Clinical Case Report

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A CARE-compliant article: a case report of primary adenocarcinoma of the anal glands

Review of literature

Yong Ji, MD, Youxin Zhou, MD*

Abstract

Rationale: Adenocarcinoma of the anal canal is an uncommon malignancy. Primary adenocarcinoma, in particular, is extremely rare.

Patient concerns: A 61-year-old man was referred to our institution with complaints of repeated hematochezia.

Diagnosis: Digital rectal examination revealed a hard palpable ulcer in the anal canal, measuring 2 cm × 2 cm in size, at the 5 o'clock direction (in the lithotomy position). The pelvic enhanced magnetic resonance imaging revealed anal verge occupying mass. A diagnosis of carcinoma of the anal canal was considered. Colonoscopic examination revealed a poorly differentiated adenocarcinoma of the anal canal.

Interventions: The patient underwent abdominoperineal resection (APR) of the rectum, and was administered 6 courses of adjuvant chemotherapy with mFOLFOX.

Outcomes: The patient was followed up for more than 1 year after operation, and no local recurrence or distant metastasis occurred.

Lessons: The diagnosis and treatment of this disease is still a huge challenge because its incidence is very low. A study of more cases is required for uniformity in diagnosis and for the development of treatment protocols.

Abbreviations: APR = abdominoperineal resection, IHC = immunohistochemistry, WHO = World Health Organization.

Keywords: adenocarcinoma, anal canal, immunohistochemistry

1. Introduction

Carcinoma of the anal canal accounts for about 1% of all gastrointestinal cancers.[1] Squamous cell carcinomas constitute the majority, with adenocarcinoma accounting for less than 10% of all anal cancers.[2] The World Health Organization (WHO) classification of tumors[3] categorizes anal malignancies as follows: adenocarcinoma including rectal type adenocarcinoma, anal gland adenocarcinoma, fistula-related mucinous adenocarcinoma, and intraepithelial adenocarcinoma (i.e., Paget disease). Primary adenocarcinomas of the anal glands are extremely rare. In this article, we present a case of primary adenocarcinoma of the anal glands, along with a review of literature.

2. Case report

A 61-year-old man was transferred to our institution with complaints of repeated hematochezia, which had lasted for 6 months. The patient had no significant medical history. He was hemodynamically stable on admission. Digital rectal examination showed a hard palpable ulcer in the anal canal, measuring 2 cm × 2 cm in size, at the 5 o'clock direction (in the lithotomy position) and the examining fingertip was covered with a sanguineous discharge. There was no evidence of any anorectal fistula or Paget disease.

No abnormalities were found on examination of the blood. The preoperative immuno-examination showed normal results, including negative HIV and syphilis antibodies. The enhanced computed tomography of the chest and abdomen showed slight thickening of the wall of the anal canal. No enlarged lymph nodes were found in the abdomen, pelvic cavity, and groin. The findings of the chest scan were normal. Pelvic enhanced magnetic resonance imaging revealed anal verge occupying mass, and it also found no swollen lymph nodes in the pelvic cavity and groin. A diagnosis of carcinoma of the anal canal was considered. The colonoscopic examination revealed a poorly differentiated adenocarcinoma of the anal canal. The patient underwent abdominoperineal resection (APR) of the rectum. The surgical specimen (Fig. 1) showed the gross shape and location of the tumor. Histopathological evaluation of the surgical sample

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Department of General Surgery, People Hospital of Jingjiang, YangZhou University Medical Academy, Jingjiang, Taizhou, China.

* Correspondence: Youxin Zhou, Department of General Surgery, People hospital of jingjiang, YangZhou University Medical Academy, Zhongzhou Road No.28, Jingjiang, Taizhou 214500, China (e-mail: zhouyouxin@yahoo.com).

