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Case report

Development of a mucinous adenocarcinoma on a sigmoid colpoplasty for vaginal agenesis: About a case report and review of the literature

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A B S T R A C T

We report a case of mucinous adenocarcinoma developed on sigmoid colpoplasty, performed for a congenital agenesis vaginal. The cancer development of neovagina remains exceptional. Its management consists, in the majority of cases, in surgery for a complete excision. Adjuvant treatments are associated according to the pathological results and the neovagina reconstruction technique performed.

1. Introduction

Vaginal agenesis can be isolated or, integrated as part of Mayer-Rokitansky-Küster-Hauser syndrome has an incidence of 1/4500 to 5000 women. The diagnosis was made following primary amenorrhea associated or no with abdominal pain (Committee on Adolescent Health Care, 2018). This pathology impacted on women's sexual life, their psyche and fertility. First-line management was vaginal elongation. Several surgical procedures are described to create a neovagina: bowel vagino-plasty with a small intestine or the sigmoid, the Williams surgery using the skin of labia majora, a split-thickness or full thickness skin graft placed over a vaginal mold into an omental flap, or a gracilis flap and the Davydov procedure (Schober, 2007; Dargent et al., 2004; Callens et al., 2014). However, its implementation exposes more frequent complications such as bladder or rectal wounds, graft necrosis, fistulas, inflammatory bowel diseases and mucinous adenocarcinoma (Schober, 2007; Dargent et al., 2004; Callens et al., 2014). Cancer of neovagina remained exceptional (Schober, 2007). Fourty-four (with 5 cases in transgender patients) cases of neovagina cancer have been reported in the literature (Schober, 2007; Reyes Claret et al., 2017; Fierz et al., 2019; Fernández-Ruiz et al., 2019; Kokcu et al., 2011; Liebrich et al., 2006; Wielgos et al., 2008; Yamada et al., 2018; Kita et al., 2015; Lambert et al., 2013; Bogliolo et al., 2015). Only 13 cases of mucinous adenocarcinoma are described (Table 1). We described the fourteenth case in this report.

2. Case report

A 67-year-old patient with postmenopausal vaginal bleeding underwent hysteroscopy with biopsy. Pathology result found an endometrioid endometrial adenocarcinoma. The patient has been referred to our department for further treatment.

In her medical history, she had a congenital vaginal agenesis with a unilateral renal atrophy. A neovagina by sigmoid colpoplasty was performed when she was 27 years old. At 48 years old, she presented a breast cancer without recurrence. She had no other personal history or risk factors. The only family history found a colon cancer in her mother after 65 years old. Therefore, the patient had no indication for colonoscopy follow-up.

Clinical examination revealed a lesion infiltrating the neovaginal wall with a budding part in the neovaginal lumen. The size is estimated at 2 cm. Cervix was normal. Vaginal touch revealed induration of the vaginal wall facing the budding zone. We completed the work-up with a pelvic magnetic resonance imaging showed an infiltrating mass of uterus, with vaginal and 50% myometrial invasion (Fig. 1). The thoraco-abdomino-pelvic scan did not show other lesions. In view of the history of colpoplasty with the sigmoid, and clinic examination, a pathological reading of the initial biopsy was requested. It ultimately concluded it was a mucinous adenocarcinoma. So, a total colonoscopy was performed and didn't reveal any digestive tumors.

A total radical hysterectomy (B1 type of Querleu-Morrow classification, 2017) with bilateral salpingo-oophorectomy and subtotal vaginectomy were performed by two oncologists' surgeons: a gynecologist and a digestive. A part of meso-neovagina and lymph nodes were

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removed (Fig. 2). The post-operative care was simple and patient returned at home after 5 days of hospitalization. The pathology found a mucinous adenocarcinoma developed in the colonic mucosa of the neovagina with a myometrial infiltration. Margins and ganglions were not affected. A microsatellite phenotype did not find an instability. An adjuvant chemotherapy with 5-fluorouracil was performed because the cancer is classified T4N0M0 (myometrial invasion).

