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Malignant Transformation to Mucinous Adenocarcinoma in Chronic Fistula-in-ano

Kronik Anal Fistülde Müsinöz Adenokarsinomaya Malign Dönüşüm

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ABSTRACT

Malignant transformation in chronic fistula-in-ano (FIA) is rare, typically occurring due to long-term inflammation in untreated fistulas, though the exact cause remains unclear. These cancers are often aggressive, and their symptoms can resemble those of a benign fistula, leading to delayed diagnosis. We report a 71-year-old gentleman with supralelevator FIA who developed perianal mucinous adenocarcinoma. The patient had suffered from a recurrent fistula for 40 years despite multiple surgeries and presented to our centre with a non-healing FIA. Magnetic resonance imaging (MRI) revealed a complex fistula with several openings, and histopathology confirmed adenocarcinoma with mucinous differentiation. Chronic FIA is a common but its rare potential to transform into perianal mucinous adenocarcinoma emphasizes the need for early detection and intervention. Although uncommon, malignant transformation should be considered in longstanding or recurrent complex FIA, particularly when symptoms persist despite previous treatment. Early imaging, such as MRI, and multiple biopsies are crucial for identifying malignancy and ensuring proper treatment, especially radical surgery.

Keywords: Anal fistula, anal gland, perianal gland neoplasm, mucinous adenocarcinoma, rectal fistula

Öz

Kronik anal fistülde (FIA) malign dönüşüm nadir görülmekte olup, genellikle tedavi edilmemiş fistüllerde uzun süreli enflamasyonla ilişkilendirilmekle birlikte, kesin etiyojisi henüz aydınlatılamamıştır. Bu maligniteler sıklıkla agresif seyretmekte ve klinik bulgularının benign fistüllerle benzerlik göstermesi nedeniyle tanıda gecikmelere yol açabilmektedir. Bu çalışmada, supralelevator anal fistülü bulunan ve perianal müsinöz adenokarsinom gelişen 71 yaşındaki bir erkek hastanın sunulması amaçlanmıştır. Hasta, birden fazla cerrahi girişime rağmen 40 yıldır tekrarlayan anal fistül öyküsü bulunması ve fistülün iyileşmemesi nedeniyle merkezimize başvurmuştur. Manyetik rezonans görüntüleme (MRG) sonucunda birden fazla dış açıklığı bulunan kompleks bir fistül saptanmış, histopatolojik inceleme ile müsinöz farklılaşma gösteren adenokarsinom tanısı doğrulanmıştır. FIA yaygın görülen bir klinik durum olmakla birlikte, nadiren perianal müsinöz adenokarsinomaya dönüşebilmesi, erken tanı ve tedavinin önemini ortaya koymaktadır. Özellikle uzun süredir mevcut olan veya tekrarlayan kompleks anal fistüllerde, önceki tedavilere rağmen semptomların devam etmesi durumunda malign dönüşüm olasılığı göz önünde bulundurulmalıdır. Malignitenin erken dönemde saptanması ve uygun tedavi stratejisinin belirlenmesi açısından MRG gibi görüntüleme yöntemlerinin erken dönemde uygulanması ve çoklu biyopsilerle histopatolojik değerlendirmenin yapılması büyük önem taşımaktadır. Bu yaklaşım, özellikle radikal cerrahi gerektiren olgularda tedavinin doğru biçimde planlanmasına katkı sağlayabilir.

Anahtar Sözcükler: Anal fistül, anal bez, perianal bez neoplazisi, müsinöz adenokarsinom, rektal fistül

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INTRODUCTION

Perianal malignancies arising from abscesses or fistulas can either be adenocarcinomas or squamous cell carcinomas, with adenocarcinomas being more common (2.9-10%) (1). Among these, mucinous adenocarcinomas are the most frequently observed subtype (1). Mucinous adenocarcinomas are characterized by the secretion of extracellular mucin, which makes up more than 50% of the tumour volume (1). Perianal fistulas are a common problem, with around 90% caused by infected anal glands, often leading to perianal abscesses (2). Approximately 10% of perirectal fistulas are linked to other factors, such as Crohn's disease, trauma, human immunodeficiency virus, sexually transmitted infections, radiation therapy, or foreign bodies (2).

