular and angular contours and rare images of mitosis. Depth extension sometimes > 2/3 of the thickness of the neck. Genetics of malignant adenoma: mutation in the 19p13.3 STK11 gene responsible for Peutz–Jeghers syndrome.

The treatment is surgical: with extended lymphadenectomy colpospectomy.

The prognosis is poor because of late diagnosis (5 year survival in stage 1 is 50%) and of the frequency of pelvic and peritoneal metastases [3,6].

Conclusion
ADK with minimal deviation is a rare histological type of adenocarcinoma. This tumor is often diagnosed around age 50 and frequently associated with ovarian carcinoma, mucinous adenocarcinoma in type or sex cord tumors in tubules ringed. Other predisposing factors are exposure to diethylstilbestrol and the association to HPV 18.

Imaging does not bring a great help in diagnosis. A cervical papanicolaou test is most often normal. The diagnosis is basically based on deep cervical biopsy or the conization piece. The standard histological diagnosis is essential to passing the plan glands. The essential histological diagnosis criterion is the exceeded plan of the glands.

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