Vaginal clear cell carcinoma in a young patient with ectopic termination of the left ureter in the vagina

Abstract The association of clear cell adenocarcinoma of the vagina and vaginal adenosis with prenatal exposure to diethylstilbestrol (DES) is well-documented in the United States. In Europe, however, DES was never used in the therapy of threatened abortion and, therefore, clear cell adenocarcinoma and vaginal adenosis remained rare diseases. We report on the clinical and pathological features of a case of clear cell adenocarcinoma of the upper vagina in a 17-year-old German girl, who had a history of hypoplasia of the left kidney with an ectopic termination of the ureter in the upper vagina, removed surgically 2 years before. No previous report of a similar coincidence of vaginal clear cell carcinoma and a congenital disorder of the genitourinary tract exists. Congenital anomaly of the ureter interfering with the development and the differentiation of the distal Müllerian tract and its epithelium might have provided a similar histological basis for carcinogenesis in our patient to that in those provided exposed to DES.

Key words Clear cell adenocarcinoma • Vaginal Ureteral ectopia

Introduction

Clear cell carcinoma of the vagina is a rare tumour occurring in the upper vagina of children and young adults. In about two-thirds of all cases reported, a history of intrauterine exposure to diethylstilbestrol (DES) was confirmed in the United States (8), pointing to the possible role of DES in the pathogenesis of this rare neoplasm. In Europe where DES had seldom been used in pregnant women, clear cell carcinoma of the vagina as well as vaginal adenosis are extremely rare. While the hypothesis of DES-related oncogenesis in the USA was strengthened by the findings in animal models (10, 11), the histogenesis of vaginal clear cell carcinoma without prenatal exposure to DES remains obscure, though there are no differences regarding morphology nor the clinical aspects of these tumours.

We report on a case of vaginal clear cell carcinoma in a patient without preceding exposure to DES, but with a history of a hypoplastic left kidney and ectopic termination of the ureter in the upper vagina.

Clinical history

A 17-year-old nulliparous woman presented with continuous vaginal bleeding. She was diagnosed as having an ectopic ostium of the left ureter into the left lateral fornix of the vagina at the age of 6. The ureter and a hypoplastic left kidney had been surgically removed in 1991 when the patient was 15. No vaginal tumour had been found and there was no history of intrauterine exposure to hormones by maternal intake of DES of treatment with agents known to be oestrogen modulators such as tamoxifen or danazol.

On examination with the vaginoscope a polypoid mass was seen in the upper vagina and the right anterior wall. The cervix uteri could not be identified behind this tumour. Vaginal endosonography and CT scanning revealed a normal-sized uterus and ovaries, the tumour being restricted to the vagina without evidence of intrauterine or abdominal spread. The right kidney and ureter were of normal size and shape on intravenous pyelogram.

The patient was treated by radical hysterectomy, partial vaginectomy, and bilateral pelvic lymph node dissection with preservation of the ovaries. Following surgery, the patient received intensive intravaginal radiotherapy (40 Gy, 5 fractions) using high dose brachytherapy.
Fig. 1 Surgical specimen of hysterectomy and partial vaginectomy showing polypoid tumour masses in the vagina

Fig. 3 Remnants of Gartner’s duct in the lateral vaginal wall, showing no relation to the surrounding tumour infiltrate

Materials and methods

The tumour was investigated using H&E, Di-PAS and Gordon-and-Sweet stains. Immunohistochemistry was performed on paraffin and fresh frozen sections using antibodies against cytokeratins, vimentin, carcinoembryonic antigen (CEA) (DAKO), oestrogen receptor, progesterone receptor (Abbott) and the proliferation associated antigen Ki-67.

Pathological findings

A polypoid large tumour with central ulceration and a maximal diameter of 5.5 cm was found in the vagina in the surgical specimen (Fig. 1). The main tumour mass was located in the upper vagina, resulting in the destruction of the lower cervix and portio uteri with smaller parts of the tumour extending to the lower vagina. Since parts of the tumour reached the margins of surgical resection, a further part of the vagina was removed, also showing small polypoid tumour masses.

The tumour showed a mixed growth pattern with papillary, tubular, cystic, and solid areas. It was largely composed of polygonal and hobnail cells with large and irregular nuclei. An abundant clear cytoplasm with negative PAS-staining could be seen in most of the tumour cells, preferably in areas with a solid growth pattern (Fig. 2). The tumour infiltrated deeply into the smooth muscle layer of the vagina, and no vascular invasion was observed. In the lateral vaginal wall small residues of Gartner’s duct were detectable (Fig. 3). However, no obvious relationship of these structures to the carcinoma was seen. In small areas inconspicuous fragments of intact squamous epithelium were found mainly in the additional tissue removed from the lower vagina. Adenosis was not evident in these structures. All lymph nodes were found to be free from tumour infiltrates.

Immunohistochemistry revealed positive reactions of tumour cells with antibodies for cytokeratins 13/14 and 8/18, but negativity for vimentin and CEA. No expression of oestrogen or progesterone receptors could be detected. The proliferation associated antigen Ki-67 was positive in up to 60% of the tumour cells.

The surgical specimen of the hypoplastic left kidney was small (approximately 2 cm maximal length) with regular glomeruli and normal vessels. Small suburothelial infiltrates of lymphocytes and plasma cells were seen in the pelvic system. A regularly differentiated transitional epithelium was found in the ureter accompanied by a scanty round cell infiltrate and slight fibrosis. No atypical cells were observed.

Discussion

Glandular lesions of the vagina are rare, the organ is normally devoid of glands and lined by squamous epithelium. The incidence of benign glandular changes (adenosis) as well as adenocarcinomas of clear cell type rose significantly in the USA in 1970 and following years, related to prenatal DES-exposure during the 1940s through the 1960s (1, 9). In countries where DES was not used during pregnancy, vaginal adenosis is only rarely observed; sporadic cases of malignant epithelial tumours with glandular differentiation are mainly found to be endometrioid type, mucinous and mesonephric carcinomas. In contrast, clear cell carcinomas are even rarer with a striking morphological and clinical similarity to the DES-related cases reported in the USA, as observed in our 17-year-old patient (7).