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Case Report

A Long-standing Perianal Fistula Hiding an Adenocarcinoma: A Case Report

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Abstract

Fistula-associated anal adenocarcinoma (FAAC) is an uncommon disease. Due to the clinical similarity in the symptoms to benign anal fistulas, FAAC can confuse clinicians and lead to delayed diagnosis. We report a case of FAAC in a patient with a 20-year history of an unhealed perianal fistula and who had recently been diagnosed with thrombocytopenia, hepatitis C, liver cirrhosis, and splenomegaly. He presented with a painful, indurated perianal fistula-producing bloody discharge which concealed an adenocarcinoma. In this report, we describe how the atypical clinical features prompted an initial biopsy via curettage and outline the therapeutic strategies for advanced FAAC. The primary tumor demonstrated a 14% reduction in size following multimodality treatment, including concurrent chemoradiotherapy and subsequent systemic chemotherapy with targeted therapy. However, rapid disease progression with metastases to both lungs and para-aortic lymph nodes ultimately led to the patient's death. This case underscores the diagnostic challenges and aggressive nature of FAAC.

Keywords: Case report, curettage biopsy, fistula-associated anal adenocarcinoma, long-standing anal fistula

Introduction

Cancers arising in the anorectal region are heterogeneous, characterized by distinct etiological factors, histopathological features, and therapeutic strategies. Rectal cancer is usually adenocarcinoma, typically associated with sporadic genetic mutations. In contrast, anal cancer is most commonly squamous cell carcinoma (SCC), which is strongly linked to persistent infection with oncogenic human papillomavirus or human immunodeficiency virus (HIV) (ESMO guidelines 2021 for anal cancer). The treatment strategies differ between localized rectal cancer and anal SCC. Rectal cancer is typically managed by surgical resection, often preceded by neoadjuvant chemoradiotherapy, whereas anal SCC is primarily treated with definitive chemoradiation.

Fistula-associated anal adenocarcinoma (FAAC) arising from a chronic perianal fistula is a rare subtype of anal cancer of extramucosal origin. The pathologic features of FAAC are

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characterized by high histologic variability.[1] Several studies have suggested that the clinical presentations of this disease can mimic those of benign anal fistulas, thereby leading to delayed diagnosis and a high percentage of FAAC patients being diagnosed at an advanced stage.[1-3] There is no standard treatment of FAAC. Surgical resection remains the mainstay of treatment of local disease. Neoadjuvant chemoradiation therapy can be considered to improve local control. We present this case of FAAC hidden in a long-standing fistula to remind clinicians of the importance of maintaining a high index of suspicion for this disease.

Case Report

A 53-year-old male presented to our colorectal surgery clinic with progressive perianal pain and new-onset bloody discharge over the past several months. He had undergone surgical treatment for a perianal fistula of the left buttock 20 years earlier and had experienced intermittent discharge since then, but without bloody discharge or severe pain until this visit.

He denied any history of malignancy or inflammatory bowel disease. A physical examination revealed an external fistulous opening with bloody discharge and irregular scar tissue on the left buttock [Figure 1a]. The fistula tract and surrounding scar tissue formed a palpable mildly tender mass. Fistulography demonstrated a communication between the external opening and the anorectal lumen [Figure 1b]. Hepatitis screening revealed chronic hepatitis C virus infection but no evidence of hepatitis B virus infection; HIV testing was not performed. He denied a history of alcohol or drug abuse or having sex with men. Laboratory evaluations showed thrombocytopenia (46,000/μL), elevated transaminases (aspartate aminotransferase: 79 IU/L; alanine transaminase: 85 IU/L), and no leukocytosis. Abdominal ultrasonography and computed tomography (CT) revealed liver cirrhosis, splenomegaly, and esophageal varices.

Intrigued by the unhealed fistula for 20 years with the unusual presentations mentioned above, we performed curettage to acquire tissue from the fistular tract at the outpatient clinic to make a pathologic diagnosis. The pathology report showed an adenocarcinoma [Figure 2]. Subsequent colonoscopy showed no evidence of synchronous colorectal cancer but did identify a small friable lesion at the internal opening of the perianal fistula [Figure 3], which was also confirmed histologically as adenocarcinoma of similar morphology. A CT scan showed a heterogeneously enhancing mass measuring 4.7 cm × 2.6 cm in the left perianal region. Enlarged lymph nodes were noted in the left inguinal and iliac chains [Figure 4a and b]. Ultrasound-guided biopsy of the left inguinal lymph nodes confirmed metastatic adenocarcinoma. The clinical stage of the perianal adenocarcinoma was T4bN2aM1, stage 4 (AJCC 7th edition) with an elevated carcinoembryonic antigen level (25.59 ng/mL). Immunohistochemistry was positive for cytokeratin 20 (CK 20) but negative for CK 7. Molecular