In rare cases, perianal fistulas and abscesses can undergo malignant transformation, potentially developing into carcinomas. These cancers are believed to result from chronic inflammation and irritation in long-standing fistulas, though the exact link between the fistula and carcinoma remains unclear (3). The tumours are usually aggressive, often mucinous, and frequently misdiagnosed early on (4). Symptoms can initially mimic benign fistula cases, and biopsies may not detect the carcinoma, leading to a delay in diagnosis. As a result, tumours are often found at more advanced stages, typically in deeper regions like the ischioanal fossa and perineum (3). It can also be difficult to determine whether the cancer developed independently or because of the fistula (3).

Given the rarity of this condition and the lack of controlled trials, this article presents a case of perianal mucinous adenocarcinoma arising from an untreated anorectal fistula. We share our experience from a tertiary care institution and provide a review of the relevant literature to guide early diagnosis and management.

CASE PRESENTATION

A 71-year-old gentleman presented with a recurrent fistula-in-ano (FIA) that had persisted for 40 years. Despite multiple previous surgeries at different healthcare facilities, he continued to experience persistent purulent discharge. On perianal examination, several tender external openings were noted, draining pus and mucin (Figure 1). The tumour marker namely carcinoembryonic antigen was within normal range.

Colonoscopy revealed an irregular internal opening in the anal canal without evidence of ulceration or mucosal inflammation. The colonoscopy was advanced to the caecum. An incidental ascending colon polyp (Paris 1sp) was identified and removed via cold snare polypectomy. Histopathological examination of the polyp showed no dysplasia or malignancy. Magnetic resonance imaging (MRI) of the pelvis demonstrated a grade 5 complex perianal fistula (St. James's University Hospital classification) with supralelevator extension and multiple bilateral ischioanal collections (Figure 2). The fistulous tracts demonstrated heterogeneous T2 hyperintensity with enhancing solid and papillary components on post-contrast sequences, raising suspicion for malignant transformation.

The patient subsequently underwent examination under anaesthesia, debridement, and seton insertion (Figure 3). Tissue obtained from the debridement was sent for histopathological analysis, which revealed adenocarcinoma with mucinous differentiation

(Figure 4). Histopathological examination demonstrated low-grade, well-differentiated adenocarcinoma with abundant extracellular mucin comprising approximately 80% of the tumour volume, consistent with mucinous adenocarcinoma. The tumour was characterized by mucin pools containing villoglandular proliferations of neoplastic epithelial cells. A distinctive feature was the direct continuity between the neoplastic glandular epithelium and the perianal epidermis at the sinus openings, with abrupt transitions to squamous epithelium within epithelialized fistulous tracts, supporting the origin of the malignancy from a chronic FIA. Immunohistochemical staining showed CK7 negativity with positivity for CK20 and CDX2, supporting a colorectal-type adenocarcinoma phenotype.

He was clinically staged as cT4N0Mx according to the TNM staging system, consistent with locally advanced disease. A staging computed tomography (CT) scan was planned prior to multidisciplinary team discussion to determine the suitability of neoadjuvant therapy followed by radical surgery. However, the patient's condition deteriorated rapidly, and he unfortunately succumbed before completion of CT staging and further oncological planning. Written informed consent was obtained from the patient's relatives for their anonymised information to be published in this article.

DISCUSSION

Determining whether FIA preceded the development of malignancy or whether malignancy led to fistula formation can be clinically challenging. To help establish malignant transformation in chronic FIA, Rosser proposed three diagnostic criteria: The fistula should be present for at least 10 years prior to carcinoma development; the tumour identified in the rectum or anal canal should represent direct extension from carcinoma within the fistula; and the internal opening of the fistula should communicate with the anal canal rather than the tumour itself (4). Our patient fulfilled most of the reported criteria. However, the lesion was not directly visualised on colonoscopy and was identified only on MRI.



