Immunopathological study of mesonephric lesions of cervix uteri and vagina

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Summary

Seventeen cases of mesonephric cervical remnants, four cases of mesonephric cervical carcinoma and nine vaginal Gardner cysts were studied by histochemical and immunohistochemical methods for the presence of mucin, proteoglucans, glucogen, CEA, cytokeratins, secretory component and vimentin. Mesonephric lesions in contrast to endocervical glandular lesions are negative for mucin, glucogen, CEA, and secretory component and positive for vimentin, and broad spectrum cytokeratins. Mesonephric carcinomas present certain immunopathological characteristics that permit their identification and proper treatment.

Key words: Cervix mesonephric lesions vagina; Gardner cysts.

Introduction

The aim of this study was to investigate the pathological and immunopathological characteristics of mesonephric lesions of the lower female genital tract. The female genital tract is created mostly by the paramesonephric ducts of Muller. The mesonephric duct system of Wolff, extending from the parovarium to the vagina eventually regresses, leaving residual foci [1]. These remnants are usually localised in the parovarium, at the lateral wall of the uterine corpus, the cervix and the vagina, where they create Gardner's cysts [2, 3].

Mesonephric lesions in the cervix are located 3-6 mm underneath the endocervical mucosa and give rise to uncommon benign and malignant lesions. The recognition of these malignant lesions as mesonephric, is necessary for their proper treatment, because of the fact that they tend to behave as squamous infiltrating cervical tumours [4-8].

Material and Methods

The material of this study comprises 19 cases of hyperplasia that developed on mesonephric remnants in the cervix, four cases of mesonephric cervical adenocarcinoma and nine cases of mesonephric vaginal cysts. Cervical mesonephric lesions were recognized in hysterectomy specimens (9 cases) and in conization cervical specimens excised for dysplastic changes of the squamous epithelium (10 cases). The cases of cervical mesonephric carcinoma were initially diagnosed in diagnostic curretage specimens as common adenocarcinoma of the endocervix.

A pathological study was made on histological sections routinely processed and stained with hematoxylin-eosin. For the study of the histochemical properties of these lesions special methods for proteoglucans (PAS), glucogen (PAS-diastase) and epithelial mucin (Mucicarmine) were used. The cellular response to the histochemical study was reported separately for the cells and their glandular secretions. A comparative study was made with the cellular response of the superficial endocervical mucosa to the same histochemical methods. All cases were studied immunohistochemically for CEA (mab Monosan), broad spectum Keratins (Monosan), Vimentin (mab Monosan) and secretory component (Poly-Dako). A streptavidin-Biotin method was used on paraffin-embedded, formalin-fixed histological sections. The negative reaction was recorded as a negative (–) and the positive as faint (+) when less than 20% of glandular cells showed a positive staining reaction, and intense (++) when more than 20% showed a positive reaction.

Results

1. Benign mesonephric lesions were observed deep in the lateral cervical wall, at least one optical field (under a high power magnification) underneath the surface endocervical mucosa (Figure 1). In all cases, a duct or part of it was observed which focally branched into small glands, sometimes cystically dilated. The epithelium of the duct and the glands was cuboidal or flattened, the

Figure 1. — Histological section showing the mesonephric remnant in the cervical wall (H & E x 100).

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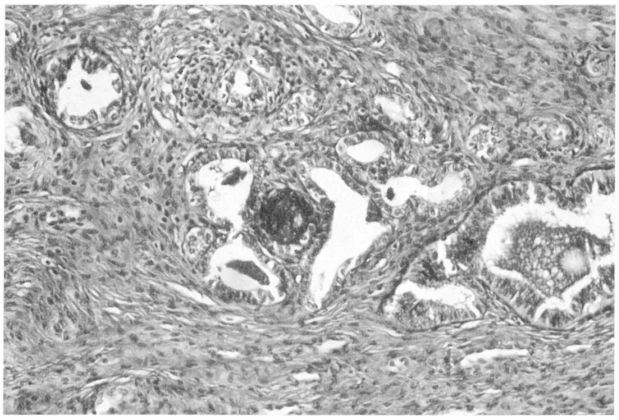

Figure 2. — Histological section of cervix showing the mesonephric glands with eosinophilic secretion (H & E x 400).

cytoplasm was amphiphil and the nuclei were round with thin chromatin. The glandular lumina contained eosinophilic secretion (Figure 2).

In all cases focal glandular hyperplasia was observed, with slight nuclear atypia, a tendency for cellular stratification, but no mitotic activity. There was no desmoplastic reaction of the surrounding cervical wall or any degree of inflammatory reaction. The mesonephric grandular cytoplasm gave a negative reaction for proteoglycans, glycogen or mucin, although a positive reaction to PAS was noted in the glandular secretion. The mesonephric vaginal cysts, measuring from 1.5-5 cm, presented cuboidal or flattened epithelium that showed a similar histochemical reaction.

