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CASE REPORT

Carcinoma of the Neovagina: Case Report and Review of the Literature

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Background. **Carcinoma of the vagina is a rare disease, and it is even more rare in the neovagina. Nevertheless, it has been well described. The aim of this report was to analyze the reported cases and to add observations concerning a risk profile for this rare occurrence of carcinoma.**

Case report. **The 29-year-old patient's history included congenital absence of vagina as a result of Rokitansky–Kuster syndrome. In 1987, when the patient was 17 years old, a neovagina was constructed by dissection between the bladder and the rectum, according to the Warthon method, and the apex of the neovagina was covered with Dura-mater. In 1990 the patient underwent radiation treatment with brachytherapy three times in combination with surgical treatment, because of granulation tissue in the neovagina. In 1999 several specimens of the granulation tissue were removed and histological examination showed intermediate differentiated squamous cell carcinoma. Total exenteration with pelvic and lower paraaortic lymph node dissection was performed, and the patient received a continent neobladder (Mainz Pouch I), colostoma, and sigma neovagina. Two months later in January 2000 the patient showed local recurrence and after local excision the patient received radiotherapy. The follow-up to June 2001 showed no evidence of disease.**

Conclusion. **All patients with vaginoplasty should undergo regular 1-year follow-ups, including smear analysis because of the possibility of the development of carcinoma. Granulation tissue arising in a neovagina should be biopsied and no prosthesis should be used until lesions have healed completely. Patients who have undergone radiation of the neovagina carry an additional risk.**

Key Words: **vaginal agenesis; neovagina; radiation; squamous cell carcinoma; cancer.**

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INTRODUCTION

Vaginal malformations are unusual and they range from vaginal shortening in patients with androgen insensitivity to complete agenesis as part of Rokitansky syndrome. Vaginal reconstruction has become an established method to restore sexual function after ultraradical surgery and/or irradiation for the treatment of gynecological malignancies. In 1817 Dupyuhen first described an attempt to construct an artificial vagina, and Baldwin and Schubert used ileum and rectum to create a neovagina. In 1921 Graves used the labia minora as donor tissue and Wharton used a perineal pouch for forming a neovagina. McIndoe and Bannister reported the first use of split-thickness dermal grafts in 1938 [1] and in 1972 Rothman created a vagina using the pelvic peritoneum. In recent decades various treatments have been described for neovaginal construction or vaginal reconstruction, using myocutaneous flaps, intestinal implants, vulvovaginoplasty with labia, and/or split-skin grafts or human amniotic membrane [2] to line a surgically dissected vagina. Another method is the formation of an artificial canal between the rectum and the bladder by opening the septum. Carcinoma of the vagina is rare, and in a neovagina is even more unusual, although it has been well described. In 1929 Ritchie described an adenocarcinoma arising in an ileum neovagina 13 years after reconstruction [3], and since then 15 cases have been reported. According to Lathrop local carcinogenic environmental factors cause the oncogenic potential of the transplanted tissue [4]. The aim of this case report and review was to analyze the reported cases of neovaginal carcinoma and to add observations concerning a risk profile for this rare occurrence of disease. Described is the first case in the literature of carcinoma arising in a neovagina after using Dura-mater in the reconstruction.

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TABLE 1
Age at Reconstruction and Diagnosis, Time between, Symptoms, and Physical Examination

Reference	Age at reconstruction (years)	Procedure	Age at diagnosis (years)	Years/between	Symptoms	Physical examination
Ritchie [3]	13	Ileum	26	13	Vaginal discharge, lower abdominal pain	2-cm mass, posterior vagina
Lavand [5]	18	Colon	33	15	Vaginal bleeding, fistula	Indurate firm area, posterior vagina
Barclay [6]	21	Skin graft	26	5	No information	Upper vagina
Jackson [7]	17	No transplant	25	8	Asymptomatic	4-cm exophytic lesion, posterior vagina
Duckler [8]	17	Skin graft	36	19	Vaginal bleeding, dyspareunia	Irregular mass, posterior vagina
Rotmensch *et al.* [9]	18	Skin graft	33	15	Vaginal discharge, lower abdominal pain	Nodular infiltrating area, apex of vaginal cuff
Jaeger and Engel [10]	No information	Sigmoid	42	No information	Vaginal bleeding	No information
Rummel *et al.* [11]	17	Skin graft	30	13	Vaginal bleeding	No information
Hopkins and Morley [12]	17	Skin graft	42	25	Vaginal bleeding	4 cm, mid and lower left vaginal wall
Balzer and Zander [13]	No information	Skin graft	No information	No information	Vaginal bleeding	No information
Balik *et al.* [14]	19	Peritoneum	38	19	Vaginal bleeding, vaginal discharge	Necrotic mass, posterior vagina
Munkrarah *et al.* [15]	21	Skin graft	45	24	Vaginal bleeding, polyp at posterior wall of the neovagina, recto-vaginal fistula	Restricted on the polyp
Borutto and Ferraro [16]	21	Ileum	60	39	Vaginal bleeding	Lower two-thirds of the right vaginal wall
Bobin *et al.* [17]	22	No transplant	43	21	Vaginal bleeding, vaginal discharge	4 cm, apex of vagina
Schult *et al.* [18]	16	Not described	32	16	Recurrent recto-vaginal fistula	Huge tumor with extension over the entire pelvis
Present case	17	Warthon/Dura	29	12	Recurrent vaginal infection, fistula	Irregular infiltration of the complete neovagina