Figure 1. Perineal examination during initial visit showing several external openings, which were tender to the touch, draining pus and mucin.

Perianal mucinous adenocarcinoma arising from chronic anorectal fistulas is rare. The exact relationship between chronic fistulas and malignant transformation remains unclear, although long-standing inflammation is considered a contributing factor. These tumours often grow slowly within the ischioanal region and may not extend into the bowel lumen, which can delay diagnosis. Therefore, early detection requires a high index of suspicion, particularly in patients with long-standing or recurrent fistulas. Tissue biopsy is essential when malignancy is suspected, and pelvic MRI may help differentiate between inflammatory fistulous disease and malignant transformation (5).

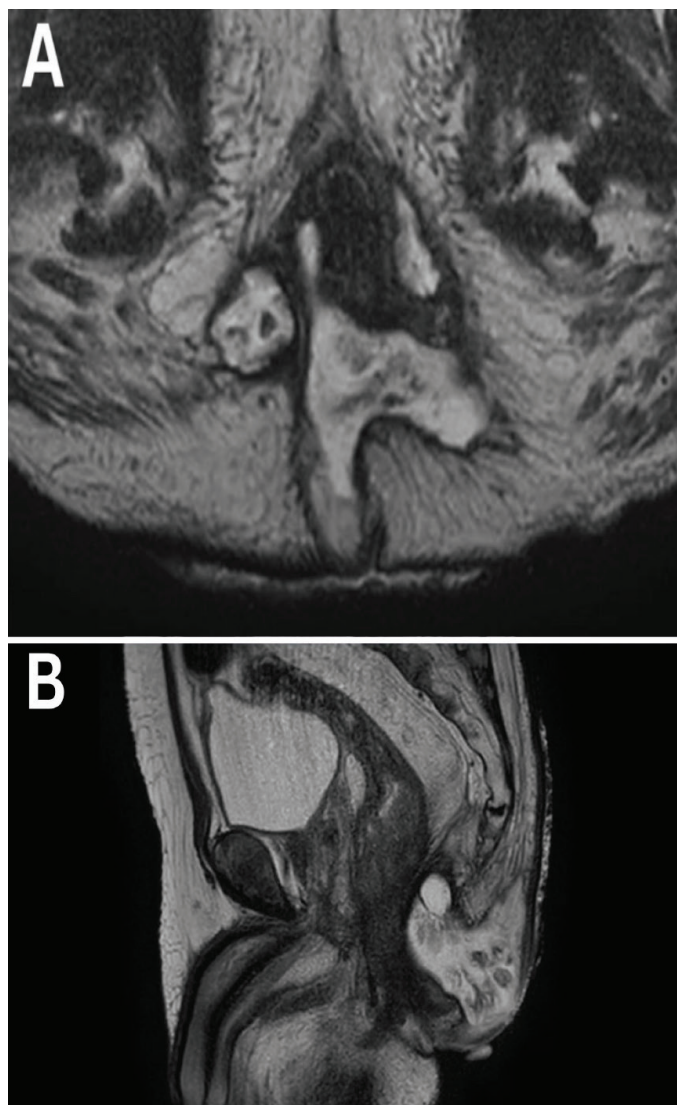


Figure 2. T2-weighted pelvic MRI demonstrating a grade 5 complex perianal fistula (St. James University Hospital classification) with supralelevator extension and multiple bilateral ischioanal collections. The fistulous tracts communicate with the anal canal and extend across the sphincter complex with horseshoe configuration. The lesions show heterogeneous T2 hyperintensity with enhancing solid and papillary components on post-contrast sequences, with irregular thickening of the lower rectal wall, features suspicious for malignant transformation. Axial (A) and sagittal (B) views are shown.

MRI: Magnetic resonance imaging.

Surgery remains the cornerstone of treatment, with adequate oncologic resection being critical for favourable outcomes. In many cases, radical procedures such as abdominoperineal resection are required to achieve complete tumour removal, as local excision alone is often insufficient. Neoadjuvant therapy may improve recurrence-free survival in selected patients; however, there is currently no consensus regarding the optimal use of neoadjuvant or adjuvant chemotherapy and radiotherapy, and treatment should be individualized. Early recognition and appropriate management are essential to prevent disease progression and improve prognosis (5).