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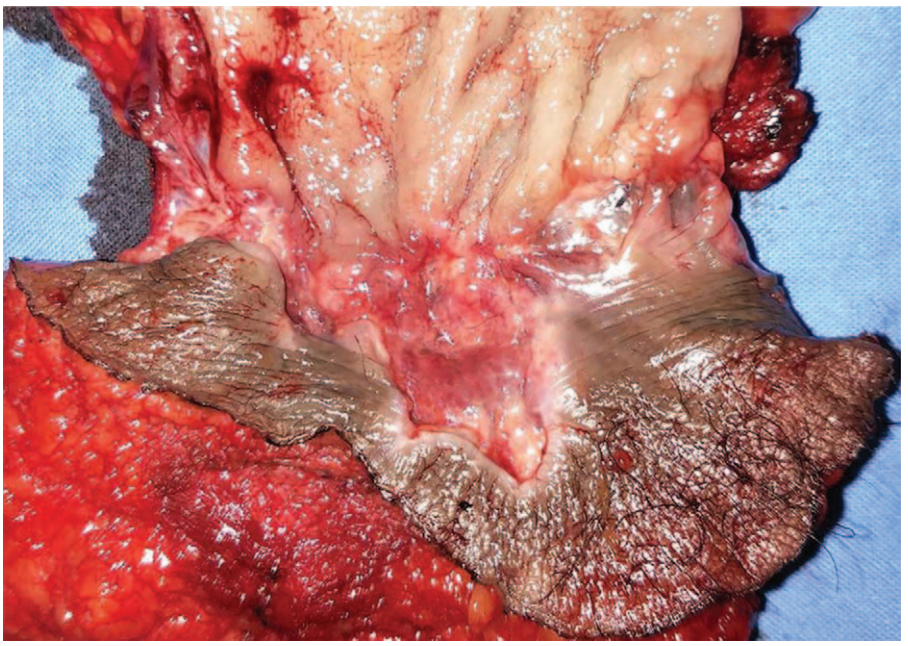

Figure 1. Surgical specimen. The operative specimen showed that the tumor invaded the dentate line upward and invaded the perianal skin downward. The tumor is an irregular, ulcerative type with a size of about 2*2 cm. However, according to this specimen, it is still difficult to identify the derivation of the tumor.

revealed a poorly differentiated adenocarcinoma of the anal canal (Fig. 2). No metastases were found in the 10 mesenteric lymph nodes. Immunohistochemical staining showed CK7 positivity (Fig. 3). The patient was started on adjuvant chemotherapy with mFOLFOX (5-Fluorouracil 5 g, Leucovorin 0.6 g, oxaliplatin 0.17 g, every 2 weeks) 2 weeks after the operation. Chemotherapy lasted for 6 cycles. The date of last follow up was June 2, this year, which is about 1 year and 4 months after surgery. The present value of CEA is 3.29 ng/mL, and the enhanced computed tomography of the chest and abdomen did not reveal any local recurrence or distant metastasis.

3. Discussion

Adenocarcinoma accounts for about 10% (5%–19%) of all cancers of the anal canal.[4] Most tumors have a colorectal

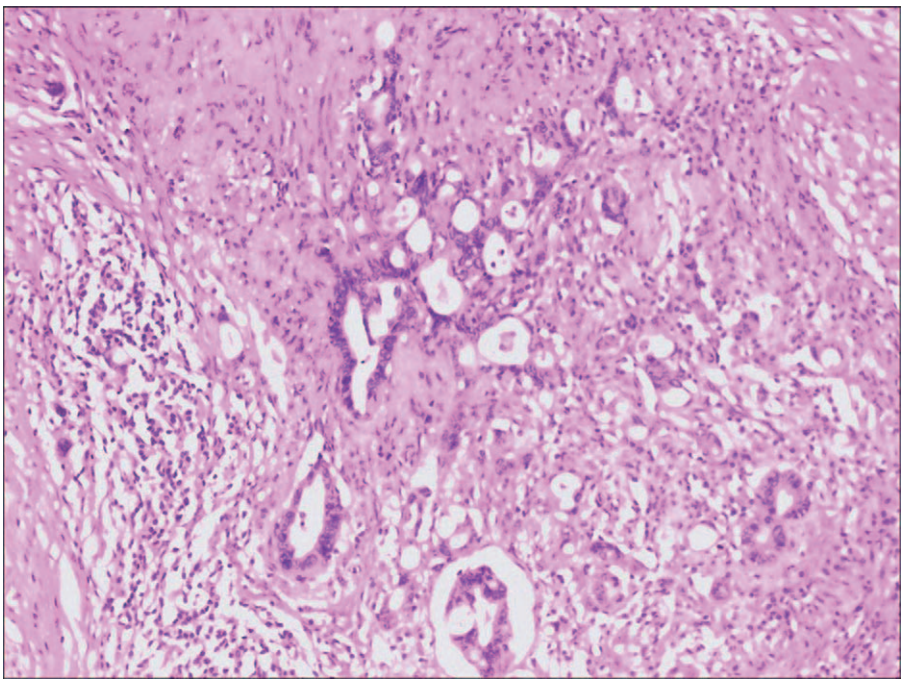

Figure 2. Histopathological evaluation revealed a poorly differentiated adenocarcinoma of the anal canal. What's more, the cancer cells were small tubular or strip like, disorderly distributed, without secreted mucus in the cytoplasm, and invading the muscular layer of the anal canal. (HE.×20). HE = hematoxylin-eosin.