CASE REPORT

The 29-year-old patient's history included congenital absence of vagina as a result of Rokitansky–Kuster syndrome. The karyotype was normal. In 1987, when the patient was 17 years old, a neovagina was constructed by dissection between the bladder and the rectum, according to the method of Warthon. The apex of the neovagina was covered with Dura-mater to prevent arising of granulation tissue (surgery performed by Prof. Kuhn, Chairman at the University of Göttingen, Germany, Department of Gynecology and Obstetrics). In 1990 the patient underwent three 4-Gy radiation treatments with brachytherapy in combination with surgery for biopsy specimen, because of granulation tissue in the neovagina. The histological examination of the specimen showed granulation tissue with no sign of malignancy. Between 1989 and 1995 the patient had regular yearly PAP smears with PAP IIw. Between 1995 and 1999 the patient lived in France and PAP smear results are not available. In the years following surgery, the patient had a normal sex life but did insert a prosthesis day and night for at least 12 years until October 1999. She was unmarried, was a smoker, and worked as an independent lawyer. We first saw the patient because of vaginal discharge and recurrent and therapy-resistant vaginal infections. On October 13, 1999, examination under general anesthesia revealed epithelium in the lower 2 cm of the neovagina, granulation tissue in the upper 6 cm, and a 7-mm-long, 2-mm-wide bright recto-vaginal fistula. Several specimens of the granulation tissue were removed and the histological examination showed intermediate differentiated squamous cell carcinoma. Under these conditions, 7 days later a total exenteration with pelvic and lower paraaortic lymph node dissection was performed, as well as provision of a continent neobladder (Mainz Pouch I), colostoma, and sigma neovagina. The postoperative period was, except for a small leakage of the neobladder, uneventful. The patient was discharged 23 days after surgery and returned to normal life.

The excised exenteration block showed an intermediate dif-

TABLE 2
Primary Treatment, Histopathology of Tumors and Lymph Nodes, and Results of Treatment and Additional Clinical Data

Reference	Primary treatment	Pathology	Lymph nodes	Result/therapy	Additional clinical data
Ritchie [3]	Radiation	Adenocarcinoma	No information	Died after 6 month	
Lavand [5]	Radiation	Adenocarcinoma	No information	?	
Barclay [6]	Radiation and radium and isolated pelvic perfusion with nitrogen mustard	Advanced epidermoid tumor	No information	Died of progressive disease	
Jackson [7]	Radiation	Squamous cell carcinoma	No information	Recurrence after 3 months	
Duckler [8]	Posterior exenteration	Squamous cell carcinoma	Free	Disease-free followed-up for 1 $\frac{1}{2}$ year	18 years past chronic irritation, biopsies showed leukoplacia, dysplastic changes
Rotmensch *et al.* [9]	Total exenteration	Squamous cell carcinoma	No information	Disease-free followed-up for 10 months	
Jaeger and Engel [10]	Radiation	Adenocarcinoma	No information		
Rummel *et al.* [11]	No information	Squamous cell carcinoma	No information		
Hopkins and Morley [12]	Radiation	Squamous cell carcinoma	No information	Recurrence after 3 years; died 4 years after diagnosis of uraemia	Additional squamous cell carcinoma *in situ* of the vulva
Balzer and Zander [13]	No information	Squamous cell carcinoma	No information		
Balik *et al.* [14]	Radiation	Squamous cell carcinoma	No information	No information	
Munkrarah *et al.* [15]	Complete dissection of the neovagina?	Mucinous adenocarcinoma	No information	No evidence of disease	Vaginal bleeding and apical nodule 3 years before
Borutto and Ferraro [16]	Complete removal of the neovagina	Adenocarcinoma	No information	No information	No information
Bobin *et al.* [17]	Radiation followed by posterior exenteration/ IORT	Squamous cell carcinoma	Free	Recurrence after 6 month	1989 mild dysplasia, 1995/1996 inflammatory pseudopolyps
Schult *et al.* [18]	Total exenteration, followed by radiation	Squamous cell carcinoma	No information	Radiotherapy, 4-month follow-up no evidence of disease	Prosthesis, recurrent recto-vaginal fistula over 2 years
Present case	Total exenteration	Squamous cell carcinoma	Positive	Recurrence after 4 months, local excision, radiation, after 1 year no evidence of disease	Recurrent inflammation, therapy-resistant

ferentiated squamous cell carcinoma that covered the entire neovagina with infiltration of the muscularis of the bladder. The tumor was also infiltrating under the rectal mucosa. The maximum depth of infiltration was 18 mm. The fistula was tumor-dependent. The margins were microscopically negative for malignancy. We found regional lymphangiosis. The 30 pelvic and paraaortic lymph nodes that were removed were negative, but there was an additional mesenteric lymph node with a metastasis. Two months later in January 2000 the patient showed a palpable inguinal lymph node on the left side and an induration 1 cm lateral the left labia majora. On 25 January 2000 we removed the suspect induration and performed a lymph node extirpation inguinal on the left side. The histological examination revealed locoregional and lymph nodular progression of disease. The analysis for low and high human papilloma virus in the tumor material was not significantly positive. From 11 February to 20 March the patient received local radiation of 59.4 Gy (39.6 Gy with four-field technique and 19.8 Gy with vulvar rotation field and a.p.–p.a. field). Through June 2001 the patient showed no evidence of disease and has, as far as possible, resumed normal life.