3. Discussion

The cancer development in a neovagina remains exceptional (Schober, 2007; Hiroi et al., 2001). This phenomenon can be described in two main groups: the recurrence of the cancer that caused the neovagina, or the cancer development from the tissues that allowed the neovagina. Our case report is an example of its latter group. It was following a genital malformation that patient underwent a neovagina reconstruction with sigmoid. Therefore, we will limit our discussion to this group.

Mainly two histologic types of tumors are described: mucinous adenocarcinoma and squamous cell carcinoma. In general, a neovagina squamous cell carcinoma was preferentially diagnosed when neovagina was performed with skin of labia majora, a split-thickness or full thickness skin graft, while mucinous adenocarcinoma is more commonly described in the case of colon or small intestine transposition. The type of cancer seems to be related to the type of tissue used in the reconstruction (Schober, 2007; Yamada et al., 2018; Hiroi et al., 2001).

In the literature, only 13 cases of neovagina mucinous adenocarcinoma were described, in the majority of cases, neovagina was performed by digestive tract transposition *(*Table 1*)*. Munkarah *and al.* (Munkarah et al., 1994) described a case of mucinous adenocarcinoma developed in neovagina performed by split thickness dermal. However it is a rectal cancer developed on a fistula between the rectum and the neovagina. This rectal cancer later spread to the neovagina.

The mucinous adenocarcinoma origin in neovagina is considered to be multifactorial. In part, it is believed to be identical to the risk factors for cancers of the intestine or colon: lifestyle, environmental factors, hereditary components (Sterpetti and Sapienza, 2019). In our case, the patient had a first-degree family history of digestive cancers. But there was no indication for personalized colorectal cancer screening in our patient because of this single-family history after the age of 65. The patient did not smoke, was not alcoholic or obese. Therefore, she did not have any major risk factors for developing colorectal cancer.

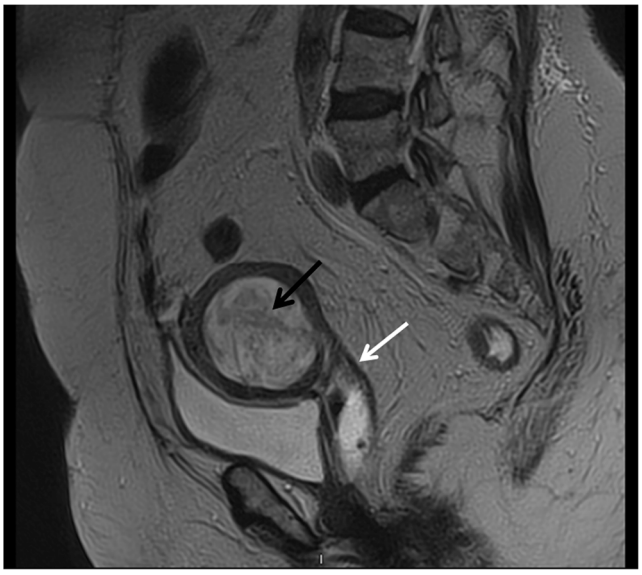

Fig. 1. Magnetic resonance imaging *(sagittal section)*. Mass in uterin cavity *(black arrow)* with neovagina infiltration *(white arrow)*.

Histological sections of neo-vaginal cancers show significant inflammation of the mico-environment, like in our case report. Also, histological sections of the transplanted digestive tract show significant inflammation. This inflammation appears to be identical to that found in chronic inflammatory bowel diseases (Sterpetti and Sapienza, 2019). In our case, we did not compare to other cases of neo-vaginal cancers because we did not have any. Also the anatomopathologists found a microenvironment rich in inflammation cells in our case as described in the literature, but we could not make a comparison because of only one case in our possession. How was this inflammation in a transplanted digestive tract explained? Different factors could be involved in this greater inflammation in this context compared to cancers of the

Table 1
Neovagina adenocarcinoma by digestive tract.

