

Concurrent Occurrence of Rectal Adenocarcinoma and Vulvar Keratinizing Squamous Cell Carcinoma: Case Report and Literature Review

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Abstract. *Introduction.* Vulvar carcinoma is a rare malignancy, whereas rectal cancer is a more common oncological condition. However, the simultaneous occurrence of these two diseases is exceptionally rare. *Case presentation.* A 76-year-old woman presented with rectal bleeding and was previously diagnosed with keratinizing squamous cell carcinoma G1 of the vulva, unrelated to HPV. Imaging revealed tumor-like masses in the vulva and rectum, with pathological lymph nodes. Biopsy confirmed rectal adenocarcinoma *in situ*. She underwent obstructive rectal resection, colostomy formation, vulvar resection, and lymphadenectomy. Postoperative antibiotic therapy was administered and discontinued after seven days due to stable inflammatory markers. The patient was discharged in good condition, with planned rehabilitation in a sanatorium. *Conclusion.* Rectal adenocarcinoma and vulvar keratinizing squamous cell carcinoma concurrent occurrence is very rare. The risk factors for vulvar cancer (HPV, smoking, immunosuppression, lichen sclerosus) and rectal cancer (genetic predispositions, lifestyle factors (e.g., smoking, alcohol consumption), inflammatory bowel diseases) differ. However, genetic syndromes and certain interactions between lifestyle factors may lead to the concurrent occurrence of these two tumors. Given the complexity of managing two primary tumors, a multidisciplinary surgical approach was essential in our case. Further research is needed to explore possible biological links and optimize diagnostic and treatment strategies for such rare oncological presentations.

Keywords: rectal carcinoma, vulvar carcinoma, vulvar cancer risk factors, rectal cancer risk factors, vulvar squamous cell carcinoma and rectal adenocarcinoma.

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Tiesiosios žarnos adenokarcinomos ir vulvos ragėjančios plokščiakūstelinės karcinomos pasireiškimas kartu: klinikinio atvejo analizė ir literatūros apžvalga

Santrauka. Įvadas. Vulvos karcinoma – retas piktybinis navikas. Tiesiosios žarnos vėžys – dažnesnis onkologinis susirgimas. Abi šios ligos kartu pasireiškia itin retai. **Klinikinis atvejis.** 76 m. moteris kreipėsi dėl kraujavimo iš tiesiosios žarnos. Prieš tai pacientei ambulatoriškai diagnozuota vulvos ragėjanti plokščiakūstelinė karcinoma (G1), nesusijusi su žmogaus papilomos virusu (ŽPV). Vaizdiniai tyrimai atskleidė esant navikines mases vulvoje ir tiesiojoje žarnoje bei patologinius limfmazgius. Atlikus biopsiją, patvirtinta tiesiosios žarnos naviko adenokarcinoma *in situ*. Pacientei atlikta obstrukcinė tiesiosios žarnos rezekcija, suformuojant kolostomą, vulvos rezekcija ir limfadenektomija. Pooperaciniu laikotarpiu taikyta antibiotikoterapija. Ji nutraukta po septynių dienų dėl stabilių uždegiminių rodiklių. Pacientė išleista iš ligoninės geros būklės, jai suplanuota reabilitacija sanatorijoje ir adjuvantinė terapija. **Išvada.** Tiesiosios žarnos adenokarcinoma ir vulvos ragėjanti plokščiakūstelinė karcinoma kartu pasireiškia itin retai. Vulvos vėžio rizikos veiksniai (ŽPV, rūkymas, imunosupresija, *lichen sclerosus*) ir tiesiosios žarnos vėžio rizikos veiksniai (genetinė predispozicija, gyvenimo būdo veiksniai, tokie kaip rūkymas, alkoholio vartojimas, uždegiminės žarnyno ligos) skiriasi. Vis dėlto tam tikri genetiniai sindromai ir gyvenimo būdo veiksnių sąveikos gali lemti šių dviejų atskirų navikų išsivystymą. Kalbamuoju atveju, atsižvelgus į dviejų pirminių navikų gydymo sudėtingumą, galima teigti, kad itin svarbus multidisciplininis chirurginis gydymas. Būtinai tolesni tyrimai, siekiant nustatyti galimus biologinius ryšius ir optimizuoti tokių retų onkologinių atvejų diagnostikos ir gydymo strategijas.