Chronic and recurrent FIA should raise suspicion for malignant transformation, particularly in longstanding disease with persistent discharge or atypical features. Pelvic MRI and tissue biopsy play an important role in differentiating complex inflammatory fistulas from underlying mucinous adenocarcinoma, especially when colonoscopy findings are inconclusive. Early recognition and timely multidisciplinary management are essential, as delayed diagnosis often results in locally advanced disease requiring radical treatment.



Figure 3. Perineal examination (post operative) following the examination under anesthesia and Hanley procedure, external openings were identified at 7 o'clock and 8 o'clock positions (3 cm from the anal verge), along with a supralelevator internal opening at 8 o'clock (8 cm from the anal verge). Another external opening was located at 3 o'clock. The openings were interconnected at the 8 o'clock position. A mucin-filled cavity was present at all external openings.

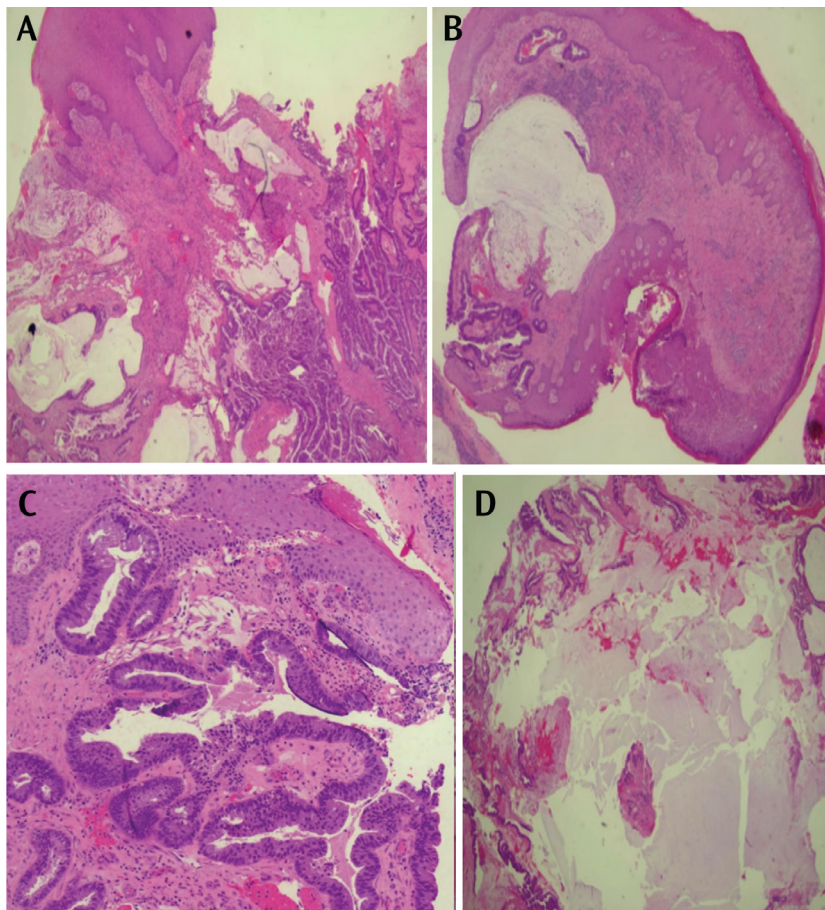


Figure 4. Carcinomatous glands infiltrating beneath inflamed squamous epithelium (A) and associated with mucinous production (B). (C) Malignant glands displaying moderate nuclear pleomorphism and loss of nuclear polarity. (D) Malignant glands accompanied by extracellular mucin pools.

Ethics

Informed Consent: Written informed consent was obtained from the patient's relatives for their anonymised information to be published in this article.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: K.H.H., A.B.K., Concept: F.H., Design: F.H., Analysis or Interpretation: A.B.K., Literature Search: F.M.A.H., Writing: F.M.A.H.

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