Case in the literature	Origin of neovagina	Transplanted tissue	Time cancer development (years)	Treatment performed
Yamada K, 2018 (Yamada et al., 2018)	MRKH syndrome	Sigmoid	53	Total pelvic exenteration
Borruto F, 1990 (Fierz et al., 2019)	*No information*	Ileum	39	*No information*
Ursic-Vrscaj M, 1994 (Fernández-Ruiz et al., 2019)	SCC of the cervix	Sigmoid	22	Surgical excision
Schouten van der Velden AP, 2005 (Kokcu et al., 2011)	Sarcoma botyroides of bladder and uterus	Sigmoid	14	Total pelvic exenteration
Kita Y, 2015 (Kita et al., 2015)	MRKH syndrome	Sigmoid	40	Abdominoperineal resection + S-1 orally
Andryjowicz E, 1985 (Wielgos et al., 2008)	SCC in situ of the vagina	Cecum	3	Radical resection of neovagina
Lambert AE, 2013 (Lambert et al., 2013)	MRKH syndrome	Sigmoid	19	Chemotherapy
Bogliolo S, 2015 (Bogliolo et al., 2015)	Partial vaginal agenesis and bicornuate uterus	Vascularised graft of the rectum-sigma	48	Total radical hysterectomy B2 type, subtotal vaginectomy + adjuvant local radiation
Hiroi H, 2001 (Kita et al., 2015)	MRKH syndrome	Sigmoid	30	Radical resection of neovagina + radiotherapy
Ritchie RN, 1929 (Bogliolo et al., 2015)	Pelvic chronic abscess	Ileum	6	Radium treatment and x-ray therapy over the pelvis
Lavand-Homme P, 1938 (Borruto and Ferraro, 1990)	*No information*	Ileum	–	*No information*
Auber G, 1989 (Ursic-Vrscaj et al., 1994)	Total vaginal agenesis	Ileum	39	Local excision + cobal radiotherapy
Munkarah A, 1994 (Schouten van der Velden et al., 2005)	Total vaginal agenesis	Split thickness dermal	21	Radical resection of neovagina
Our case	Total vaginal agenesis	Sigmoid	40	Posterior pelvectomy and chemotherapy

MRKH syndrome: Mayer-Rokitansky-Küster-Hauser syndrome, SCC: squamous cell carcinoma.

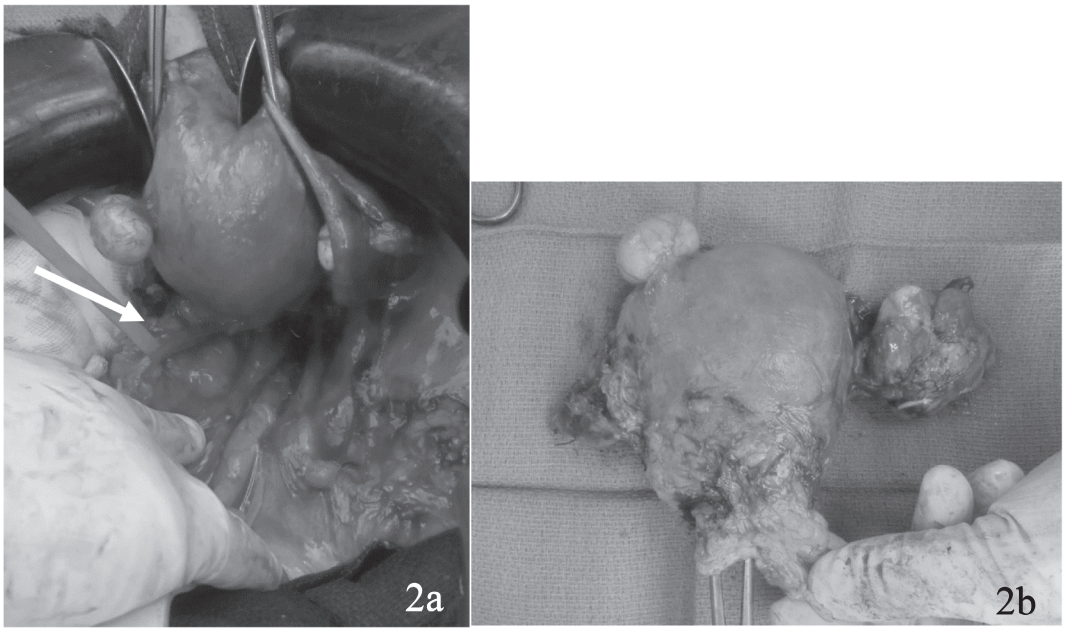

Fig. 2. Peri-operative view: 2a: Vascularization identification of the neovagina *(white arrow),* 2b: Total colpo-hysterectomy and bilateral annexectomy with excision of the meso and upper part of the colpoplasty in accordance with colon cancer surgery *(white arrow)*.