Reikšminiai žodžiai: tiesiosios žarnos karcinoma, vulvos karcinoma, vulvos vėžio rizikos veiksniai, tiesiosios žarnos vėžio rizikos veiksniai, vulvos plokščiakūstelinė karcinoma, tiesiosios žarnos adenokarcinoma.

Introduction

A significant proportion of malignant tumors originate from the skin of the labia, while those arising from the clitoris or vestibular glands are exceedingly rare [1]. Vulvar cancer accounts for only 4% of all gynecological malignancies, and as of 2020, it represented 0.8% of all cancers globally [2, 3]. The most common subtype of vulvar cancer is squamous cell carcinoma, comprising more than 90% of all vulvar carcinomas. Globally, the incidence of vulvar cancer reaches approximately 30 000 cases annually [2]. Vulvar cancer predominantly affects postmenopausal women [1].

The incidence of colorectal cancer continues to rise annually, particularly in developing countries. It is the third most common malignancy and the second leading cause of cancer-related mortality worldwide [4]. In 2018, the number of colorectal cancer cases reached 1.8 million [5, 6]. Rectal cancer accounts for approximately one-third of all colorectal cancer cases [6]. About 90% of colorectal carcinomas are adenocarcinomas [5]. According to the literature, approximately 65% of colorectal cancer cases occur sporadically, without a family history or inherited genetic mutations [5]. The remaining cases are associated with familial factors, with 5% of these being attributed to hereditary cancer syndromes [5].

The concurrent occurrence of rectal adenocarcinoma and keratinizing squamous cell carcinoma of the vulva is exceedingly rare and is sparsely documented in the literature. Thus, we aim to present this unique case observed in our clinic. Additionally, we analyzed clinical cases similar to ours (Table 1) and conducted a literature review to assess the risk factors for vulvar and rectal cancers.

Case presentation

A 76-year-old woman with type II diabetes mellitus and arterial hypertension presented with complaints of rectal bleeding during defecation. Earlier, she had reported itching and lesions in the vulvar region, leading to outpatient evaluation for vulvar carcinoma. A biopsy confirmed keratinizing squamous cell carcinoma G1, unrelated to HPV. Cancer marker tests were performed: CA19-9 level was 38.6 U/mL, and CEA level was 46.6 ng/mL. Contrast-enhanced computed tomography (CT) of the chest, abdomen, and pelvis revealed tumor-like masses involving the labia minora and vagina, as well as suspicious changes in the rectum. Pathological lymph nodes were identified in the inguinal region, measuring up to 3.4x1.7 cm, and pararectally, up

to 1 cm in size. Fibrocolonoscopy revealed a circumferential, ulcerated, lumen-narrowing tumor extending from 5 cm to 15 cm above the anal verge. Biopsy from the rectal tumor confirmed adenocarcinoma in situ, unclassified. For further assessment, magnetic resonance imaging (MRI) with intravenous contrast was performed (Figure 1). A tumor measuring approximately 7.9 cm in length was detected in the middle third of the rectum, growing into the intestinal lumen and invading all layers of the rectal wall in certain areas. The tumor exhibited DWI restriction features. Several lymph nodes in the mesorectum appeared pathological. According to MRI imaging findings, the rectal cancer is classified as cT3N1, MRF (-).