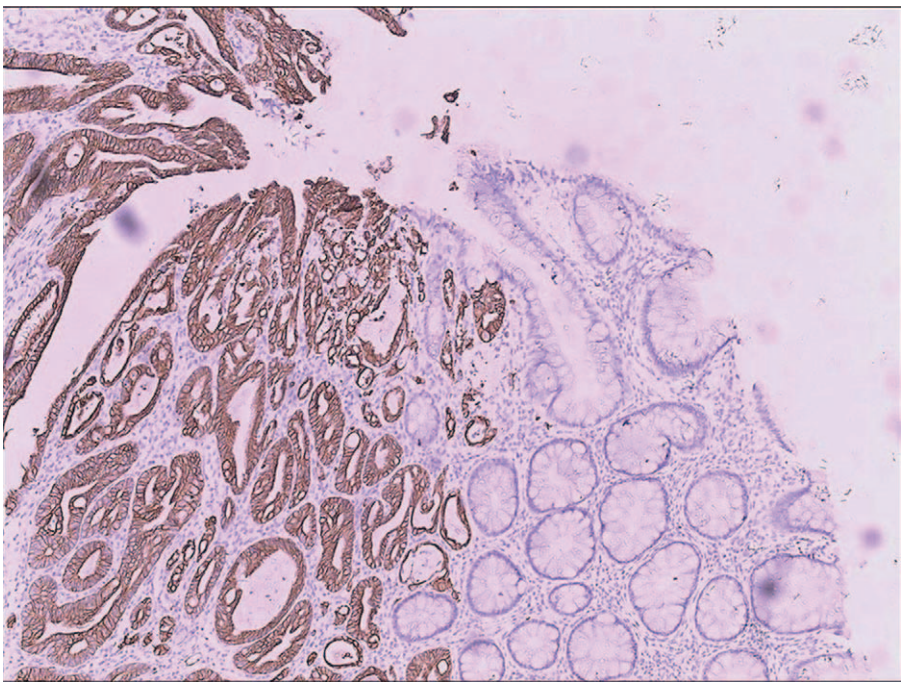

Figure 3. The glands are positive for CK7.(IHC.×20). IHC = immunohistochemistry.

phenotype and represent tumors originating either from the colorectal zone in the upper portion of the anal canal or from the glandular cells of the mucosa of the anal transitional zone. The WHO classification of tumors[3] categorizes anal malignancies as follows: adenocarcinoma including rectal type adenocarcinoma, anal gland adenocarcinoma, fistula-related mucinous adenocarcinoma, and intraepithelial adenocarcinoma (i.e., Paget disease). In routine practice, adenocarcinoma of the anal canal represents a unique challenge both for pathologic diagnosis and for clinical management. There is a lack of experience in its diagnosis and treatment as it is an extremely rare disease entity.

Various etiological factors including chronic local inflammation, anal fistula, and Crohn's disease have been implicated in its development.[5] Crohn's disease or other inflammatory conditions that result in chronic anal fistula may predispose to the development of fistula-associated adenocarcinomas.[6] High-risk HPV types may play a role, as their presence has been documented in at least some cases of anal adenocarcinoma.[7] However, as in the case of many cancers, the exact risk factors are unknown.

The diagnosis of any disease depends on its clinical manifestations, findings on physical examination, and on adjuvant examination. Adenocarcinoma of the anal canal is no exception. The clinical manifestations of anal cancer are frequently late and nonspecific and generally relate to the size of the tumor and the extent of infiltration. Anorectal bleeding is the most common presenting sign of anal cancer, occurring in 45% of patients. Anorectal pain and fullness are present in 30% of patients, while 20% present with no symptoms. Other symptoms include thin-caliber stools and changes in bowel movements, and in addition, the sensation of incomplete evacuation.[8,9] This case presented with clinical manifestations of reduplicated hematochezia. The findings indicate that attention must be paid to senile patients with repeated long-term hematochezia. Unfortunately, the diagnosis of anal cancer is often delayed, because anorectal bleeding is initially thought to be caused by hemorrhoids. Most anal canal cancers are located near the anus. Digital rectal examination is of great significance in the diagnosis of this disease. Additionally, it can be easily distinguished from hemorrhoids, in this manner. Careful digital examination of the anal region can provide essential information regarding the presence, the site, and the extent of involvement. For all patients with hematochezia, rectal examination is absolutely essential. Colonoscopy is also indispensable, as it can help determine the location, the shape, the size of the tumor, and most importantly, the pathological type and differentiation of the tumor on biopsy. Imaging examinations, such as computed tomography, endoscopic ultrasonography, and magnetic resonance imaging, can help us determine whether tumors have local infiltration, distant metastasis, and lymph node metastasis. The results can provide an important reference to formulate corresponding treatment strategies and evaluate the prognosis.