digestive tract in a physiological position or transplanted in other conditions. Firstly, the vaginal physiological bacterial environment contaminating the transplanted gastrointestinal tract during reconstruction may contribute in part to this inflammation (Sterpetti and Sapienza, 2019). In particular, HPV infection, a risk factor for various cancers (cervix, vulva, vagina, otho-rhino-laryngeal sphere), and involved in their carcinogenesis, could contribute to the development of cancer (Schober, 2007). Secondly, the reconstruction of a vagina is intended to play the role of a vagina, intervening in the sexual activity of patients. Hiroi *and al.* (Hiroi et al., 2001) have hypothesized that micro lesions secondary to coitus could contribute to the maintenance of chronic inflammation, which is conducive to the development of cancer. However, Sterpetti *and al.* (Sterpetti and Sapienza, 2019) reported in their series of 8 cases of mucinous adenocarcinoma of the neo-vagina that in 50% of cases, the patients had not had sexual activity since the neo-vaginal surgery. Thus, coitus could be a factor in the development of neovaginal cancer, but not sufficient on its own to promote cancer. Thanks to sigmoid colpoplasty, our patient had sexual intercourse, and never had a child or childbirth. In total, several associated factors could promote the carcinogenesis of a neo-vagina (Schober, 2007; Yamada et al., 2018; Hiroi et al., 2001; Sterpetti and Sapienza, 2019).

The risk of developing mucinous adeocarcinoma in a neovagina constructed from the digestive tract has a median of 30 years, and a mean of 29 years according to our literature review *(*Table 1*)*. It is necessary to inform patients of the need for very long-term monitoring in this reconstruction. Patients should be informed of the clinical signs leading to a consultation with a physician.

There is no consensus about care plan of neovagina mucinous adenocarcinoma. The aim of surgery was a total tumor resection with healthy margins. In the majority of cases, a radical hysterectomy was performed according to Wertheim-Meigs'surgical procedure (Schouten van der Velden et al., 2005), or Querleu-Morrow classification like in our case (Dargent et al., 2004). If the patient had not a uterus, a radical colpectomy can be performed (Callens et al., 2014). Sometimes, a pelvectomy remained necessary due to adhesions or tumor infiltration (Borruto and Ferraro, 1990). Surgical management of these patients must be performed by oncologist surgeons. The association of a gynecologist and a digestive surgeon appeared the best care plan, like in our report. Association of a digestive surgeon allows the expertise of oncology digestive care to that of the reconstruction of the neovagina often carried out by gynecological surgeons. It was necessary to inform patients about risk of surgery such as conversion to posterior or total pelvectomy, with or without stoma or bladder reconstruction. The reconstruction of a neovagina should be discussed with the patient in preoperatively by evaluating which technique can be proposed. The surgeon should inform the patient that depending on the perioperative findings, this neovaginal reconstruction may not be performed in some cases.

In the case of other vaginal reconstruction techniques, cancers can also develop (Schober, 2007), with a low incidence (Schober, 2007). The creation of a neovagina can follow a congenital malformation as in our case. It can follow surgery, especially oncology surgery (Schober, 2007), or a sex change (Reyes Claret et al., 2017; Fierz et al., 2019; Fernández-Ruiz et al., 2019; Kokcu et al., 2011; Liebrich et al., 2006). In all cases, whatever the cause of neovagina creation and the technique used, it seems necessary to follow the patients in the very long term. They should be informed of this risk and of the symptoms that should make them consult. Faced with this rare pathology, it would be interesting to have an international database, in order to better evaluate the different techniques of vaginal reconstruction, and their long-term evolution.

4. Conclusion

Mucinous adenocarcinoma is mainly found in neovaginal created by a digestive tract transposition. Its management was similar to that of the digestive tract in an anatomical position. However, multidisciplinary management remained essential in the absence of guidelines. It was necessary to carry out a very long-term follow-up, whatever the technique used, of patients with a neovagina.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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