



Colonic Adenocarcinoma of a Neovagina in a Patient with Mullerian Agenesis

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Abstract

Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome, also known as Mullerian agenesis, is a largely sporadic disorder resulting in absence or hypoplasia of the vagina, uterus, and fallopian tubes. In order to foster adequate psychosocial development and sexual intercourse, a number of surgical procedures are available, one of which is the creation of a neovagina from a segment of sigmoid colon. In this report, we describe a patient who presented at age 17 amenorrhea and was found to have MRKH. She underwent vaginal reconstruction with a neovagina from a segment of her sigmoid colon at age 19. Subsequent to this procedure, the patient developed carcinoma of the breast and renal cell carcinoma, and in addition developed an invasive mucinous adenocarcinoma of her neovagina. This is only the third case of an adenocarcinoma arising in a neovagina in the setting of MRKH, and the first case described with an accompanying adenomatous component. All three cases to date demonstrated a mucinous phenotype. Overall, this case emphasizes that neovaginal mucosa may undergo neoplastic transformation, and that recognition of this possibility is important in long-term follow up care for patients affected MRKH treated by surgical reconstruction.

Keywords: Mullerian agenesis; MRKH; Neovagina; Adenocarcinoma

Introduction

Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome, also known as Mullerian agenesis, is caused by incomplete development of the Mullerian Ducts, resulting in underdeveloped or absent vagina, uterus, and fallopian tubes [1]. The condition is usually detected in late adolescence with failure of menstruation. After gonadal dysgenesis, MRKH is the second most common cause of primary amenorrhea [2]. Nonsurgical vaginal dilation or surgical creation of a neovagina are among the treatment options, and allow for normal sexual intercourse [3,4].

Case Report

A 49 year old woman presented initially at age 17 with primary amenorrhea and was diagnosed with Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome, or Mullerian agenesis. The patient was said to have a "pea-sized" uterus and completely absent vagina and fallopian tubes. She had a neovagina created from a segment of her sigmoid colon at age 19. No signs of androgen excess were noted.

At age 38, the patient was diagnosed with clear cell renal cell carcinoma, and at age 44, she was diagnosed with infiltrating ductal carcinoma of the right breast. Her family history was remarkable for ovarian cancer, as well as colon cancer in her mother and maternal grandmother, the latter passing away at age 36 of metastatic disease. Because of her past medical history and family history of multiple malignancies, the patient had yearly mammograms and colonoscopies. Her most recent colonoscopy in 2013 revealed two tubular adenomas. Shortly thereafter, she suffered a fall and a right hip fracture, at which

time a 3 cm vaginal mass was also detected. The patient was otherwise unaware of the mass and reported no pain, hemorrhage, or other symptoms aside from an intermittent, yellow vaginal discharge. In addition, during the course of her follow up for neovagina surgery, the patient had two vaginal biopsies, one 15 years prior to the current presentation, and a more recent biopsy one year prior to presentation, both of which were benign. The specific indication for these biopsies was not indicated in the medical records. After recovery from hip surgery, the vaginal mass was biopsied and excised, and the neovagina was subsequently resected.

Excision of the vaginal mass showed invasive, moderately differentiated adenocarcinoma arising in a villous adenoma (Figure 1). Carcinoma extended to the margin of both the excision specimen, and additional excised mucosa segments, so resection of the remainder of the neovagina was performed. After examination of the entire tumor specimen, the carcinoma was further characterized as invasive moderately differentiated, mucinous adenocarcinoma (Figure 2). One out of five lymph nodes were positive for metastatic adenocarcinoma. The remainder of the neovagina showed no additional lesions (Figure 3).

Discussion

In this case report, we demonstrate mucinous adenocarcinoma arising in a villous adenoma, and involving a neovagina created from a segment of sigmoid colon in a patient with MRKH. To our knowledge, this is only the third such case reported in the literature. Munkarah et al. [5], reported a case of mucinous adenocarcinoma arising in a neovagina, although this case was complicated by rectovaginal fistula, which led the authors to speculate that chronic inflammation in the affected segment of tissue contributed to the development of

carcinoma. An additional case was reported by Hiroi et al., in which a mucinous adenocarcinoma arose in a neovagina 30 years after the surgical reconstruction, essentially identical to the case reported here [6]. It is interesting that all three reported cases to date had a mucinous phenotype, although the numbers are presently too few to establish statistical significance. The case reported here is the only case so far described to have arisen in adenomatous tissue.

MRKH syndrome is a rare, largely sporadic congenital syndrome with no specific genetic linkages known aside from familial clustering. The incidence of MRKH is approximately 1 in 5,000 females [7]. A possible atypical form of the disorder is linked to WNT4 mutation and associated with androgen excess [1]. It has been postulated that the Mullerian duct system ceases development sometime around days 44-48 of gestation. Individuals with MRKH syndrome have a chromosomal pattern of 46, XX with normal functioning ovaries, external genitalia, breast and pubic hair development, while the extent of development of the vagina, cervix and uterus can vary. MRKH may be isolated (type 1), or associated with other malformations, typically of the urinary tract [7,8] (type 2).