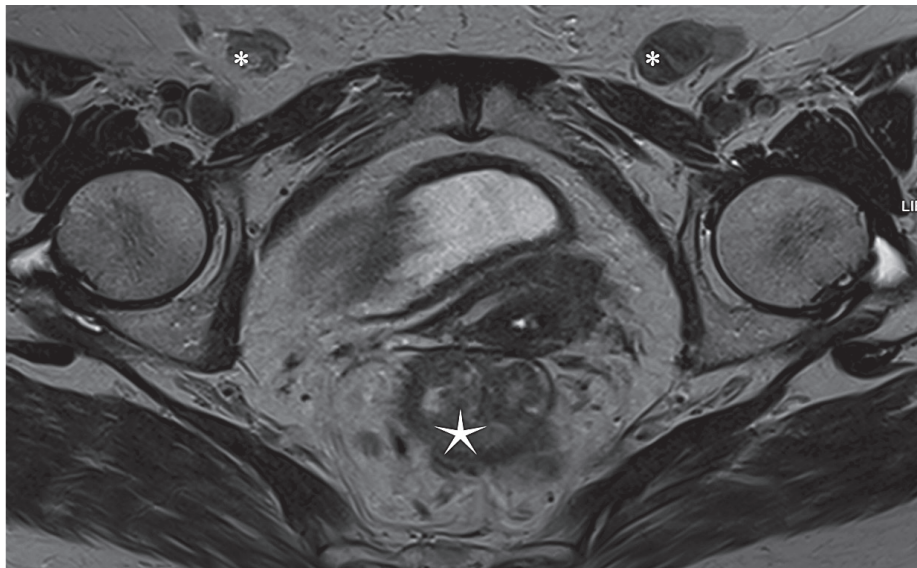


Figure 1. MRI

* – clusters of enlarged lymph nodes, ★ – cancerous mass in rectal region.

The patient underwent surgery via a laparotomy incision, which included obstructive rectal resection with the formation of a colostomy on the left side of the abdomen. A pathological lymph node near the left external iliac artery (a. iliaca externa sin.) was excised. A drainage tube was inserted into the pelvis through the left iliac region. Through separate skin incisions in both groins, enlarged clusters of lymph nodes, fixed to subcutaneous tissues and resembling pathological nodes, were removed. Bilateral vulvectomy was performed, including removal of the clitoris, with 1 cm margins of healthy tissue and resection of approximately 5 mm of the posterior vaginal wall at the vaginal entrance (Figure 2). Antibiotic therapy with cefuroxime and metronidazole was initiated due to the high risk of infection associated with an open bowel lumen during surgery, and preoperative antibiotic prophylaxis with cefazolin was administered.

Histological examination of postoperative specimen confirmed infiltrative colonic adenocarcinoma, classified as pT3, N1b, Mx, LVi0, R0, G2, with metastases found in 6 out of 18 examined lymph nodes within the surrounding adipose tissue of the colon. Histological examination of another specimen revealed keratinizing squamous cell carcinoma of the vulva, unrelated to HPV, classified as pT1b, N2c, R1, G1, with metastases detected in one para-iliac lymph node, three lymph nodes in the left groin, and two lymph nodes in the right groin.

Antibiotic therapy was discontinued after seven days as inflammatory markers did not progress. Observing a favorable clinical condition, the patient was discharged home 12 days postoperatively (Figure 3). A third-stage rehabilitation program and radiotherapy were planned.

