

Mucinous adenocarcinoma arising from a chronic perianal fistula: A case report and literature review



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ABSTRACT

Perianal fistula is a common disease affecting the general population but development of mucinous adenocarcinoma (MA) in a chronic perianal fistula is a rare entity. Due to the rare nature of the disease, there are no established guidelines regarding the diagnosis and management of the condition. The aim of this article is to report a case of MA perianal region that we managed surgically with an extra levator abdominoperineal resection and flap reconstruction.

Key words: Mucinous adenocarcinoma in perianal fistula; Extra levator abdomino-perineal resection; Perianal fistula

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INTRODUCTION

Perianal fistula is a common disease among the general population. There is a risk for malignant transformation of chronic perianal fistulae, especially those persisting for more than 10 years. It is known that perianal fistulae and abscesses arise from the anal glands and ducts, but the origin of these carcinomas are controversial. The current hypothesis for carcinomatous change is chronic inflammation leading to transformation of the rectal mucosal cells or focal adenomatous hyperplasia of the anal glands.¹ Due to the rarity of occurrence of this complication, its etiological relations have not been extensively studied.

The carcinoma may be adenocarcinoma or squamous cell carcinoma, among which adenocarcinoma is the more common type.^{2,3} An extremely rare complication is the transformation into mucinous variety of adenocarcinoma. Mucinous adenocarcinoma (MA) of perianal region constitutes only 2–3% of large intestine neoplasms.⁴ It has an indolent course and even though inguinal lymph node metastasis may occur in advanced cases, distant metastasis is rare. It is a locally aggressive tumor and has a high risk of local recurrence post-treatment.⁵

A patient with early MA of perianal region will be having only the subtle symptoms of a benign pathology due to the absence of tumor inside the bowel and its indolent growth deep into the ischioanal fossa. This causes delay in diagnosis

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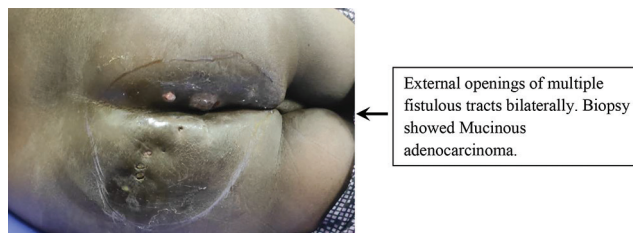
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and treatment which leads to a poorer prognosis as most patients would have developed locally advanced disease.

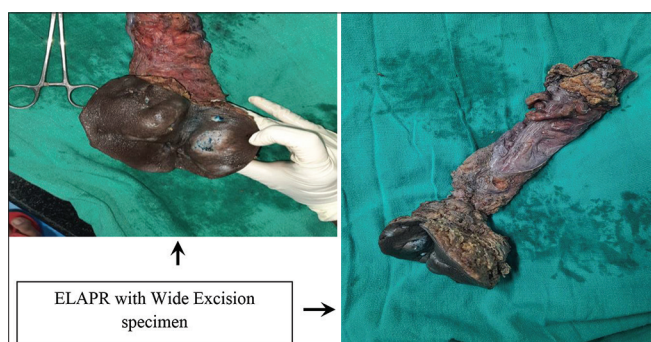
The currently accepted treatment strategy is combined pre- and post-operative chemoradiation with surgery and wide resection margins.⁶ The aim of this case report is to present our experience in a case that underwent pre-operative concurrent chemoradiation and abdominoperineal resection (APR) with wide local excision and to discuss the outcome. Written informed consent was taken from the patient before preparation of this case report and any accompanying images.

CASE REPORT

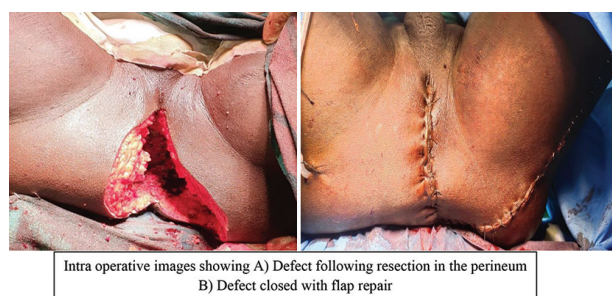
A 48-year-old male presented to us with complaints of multiple discharging wounds in the perianal region for the past 12 years. On clinical evaluation, he was found to have multiple fistulae-in-ano. He underwent a colonoscopic evaluation in 2019 which revealed a sigmoid polyp and polypectomy was done. Histopathological evaluation of the polyp was done and was reported as tubulovillous adenoma with high-grade dysplasia. He was symptomatically managed for the perianal fistula, but lost in follow-up. Patient presented to us after 1 year in 2021 with the same complaints and a perianal biopsy was done.



The histopathological examination report came as MA of perianal region. The patient was evaluated and after a multidisciplinary discussion, he was taken up for sigmoid loop diversion colostomy in September, 2021. He underwent neoadjuvant chemoradiation with 45 Gy units in 28 fractions along with Capecitabine. The neoadjuvant therapy was completed in April, 2022.