The clinical differential diagnoses include 5-alpha reductase deficiency, androgen insensitivity syndrome, congenital adrenal hyperplasia, hermaphroditism, mullerian-inhibiting substance deficiency, and Turner syndrome. Chromosomal analysis can exclude karyotypic abnormalities of the X chromosome and androgen insensitivity syndrome [2,3]. Imaging modalities, including ultrasound, MRI, and laparoscopy can be used to determine length of obstruction of the vagina, evaluation of the uterus and fallopian tubes, and presence of a cervix [9].

The presence of multiple malignancies in this patient raises the issue of hereditary tumor syndromes. Hereditary non-polyposis colon cancer or Lynch syndrome may be suggested by the presence of colon cancer in the patient's mother and maternal grandmother who became symptomatic and died in her 30s. On the other hand, the constellation of renal cell carcinoma, breast carcinoma, and colorectal carcinoma does not fit well with any known tumor syndrome. Microsatellite testing has not been performed to date.

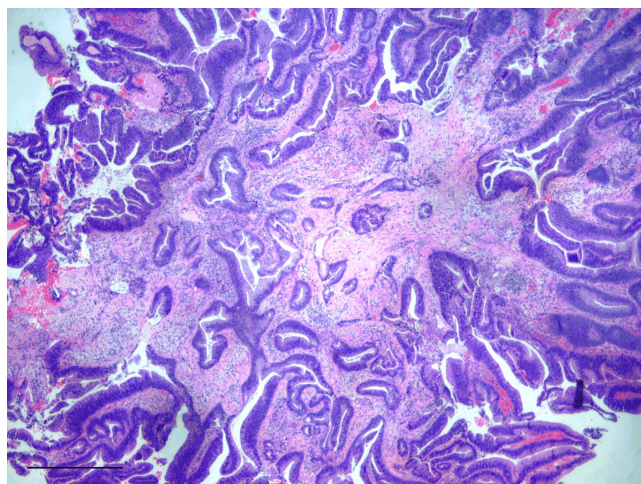


Figure 1: Photomicrograph of invasive, moderately differentiated adenocarcinoma arising in a villous adenoma (scale bar=250 μ m).

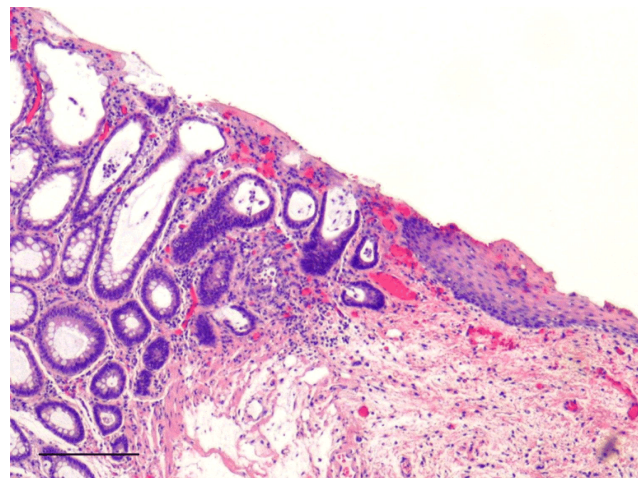


Figure 2: Mucinous component of invasive adenocarcinoma (scale bar=300 μ m).

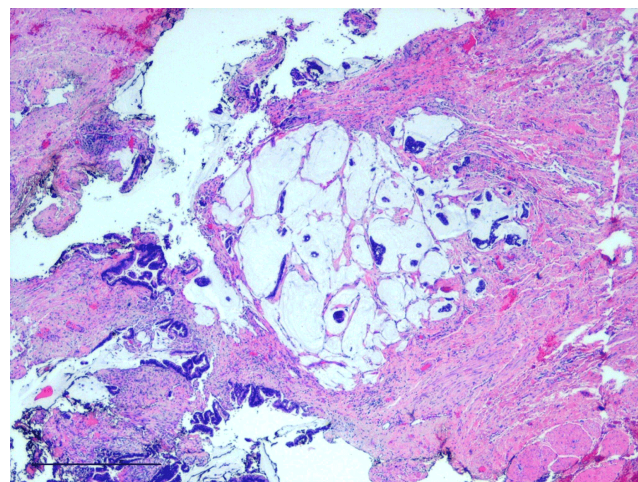


Figure 3: Neovagina uninvolved by adenocarcinoma, showing continuity between squamous and colonic mucosa (Scale bar=100 μ m).

In conclusion, we report a rare case of adenocarcinoma involving a segment of sigmoid colon used in the construction of a neovagina in a patient with MRKH. This case emphasizes that neovaginal mucosa may undergo neoplastic transformation, and that recognition of this possibility is important in long-term follow up care of patients affected MRKH treated by surgical reconstruction.

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