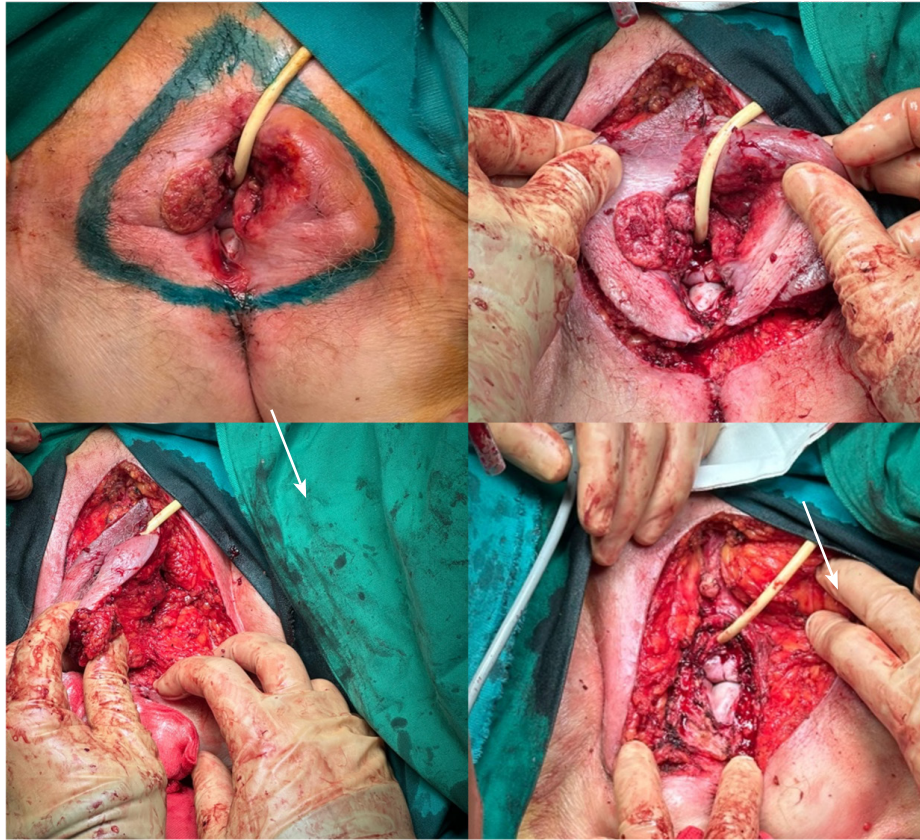


Figure 2. Vulvar resection



Figure 3. The appearance of the vulva on the day of discharge from the hospital

Discussion

Vulvar squamous cell carcinoma (VSCC) develops through two distinct pathways: an HPV-associated form, primarily affecting younger women, especially those who smoke or are immunosuppressed [1, 2], and an HPV-independent form, most common in postmenopausal women with lichen sclerosus (LS) [1, 2]. High-risk HPV types 16 and 18 are linked to 69% of VSCC cases [7], with HSIL as a precancerous lesion [1, 2], whereas LS is strongly associated with differentiated vulvar intraepithelial neoplasia (dVIN), which progresses more aggressively to carcinoma [8–10].

Colorectal cancer arises through genetic and epigenetic changes in colonic epithelium, driven by environmental and lifestyle factors [5]. Risk increases with age, male gender [4, 5], poor diet, alcohol consumption [5, 11–14], smoking [15], and genetic syndromes such as Lynch syndrome and familial adenomatous polyposis [16, 17]. Long-term dietary patterns, particularly low fiber and high red meat intake have been associated with an elevated colorectal cancer risk [5].

Given the distinct etiology and progression of these malignancies, treatment strategies must be tailored accordingly. Below, we discuss the management approaches for vulvar and rectal cancer.

Managing vulvar cancer typically includes a combination of surgical intervention and radiation therapy, in early stage cancer sentinel lymph node biopsy (SNB) procedure is performed. Surgical treatment for vulvar cancer depends on tumor size, location, and lymph node involvement [18]. Early-stage tumors (T1a) with ≤ 1 mm of stromal invasion are managed with wide local excision, while larger tumors (T1b, >1 mm stromal invasion or T2 ≤ 4 cm and the lesion is 1 cm from median line) may require wide local excision or a modified radical vulvectomy with SNB [19]. For advanced cases (T2 > 4 cm, T3 and lesion ≥ 1 cm from the median line) a radical vulvectomy combined with ipsilateral inguino-femoral lymph node dissection is advised [19].