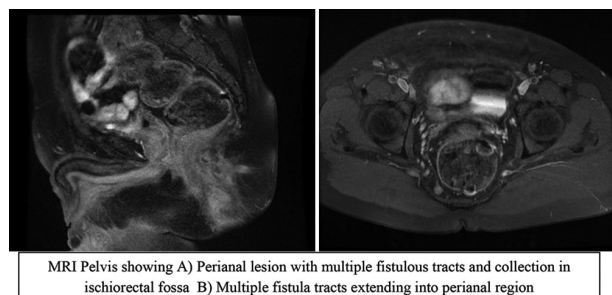


In July, 2022 he underwent extralevator APR with excision of all the fistulous tracts on both sides of the perianal area. The defect was covered with a V-Y advancement flap in the same sitting. Post-operative period was uneventful except for loss of a portion of the flap which was managed conservatively. The histopathology report shows that all resected margins were negative. He is currently taking adjuvant radiation therapy and has shown no features suggestive of local recurrence or distant metastasis.

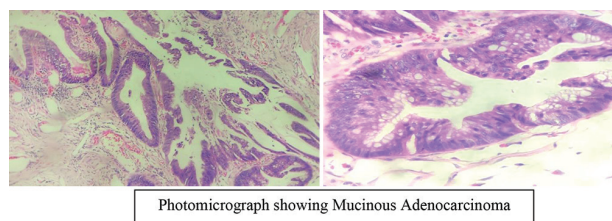


DISCUSSION

The incidence of perianal fistula in general population varies from 1.04 to 8.6/100,000 with a male preponderance.⁷ It is a very common disease but malignant transformation is a rare occurrence. Repeated friction, scarring and inflammatory reactions maybe risk factors for this transformation but etiological relations lack confirmation due to the rarity of the disease. Perianal fistulas are very common in association with Crohn's disease and the association between Crohn's disease and MA is well documented.⁸



Though initially objected, there is now compelling evidence in literature to support that chronic fistula can give rise to malignancy. In conditions where an adequately treated fistula has persistent mucoid discharge, undue induration, or prolonged healing, carcinoma should be suspected.



It has been identified that the anal glands at the level of dentate line are the etiology of most perianal abscesses and fistulae. MA is an invasive adenocarcinoma made up of malignant glandular cells with intracytoplasmic mucin. It can develop at multiple sites in the gastrointestinal tract (stomach, gall bladder, and colon), breast, thyroid, and skin but perianal MA is a rare entity.⁹

The most common clinical presentation of patients is a long standing perianal fistula and the features of malignant transformation are usually masked by the benign disease. The symptoms suggestive of malignant transformation are new onset pain, induration, or persistent mucinous discharge associated with an ulceroproliferative lesion or palpable mass in the perianal region.¹⁰ Rectal examination often reveals no findings and colonoscopic evaluation shows no lesions in the anorectum. As rectal mucosa is rarely affected, rectal bleeding or intestinal obstruction is seldom seen. As the common presentation usually mimics benign conditions, clinical suspicion is of utmost importance for early diagnosis of the condition.

Imaging studies including computed tomography, magnetic resonance imaging (MRI), and Transrectal ultrasonography may be useful in establishing the local extent of the disease and to plan the surgical approach. MRI pelvis is preferred as the mucin in the neoplasm has a specific appearance in the images.¹¹ Histopathological examination remains the gold standard for diagnosis of the disease but due to its indolent course and as rectal mucosa is not involved, multiple biopsies are often required to confirm the malignancy. Furthermore, all tissues removed during fistulectomy procedures should be subjected to thorough microscopic examination, especially in long standing perianal fistulae.¹² In many cases, the definitive diagnosis is only reached on histological examination of the resected specimen as pre-operative biopsies often fail to reveal an infiltrating carcinoma.¹³

Surgery has been the primary treatment for the condition and the preferred procedure is an APR with wide local excision. This removes the malignant tissues and decreases the risk of local recurrence when margins are clear.¹⁴ In cases with locally advanced disease, an extra levator APR with reconstruction of the perineum may be done, as it was done for our patient so as to get an R0 resection. Complementary radiotherapy can clear the large neoplastic hollows and reduce the risk of recurrence. The efficacy of chemoradiation in the management of perianal MA is still unclear. Yang *et al.*, suggested that the combination of chemo radiation is a valid option in conditions where patient is unfit or refuses surgery and when tumor was not completely resected.¹⁵ In locally advanced tumors, pre-operative chemo radiation can cause downsizing of

large neoplasms, contribute to eliminate disseminated tumor cells, and thus increase the chances of R0 resection while decreasing local recurrence (15). The use of pre-operative chemoembolization of large tumors has also been described to limit the perineal resection.¹⁶

The prognosis of perianal carcinoma is very poor despite radical surgery and the 5-year survival rate is <20% as per literature,¹ mainly due to the delayed diagnosis and advanced stage at the time of presentation. By combining the various treatment modalities, a better prognosis is expected in the future.

CONCLUSION

MA arising in a chronic perianal fistula is a rare entity and often mimics benign inflammatory conditions, leading to delayed diagnosis and advanced stage at presentation. It is associated with high level of local infiltration and lymph node metastases. Clinical suspicion is of utmost importance in identifying the disease and multiple biopsies are often required for confirmation of the diagnosis. Neoadjuvant chemoradiation followed by aggressive surgery as APR and wide local excision with negative margins with supplementary radiation or chemotherapy is appropriate in a locally advanced disease and can decrease the risk of local recurrence.

The case presented here has now completed post-operative radiotherapy and he is on regular follow-up and has shown no evidence of metastasis or local recurrence. These tumors are currently associated with a poor prognosis and high recurrence rates but with a multimodal and aggressive management, R0 resection rates can be increased and a better prognosis can be expected in the future.

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