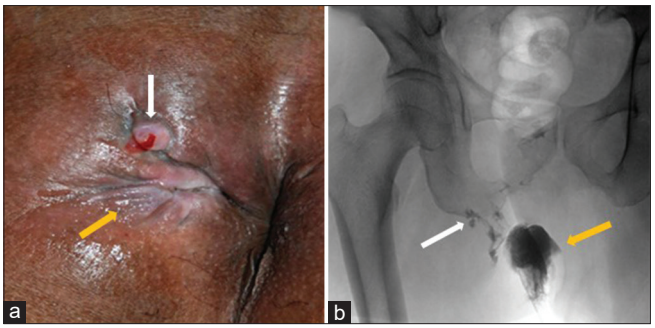

Figure 1: Perianal fistula. (a) An external opening of the fistula showing bloody discharge (white arrow) and irregular scar tissue (yellow arrow). (b) Fistulogram showed communication between the external skin opening (white arrow) and anorectal lumen (yellow arrow)

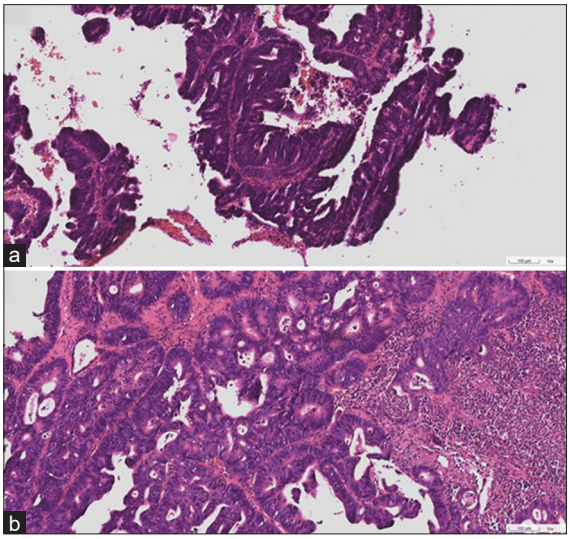

Figure 2: Adenocarcinoma. Tissue biopsy was taken from (a) the fistula tract and (b) external opening of fistula by curettage. Microscopically, the section showed irregularly shaped glands composed of hyperchromatic and pleomorphic columnal epithelium. Cytoplasmic mucin was markedly reduced. Stromal invasion of the neoplastic glands was present

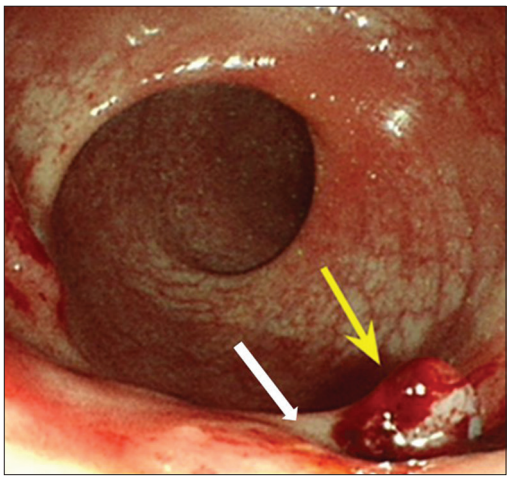

Figure 3: Colonoscopy. A mucosal protrusion (yellow arrow) at the internal opening of the anal fistula (white arrow) in the anal canal

testing showed wild-type K-RAS and N-RAS at codons 12 and 13 of exons 2, 3, and 4.

The multidisciplinary team decided on concurrent chemoradiotherapy (CCRT) as the upfront therapy, followed by systemic therapy with the FOLFIRI regimen (irinotecan and fluorouracil) plus bevacizumab. Follow-up CT showed a reduction in tumor volume by 14%. However, the cancer metastasized to the lungs and paraaortic lymph nodes within 1 year [Figure 5a and b]. Ascites and a pathological fracture of the lumbar spine occurred after 15 months of treatment. Figure 6 summarizes the adjustment of chemotherapy and targeted therapy in response to cancer progression. Unfortunately, the patient ultimately succumbed to infection.