Postoperative radiotherapy aims to lower recurrence rates and improve survival [18]. Adjuvant therapy is typically reserved for patients with advanced disease, large tumors, or positive lymph nodes [19]. If invasive disease reaches the pathological excision margins of the primary tumor and further surgical excision is not feasible, postoperative radiotherapy is recommended [18]. Radiation is highly effective in preventing recurrence in inguino-femoral lymph nodes, particularly for patients with multiple positive nodes or extracapsular spread [19]. However, its role in cases with a single positive node remains unclear [19].

Rectal cancer treatment typically follows a multimodal strategy [20]. For early-stage (cT1, cN0, M0) rectal cancer local excision is recommended (TAE, TAMIS, TEMS) or sometimes total mesorectal excision (TME) [21]. TME is often preferred for its comprehensive removal of the rectum and associated lymph nodes [21]. For locally advanced disease, treatment includes neoadjuvant chemotherapy, tailored to the clinical situation, followed by total mesorectal excision and subsequent adjuvant chemotherapy [20–22]. The choice of procedure depends on factors such as tumor size, location, and patient health [21]. In patients achieving a complete clinical response, organ-preserving options like the “watch-and-wait” approach may be pursued to avoid surgery while maintaining comparable outcomes. Total neoadjuvant therapy is an emerging protocol that improves patient compliance and targets micrometastases before surgical intervention. Advanced imaging technologies are crucial for accurate staging, treatment planning, and assessing response to therapy [20, 22].

Six clinical cases were also analyzed [23–27] (Table 1). The analysis revealed that the concurrent occurrence of rectal adenocarcinoma and keratinizing squamous cell carcinoma of the vulva is extremely rare, with only one documented case involving two distinct tumors [23]. Another similar case involved adenocarcinoma in the cecum [24]. In two other described cases, metastases were observed, but not two separate primary tumors [25, 26]. Additionally, one case associated with a MUTYH gene mutation reported the occurrence of five independent cancers, including rectal and vulvar cancers [27].

The management of such rare synchronous malignancies varies greatly depending on individual tumor characteristics and disease extent. Our clinical case is particularly rare as it required the integration of distinct treatment strategies for two different malignancies. The therapeutic approaches for vulvar cancer differ significantly from those for rectal cancer, as previously discussed. Typically, in cases like ours, rectal cancer treatment involves neoadjuvant therapy followed by surgery, whereas vulvar cancer is primarily managed with surgery, followed by adjuvant therapy. In our case the decision was made to perform an obstructive rectal resection with colostomy formation, alongside a bilateral vulvectomy and lymphadenectomy. This approach aimed to achieve complete tumor resection while minimizing the risks associated with multiple separate surgical procedures. Given the high risk of infection due to an open bowel lumen, perioperative antibiotic prophylaxis and postoperative antibiotic therapy were administered. The patient's postoperative course was uneventful, and a multidisciplinary team planned further rehabilitation and adjuvant radiotherapy to optimize long-term oncological outcomes.

Conclusions

The concurrent occurrence of rectal adenocarcinoma and vulvar keratinizing squamous cell carcinoma is exceptionally rare. In this report we reviewed vulvar and rectal cancer risk factors, treatment options and similar clinical cases described in the scientific literature, while also presenting a clinical case observed in our hospital. The treatment strategies for both malignancies depends on tumor size, location, and lymph node involvement.

Our case required a complex treatment strategy, as it involved the simultaneous management of two distinct oncological processes, posing a significant challenge in selecting the appropriate treatment strategy. During a multidisciplinary team discussion involving gynecologists, surgeons, and oncologists, it was determined that surgical treatment should be prioritized, followed by adjuvant therapy. Based on the histological findings – infiltrative colonic adenocarcinoma (pT3, N1b, Mx, LVi0, R0, G2) and keratinizing squamous cell carcinoma of the vulva, unrelated to HPV (pT1b, N2c, R1, G1) – the chosen treatment strategy was well-adapted. Importantly, no cancer cells were detected at the resection margins of the rectum, confirming clear surgical margins.