The anal canal is histologically divided into 3 parts on the basis of its lining epithelium: The colorectal zone, lined by colorectal type glandular mucosa proximally, the anal transition zone, lined by an epithelium having varying appearances in the middle, and the squamous epithelium-lined distal portion. Therefore, despite its short length, a variety of tumor types may develop in the anal canal, reflecting its complex anatomic and histological structure.[10] The rectal type is the most common type of adenocarcinoma in the anal canal and arises within the upper zone lined by the colorectal-type mucosa. Its histology is similar to that of adenocarcinoma of the large intestine. It is generally difficult or impossible to separate adenocarcinoma of the anal canal from adenocarcinoma of the lower rectum. Immunohistochemistry (IHC) showed negativity for CK7 and positivity for CK20 and CDX2, confirming the colorectal phenotype.[10,11] Carcinoma-associated with chronic fistulae-in-ano was first described by Rosser in 1934.[12] The tumor usually presents as a large, painful mass in the buttock. A long history of fistula-in-ano and multiple perirectal abscesses is considered characteristic.[13] A minimum criterion for diagnosis is an overlying nonneoplastic

mucosa, which may be ulcerated. It includes 2 groups, depending on its association with either fistulae, or with anal glands.[14]

Primary adenocarcinoma of the anal glands is extremely uncommon. It is composed of small acini and tubules originating from ducts opening onto the mucosal surface and infiltrating the surrounding tissues, without necessarily causing ulceration. The acini are lined by cuboidal cells showing scanty mucin secretion. The most recent WHO definition of anal gland carcinoma stresses on the morphology and the histogenesis. It also states that only a few reported cases have shown evidence of an anal gland-origin because of continuity between the anal gland epithelium and the tumor.[14] In a significant proportion of cases, however, a direct relation cannot be established between the tumor and the anal glands. This is because of a number of factors, which include obliteration of the point of origin, effacement of the primary tumor site, associated inflammatory changes, and the vagaries of sampling.[10] Therefore, Hobbs et al have proposed a definition of anal gland carcinoma as being a tumor composed of haphazardly dispersed CK7 positive small glands with scant mucin production, invading the wall of the anorectal area, without an intraluminal component. This definition does not require continuity of the invasive tumor with the benign anal glands. According to Hobbs et al, a primary intramural anal canal tumor composed of small dispersed glands could be considered as an anal gland carcinoma even without examination of the expression of CK.[15] In our case, the cancer cells were small tubular or strip-like, disorderly distributed, without secreted mucus in the cytoplasm, and invading the muscular layer of the anal canal, as observed after staining with hematoxylin and eosin (HE) (Fig. 2). Furthermore, the cells were CK7 positive on IHC. (Fig. 3). Our case met the prescribed criteria; hence, this was a primary adenocarcinoma of the anal glands.

Owing to the rarity of anal adenocarcinoma, most of the studies in literature contained small numbers of patients. Treatments included local excision, radiotherapy, chemotherapy, chemoradiotherapy, and APR.[16] The relevant studies indicate that a combination of radical surgical resection and pre-or postoperative chemoradiotherapy offers the best chance of survival. In the present case, APR was performed and followed by adjuvant chemotherapy.

The overall prognosis of anal adenocarcinoma is poor. In a series of 21 patients with anal adenocarcinoma, both the crude 5- and 10-year survival rates were only 4.8%.[17] The condition may be difficult to diagnose owing to its rarity and the presentation with pain, rectal bleeding, and a perianal mass. This may be attributed to a number of benign conditions.[18] Similar to other tumors, early detection, and early intervention are of great prognostic importance. Adequate attention must be paid to the clinical manifestations of repeated hematochezia, anorectal pain, and fullness. Digital rectal examination is of great importance in the diagnosis of this disease. For patients with the above clinical manifestations, rectal digital examination must be performed for every patient. If the rectal digital examination is highly suggestive of the possibility of tumors, further enteroscopy, computed tomography, and magnetic resonance imaging are needed.

4. Conclusion

We have presented a case of primary adenocarcinoma of the anal glands. We believe that the diagnosis of this disease still depends on the clinical manifestations, the physical examination, and on auxiliary examinations, particularly, rectal digital examination. The treatment of this disease is comprehensive and centered on surgery. The unified diagnostic therapeutic criteria have not yet been defined owing to a very low incidence of this disease. In conclusion, studies of more cases are required for uniformity in diagnosis and for the development of treatment protocols.

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Author contributions

Investigation: Yong Ji.
Supervision: Yong Ji.
Writing – original draft: Youxin Zhou.
Writing – review & editing: Youxin Zhou.
Youxin Zhou orcid: 0000-0001-8498-709X.

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