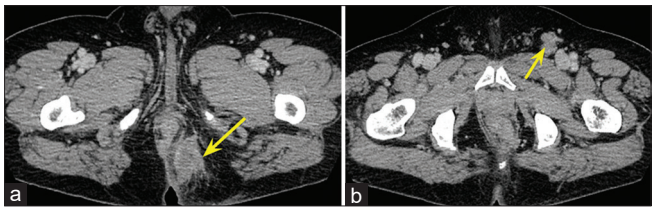

Figure 4: Clinical staging by abdominal computed tomography scan. (a) A heterogeneous enhancing tumor in the left posterior to the anus (yellow arrow). (b) Enlarged lymph nodes in the left inguinal area (yellow arrow)

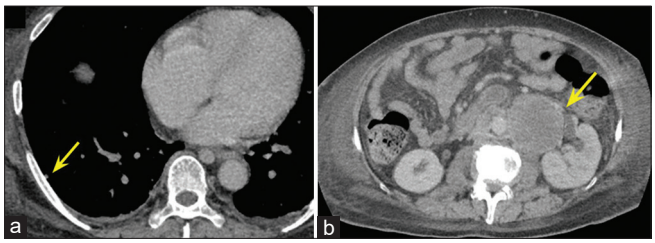

Figure 5: Computed tomography scan indicated disease progression. (a) Tiny lung nodules (yellow arrow) developed in the lung at 8 months. (b) Paraaortic lymphadenopathy (yellow arrow) developed at 11 months

Discussion

FAAC occurs in approximately 0.6% of patients with perianal fistulas.[1] The incidence is higher among patients with anal fistulizing Crohn's disease, ranging from 0.79% to 2.9%.[1,4] Carcinogenesis in chronic fistulas has been associated with persistent inflammation, a concept first proposed by Rosser in 1934. The reason why many FAAC tumors exhibit a mucinous histological subtype remains unclear.[2,3]

Regarding the differential diagnosis, adenocarcinoma arising within a fistula tract may result from implantation of colorectal cancer into a preexisting fistula, as suggested by Gomes *et al*.[5] Thus, the co-existence of colorectal cancer and an anal fistula may indicate an implantation etiology. Alternatively, a fistula harboring adenocarcinoma may be due to direct invasion by an existing adenocarcinoma, as described by Lee *et al*.[6] Rosser proposed diagnostic criteria for FAAC, including: (1) The presence of a chronic fistula for at least 10 years before the diagnosis of cancer, (2) the tumor within the anus or rectum is secondary to direct extension from cancer in the fistula, and (3) the internal opening is located in the anus.[7] The present case meets these criteria, characterized by a 20-year history of a fistula, absence of synchronous colorectal cancer, no evidence of anorectal cancer in the previous surgery, and a tumor confined entirely to the fistula tract. These features not only fulfill Rosser's criteria but also exclude the possibilities of tumor seeding or secondary invasion.

A major diagnostic challenge of FAAC lies in its similarity to benign fistulas. Thus clinicians should remain alert when encountering patients with unusual presentations such as an unhealed fistula for more than 10 years, increasing bloody discharge, and irregular scars with tumor formation, etc.[2,3] In our case, these warning signs prompted us to obtain tissue for histopathological confirmation.

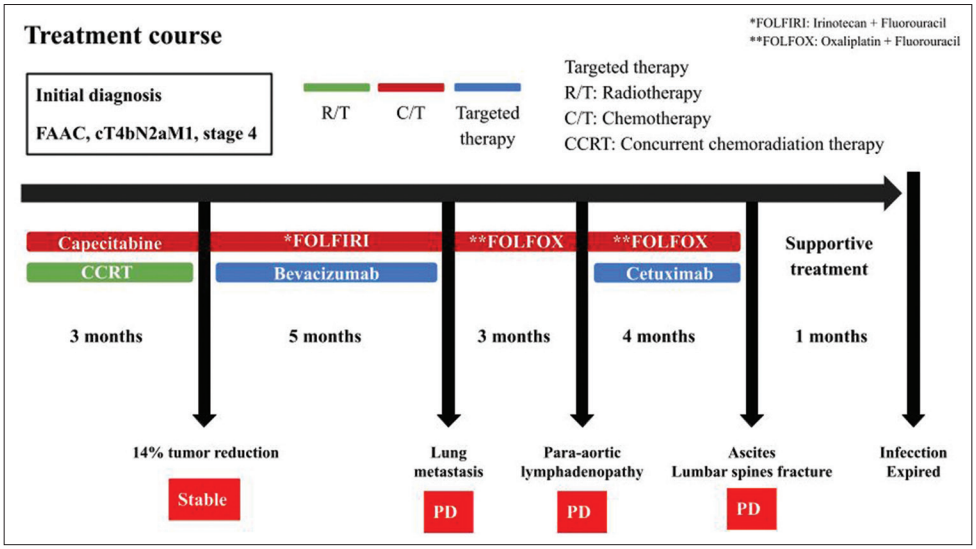

Figure 6: Clinical course. The multimodality of therapies was adjusted in response to Fistula-associated anal adenocarcinoma progression. Stable: Stable disease, PD: Progressive disease