DISCUSSION AND REVIEW OF THE LITERATURE

Including our own observation, 16 cases of carcinoma of the neovagina in patients with primary vaginal malformations have been documented. Age at reconstruction was between 13 and

22 years (median 18.1 years). In 4 cases an intestinal implant was used; 7 patients underwent vulvovaginoplasty with split-thickness skin graft following the McIndoe procedure; 2 patients had no transplanted tissue, according to the Wharton operation; 1 patient received a reconstructed vagina covered with pelvic peritoneum as described by Rothman; our patient underwent the Wharton operation and the vaginal tunnel was covered with Dura-mater; and for 1 patient the information was not available. There were no postoperative complications reported. The patients with intestinal implants did not need additional treatment. The 12 patients with preparation of a vaginal tunnel needed a vaginal dilator to prevent stenosis of the neovagina. The age at diagnosis of carcinoma was between 25 and 60 years (median 36 years). The latency period between reconstructive procedure and diagnosis of carcinoma was between 5 and 39 years (median 17.4 years). Ten patients had vaginal bleeding as first symptoms, 4 with additional vaginal discharge and 1 with dyspareunia and 4 combined with a vagino-rectal fistula. Two patients showed vaginal discharge combined with lower abdominal pain. The physical examination showed tumor masses or large irregular areas in the neovagina; in 1 case the adenocarcinoma was restricted to the vaginal polyp. These tumors were mainly located on the posterior wall of the vagina, but in 2 cases the tumor was located in the apex of the vagina. Our patient showed an irregular infiltration of the entire neovagina (Table 1). The primary treatment was, in 10 cases, radiation, in 1 case followed by posterior exenteration and IORT. In 3 cases a total exenteration was performed and 1 patient underwent a posterior exenteration as primary treatment. Histological examination showed, in 5 cases, adenocarcinoma and, in 11 cases, squamous cell carcinoma. Three patients had a rapid recurrence of the disease within 3 to 6 months after the initial treatment; 1 woman died after 6 months. One woman had a recurrence-free interval of 3 years and died 1 year later, 4 years after diagnosis. Two patients have a recurrence-free follow-up of 10 and 18 months, respectively (Table 2).

Carcinoma of the neovagina in patients with vaginal malformations is very rare and only 13 cases have been reported since 1929. Primarily, malignancy appears to be related to the use of transplanted tissue: three adenocarcinomas in intestinal implants and five squamous cell carcinomas in skin graft transplants. Four cases of squamous cell carcinoma were reported (including our own observation) without the use of skin graft transplants for the reconstructive procedure. The etiology of these tumors is still speculative. The squamous cell carcinomas could have arisen from the epithelium residuum of the embryonic uterine cervix in cases without skin graft transplants. During the development of embryological undifferentiated cells, physical agents can induce carcinogenesis. In our case the patient had inserted a prosthesis for about 12 years and had undergone radiation and surgical treatment for recurrent granulation tissue in the neovagina. The chronic irritation could have provoked the development of neovaginal carcinoma, lending support to a hypothesis in the literature describing similar chronic irritation resulting in intraepithelial neoplasia [19]. Carcinoma arising in the neovagina is distinctly clinical. Younger women are affected and, histologically, the tumors are poorly differentiated or even undifferentiated. All reported patients had large tumor masses and clinical data showed rapid progression. The prescribed therapies, including radiation and/or radical surgical procedures, are extreme. Despite poor prognosis, radical surgery including pelvic and paraaortic lymph node dissection seems to be the best option for advanced cases. Preoperative radiation may shrink the tumor and, as described by other teams using IORT in parametric involvement, we found that local radiation can afford local control in a case with rapid local progression. Despite the poor prognosis when these rare carcinomas develop, reconstructive methods to provide patients with neobladders and neovaginas in cases of total or partial exenteration should be used whenever possible. No vaginoplasty has a zero cancer risk and, in line with other teams, we recommend that these patients undergo regular 1-year follow-up, including smear analysis because cytological findings are needed for comparisons with normal vaginal epithelium [20]. All granulation tissues arising in the neovagina should undergo biopsy and histological examination, and there should be no additional physical agents such as a prosthesis until lesions have healed completely to avoid the onset of chronic irritation. Patients who have undergone radiation of the neovagina are also at risk for carcinoma of the neovagina; for example, in the case presented here, 9 years after low intensive radiation treatment of this region squamous cell carcinoma was detected.

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