2. Mesonephric adenocarcinomas consisted of small glands or compact cellular masses extending to the cervical surface and infiltrating the two-thirds of the cervical wall thickness (in 2 cases) and all of the cervical wall extending almost to the outer cervical surface (2 cases) (Figure 3). In all cases the malignant glandular cytoplasm stained clear or pale and the nuclei were small and hyperchromatic, focally of a hobnail morphology. Many

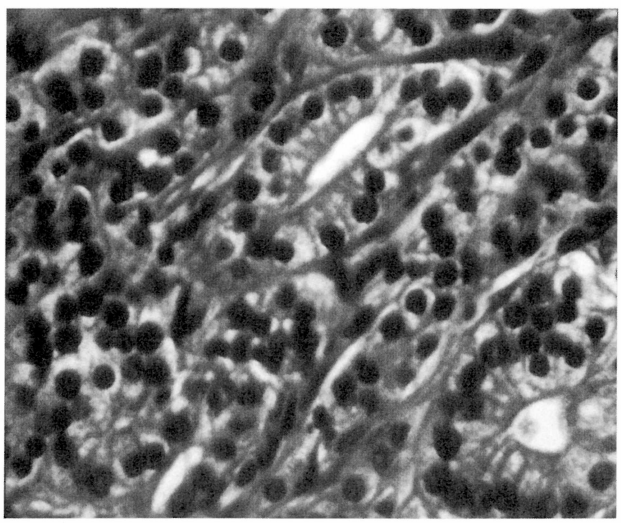

Figure 3. — Mesonephric adenocarcinoma diffusely infiltrating the cervical wall (H & E x 250).

mitoses were observed, as well as a concomitant inflammatory and stromal response. A positive reaction to the PAS histochemical method in the lumina secretion showed the presence of proteoglucans in these adenocarcinomas.

Immunohistochemistry: mesonephric lesions showed a negative immunohistochemical reaction to CEA and the secretory component. This was in contrast to the positive immunoreaction to these substances that the normal endocervical glands gave. All cases showed a positive reaction to broad spectrum keratin markers, in common with superficial endocervical mucosa and to vimentin, in contrast to endocervical mucosa.

Discussion

In the uterine cervix mesonephric remnants are observed in 0.4-27% of the specimens of uteri removed for various lesions and/or in conization specimens removed for dysplastic changes of the squamous epithelium [2-5]. The highest incidence is observed in the conization specimens where the whole of the cervix is examined in parallel sections. Until recently the possibility that these remnants could be hyperplastic and even show atypical changes was not appreciated with the result that problems in the differential diagnosis from minimal endocervical adenocarcinoma have arisen [6]. Mesonephric hyperplasia is defined as the presence of many small hyperplastic glands surrounding the main mesonephric duct without any remarkable cellular atypia or mitotic activity. Based on the architecture of the glandular structures, mesonephric hyperplasia has been classified into two different histologic types. The most common is the lobular type, characterized by tubular clusters with a central duct. This form tends to occur in young women and arises deeper in the cervical stroma. The other type is the diffuse form where clustering round the mesonephric glands is absent [7].

Thirteen of our examined cases were of lobular type and 4/17 of the diffuse type of mesonephric hyperplasia. In 4/17 cases nuclear atypia and cellular stratification but without mitotic activity was observed as well. The differential diagnosis of hyperplastic mesonephric glands must be made from a well differentiated endocervical adenocarcinoma that presents mitoses, remarkable atypia and stromal reaction in the form of desmoplasia and/or inflammatory reaction. No other therapeutic proceeding is needed in cases of hyperplasia or even atypical mesonephric hyperplasia.

Adenocarcinomas arising in mesonephric remnants are rare entities with a tendency to occur in younger patients [4-6, 8]. Mesonephric carcinoma in the past was confused with clear cell carcinoma of the cervix [9]. Only 14 cases are reported in the literature, ten pure adenocarcinomas and four of mixed type, presenting a malignant spindle cell component as well. Grossly they present as a cervical mass, deeply infiltrating the cervical wall. The most common is the ductal type consisting of glands of various size. Retiform, tubular and sexcord patterns are described as well [9].

Criteria for the diagnosis are strict. The tumor must be located deep in the cervical wall, the endocervical mucosa must be uninvolved and there must be no evidence that the patient has been exposed to DES [7-9].

The differential diagnosis of mesonephric carcinoma from hyperplasia is based on extensive and diffuse stromal infiltration and malignant nuclear morphology.

There is evidence that mesonephric carcinomas behave as squamous cell carcinomas and they are not sensitive to irradiation [6-8], thus they have to be treated by radical uterine resection with parametrial lymph node dissection. Our cases were treated with radical hysterectomy. No lymph-node metastases were observed. The differential diagnosis from common endocervical adenocarcinomas is based on the morphology in general, the coexistence of dysplastic changes of endocervical glands adjacent to the adenocarcinoma, the absence of mucin, the negative immunohistochemical reaction for CEA, and the secretory component and the positive reaction for vimentin in mesonerphric adenocarcinoma.

In conclusion, mesonephric remnants of the lower female genital system are rare entities that may give rise to hyperplastic lesions, atypical lesions and adenocarcinomas, with distinct morphological and immunopathological characteristics that permit their identification and proper treatment.

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