The prognosis of FAAC remains poor, primarily due to delayed diagnosis. The reported 5-year overall survival rate is approximately 33%.[1] More than half of patients present with locally advanced disease or with nodal or distant metastases at the time of diagnosis.[1-3] The inguinal lymph nodes are a common site of lymphatic spread, often complicating management, as in our case.[3,8]

To date, no standardized treatment guidelines are available for FAAC. Cure-intent abdominoperineal resection is recommended for the early stage of FAAC. For advanced FAAC, several studies utilized neoadjuvant CCRT with or without adjuvant therapy to enhance resectability and improve local control.[2,3,8] One case series reported seven patients who received neoadjuvant chemoradiation therapy followed by cure-intent APR, and the patients remained disease free during a follow-up period of 64.3 months.[3] These results may indicate the clinical benefit of preoperative neoadjuvant CCRT. A cure-intent surgical approach can be considered in patients without unresectable distant metastasis.

In our case, first-line CCRT followed by systemic therapy resulted in stable disease and a reduction in tumor size by 14%, but not enough to achieve R0 resection. As our case had distant metastasis to inguinal lymph nodes, the role of APR surgery was considered palliative intent. Furthermore, our patient had comorbidities including liver cirrhosis, splenomegaly and thrombocytopenia, making the surgical risks much higher. After shared decision-making with the patient and his family, he preferred to continue chemotherapy and targeted therapy after the neoadjuvant CCRT. Considering the reimbursement policy of the National Health Insurance bureau in Taiwan and the surgically incurable status, bevacizumab was selected for first-line systemic treatment, with cetuximab reserved for later-line therapy. However, the response was not satisfactory. We suspect that additional mutations in other genes such as BRAF and HER2/neu may have led to the poor response to multiple lines of targeted therapy and chemotherapy.[9,10]

Conclusion

This case illustrates that being alert to unusual symptoms can help to distinguish a malignant fistula from a benign fistula. We recommend simple curettage to harvest tissue when encountering suspicious fistulas. Biopsy under anesthesia can be the next choice to acquire tissue for thediagnosis.

Ethical statement

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of Mackay Memorial Hospital for granting the permission (approval number: 25MMHIS219e, approval date: June 23, 2025). The requirement for informed consent was waived by IRB.

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Author contributions

I-Wei Lin, contributed to acquisition of data and manuscript preparation. Ying-Wen Su contributed to the concept and design of this report. Ching-Heng Ting, contributed to acquisition and review of pathology data. Ming-Jen Chen, contributed to the design and concept of this case report as well as critical revision of manuscript. All the authors participated in the data interpretation and approved the final draft.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Harpain F, Dawoud C, Wimmer K, Schlager L, Kirchnawy S, Rizk D, *et al*. Fistula-associated anal adenocarcinoma: A 20-Year single-center experience. Ann Surg Oncol 2023;30:3517-27.
2. Leong FQ, Chan DK, Tan KK. Anal adenocarcinoma can masquerade as chronic anal fistula in Asians. Ann Coloproctol 2019;35:47-9.
3. Gaertner WB, Hagerman GF, Finne CO, Alavi K, Jessurun J, Rothenberger DA, *et al*. Fistula-associated anal adenocarcinoma: Good results with aggressive therapy. Dis Colon Rectum 2008;51:1061-7.
4. Shwaartz C, Munger JA, Deliz JR, Bornstein JE, Gorfine SR, Chessin DB, *et al*. Fistula-associated anorectal cancer in the setting of Crohn's disease. Dis Colon Rectum 2016;59:1168-73.
5. Gomes RM, Kumar RK, Desouza A, Saklani A. Implantation metastasis from adenocarcinoma of the sigmoid colon into a perianal fistula: A case report. Ann Gastroenterol 2014;27:276-9.
6. Lee SH, Zucker M, Sato T. Primary adenocarcinoma of an anal gland with secondary perianal fistulas. Hum Pathol 1981;12:1034-7.
7. Ghosh NK, Kumar A. Chronic fistula in ano associated with adenocarcinoma: A case report with a review of the literature. Ann Coloproctol 2024;40:S1-5.
8. Osone K, Ogawa H, Katayama C, Shibasaki Y, Suga K, Komine C, *et al*. Outcomes of surgical treatment in patients with anorectal fistula cancer. Surg Case Rep 2021;7:32.
9. Taniguchi H, Uehara K, Ishikawa T, Okochi O, Akazawa N, Okuda H, *et al*. BRAF V600E and Non-V600E Mutations in RAS wild-type metastatic colorectal cancer: Prognostic and therapeutic insights from a nationwide, multicenter, observational study (J-BROS). Cancers (Basel) 2025;17:399.
10. Achalla LS, Shinde RK, Jogdand S, Vodithala S. Review of the role of HER2/neu in colorectal carcinomas. Cureus 2022;14:e25409.