Table 1. Analysis of clinical cases of concurrent vulvar and rectal cancer

Authors, country, article title	Case description	Findings	Treatment
Kremzer T, Pete I, Stári O. (Hungary) <i>The primary surgical therapy of a synchronous sigmoid, rectal and vulvar cancer.</i> [23]	64-year-old woman with vulvar squamous cell carcinoma and rectal/sigmoid adenocarcinoma.	Histology: sigmoid tumor (pT3N0M0), rectal tumor (pT2N0M0), vulvar tumor (pT1N0M0).	The patient underwent sigmoid colectomy and rectal extirpation, along with vulvectomy and inguinal lymphadenectomy, followed by colostomy formation.
Vahidfar M, Abdo-lahi AH, Zarchi M. (Iran) <i>Colorectal and vulvar synchronous cancer.</i> [24]	63-year-old woman with vulvar squamous cell carcinoma and cecal adenocarcinoma.	CT: 5 cm hypoechoic liver lesion (metastasis).	The patient underwent surgical resection of the vulvar lesion and cecal adenocarcinoma, with adjuvant chemotherapy due to suspected hepatic metastasis.
Akpak YK, Dandin Ö, Gün İ, Atay V. (Turkey) <i>A rare case of vulvar skin metastasis of rectal cancer.</i> [25]	47-year-old woman with a vulvar lesion three years after abdominopereineal resection and oophorectomy for ovarian cancer metastases.	MRI: hyperintense vulvar lesions; surgical excision revealed atypical glandular structures infiltrating vulvar skin. Referred for oncology and radiotherapy.	Surgical excision of the vulvar lesion was performed, and the patient was referred for systemic oncological treatment, including chemotherapy and radiotherapy.

Authors, country, article title	Case description	Findings	Treatment
Soh JM, Scott GA, Pavlovitz BT. (USA) <i>Metastatic rectal adenocarcinoma and anal squamous cell carcinoma. [26]</i>	47-year-old woman with primary anal squamous cell carcinoma and vulvar metastases.	PET/CT: metastases in inguinal/paraortic lymph nodes; chemotherapy initiated.	Systemic chemotherapy targeting metastatic disease.
Soh JM, Scott GA, Pavlovitz BT. (USA) <i>Metastatic rectal adenocarcinoma and anal squamous cell carcinoma. [26]</i>	49-year-old woman with stage IV rectal adenocarcinoma and vulvar metastases.	PET/CT: metastases in liver, lungs, lymph nodes; treated with radiotherapy and chemotherapy.	Surgical resection, followed by chemoradiotherapy. Postoperatively, vulvar nodules were identified as metastatic adenocarcinoma, leading to palliative radiotherapy and chemoradiotherapy for metastatic disease.
Arroyave A, Nodit L, Clegg D, Russ A. (USA) <i>Forty-eight-year-old female MUTYH carrier presenting with five concurrent primary cancers. [27]</i>	48-year-old woman with multiple primary cancers, including rectal adenocarcinoma and vulvar squamous cell carcinoma.	Genetic testing: MUTYH mutation; underwent extensive surgical and chemoradiotherapy.	Radical partial vulvectomy, thyroidectomy, neoadjuvant chemoradiotherapy, and subsequent pelvic exenteration, hysterectomy, bilateral salpingo-oophorectomy, sigmoid colectomy, radical vaginectomy, and perineal proctectomy.

Author contributions

Odeta Laukaitytė – conceptualization, methodology, formal analysis, investigation, writing – original draft, writing – review and editing, visualization.

Gustė Brazytė – conceptualization, methodology, formal analysis, investigation, writing – original draft, writing – review and editing.

Tadas Latkauskas – conceptualization, methodology, formal analysis, investigation, writing – review and editing, visualization.

Saulius Paškauskas – conceptualization, methodology, formal analysis, investigation, writing – review and editing, visualization.

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