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FISTULA-IN-ANO ASSOCIATED WITH MUCINOUS ADENOCARCINOMA: CASE REPORT WITH REVIEW OF THE LITERATURE

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ABSTRACT

Objective: Fistula-associated perianal Mucinous Adenocarcinoma (MA) is a rare entity and easily overlooked by many surgeons. The aim of this case report is to highlight its possible occurrence especially in a background of chronic fistula in ano. **Case presentation:** This report will present the details of a 50-year-old male patient who was diagnosed with perianal mucinous adenocarcinoma arising in a fistula. The patient underwent neo-adjuvant chemo-radiotherapy followed by laparoscopic Abdominoperineal resection (APR) and adjuvant chemotherapy. A comprehensive review of the literature on this rare tumor will be conducted, focusing on the diagnostic and therapeutic procedures. An informed written consent, including permission to use relevant images, was obtained from the patient for this case report. **Conclusion:** while APR remains the primary surgical option for fistula associated with rectal cancer, a multidisciplinary approach that includes preoperative chemo-radiotherapy may lead to positive response rates.

KEYWORDS: Fistula, Mucinous adenocarcinoma, APR.

INTRODUCTION

One of the most common anorectal diseases is the perianal fistula so called Fistula-in-ano. The most common etiology for fistula-in-ano occurrence is the obstruction of the anal gland resulting in an abscess formation which if inadequately drained may later result in a fistula development.[1] It is found that a fistula will already be present on examination of Thirty to 70% of patients diagnosed with an anorectal abscess.[2]

The malignant transformation in a pre-existing anal fistulae might occur in some cases in association with Crohn's disease[3], but others may contain epithelioid granulomas, or extravasated mucin but without other signs of inflammatory bowel disease.[4]

From a histological perspective, carcinomas that develop in fistulas typically consist of mucinous type, although tubular adenocarcinomas and squamous neoplasia may also be present.[5]

The initial report of fistula-in-ano linked to mucous adenocarcinoma was provided by Rosser in 1934, where he documented seven cases of mucous adenocarcinoma arising from longstanding anal fistulae.[6]

Malignant adenomas of the perianal region are a rare tumor, making up less than 5% of all anal tumors.[7] It remains uncertain whether the presence of a chronic fistula contributes to the formation of these tumors, or if the fistula itself is a complication caused by these malignancies.[8]

The identification of these tumors is often delayed as their symptoms closely resemble those of benign inflammatory anorectal conditions. The delayed diagnosis results in late treatment and poor prognostic outcomes.

Fistula-in-ano related malignant adenocarcinoma is a type of tumor that grows slowly and shows low-grade features. It is known to be locally aggressive, with rare instances of spreading to other parts of the body, usually through the lymphatic system.[9]

At present, the prevailing management strategy for these tumors involves neo-adjuvant concurrent chemo-radiotherapy, followed by surgery (APR) and adjuvant chemotherapy.[10]

CASE PRESENTATION

A 50-year-old male patient who had no past medical history nor chronic medical illnesses underwent incision and drainage of perianal abscess 10 years ago at 3 o'clock. Since that time patient claimed history of recurrent perianal pain, mucous discharge and occasional lump at 3 o'clock that regress in size after spontaneous drainage of pus and mucous. The patient did not seek medical attention until 6 months ago (February 2023) when he presented to our clinic complaining of progressive perianal swelling at the same site associated with pain that he tried to decrease it with NSAIDs.

The patient did not provide a record of any family history of colorectal cancer, nor did he report experiencing fever, vomiting, weight loss, fatigue, or rectal bleeding. Upon examination, the patient appeared to be in good overall health but displayed mild distress due to perianal pain. Local examination revealed a 6×10 cm swelling on the left side of the anus, with its innermost point located approximately 3-4 cm from the anal verge. The swelling was found to have a firm consistency, to be immobile with attachment to underlying structures, to have multiple punctums, and to show no signs of active discharge (Figure 1). Digital rectal examination was unremarkable, except for a dimple in the anal mucosa at the 3 o'clock position, 2cm above the dentate line. Upon applying finger pressure to the dimple, a minimal amount of purulent discharge was observed to emerge from the swelling's punctums, prompting suspicion of an underlying fistula.

Figure 1: Left sided perianal swelling.

The comprehensive assessment for better evaluation and diagnosis comprised tumor markers, pelvic MRI, pan computerized tomography scan (Pan CT scan), and colonoscopy. The CEA level was measured at 78. The pelvic MRI with IV contrast revealed a trans-sphincter fistulous tract arising from 3 o'clock and extending downward posteriorly with peri-anal collection (Figure 2). A colonoscopy was performed and no masses were identified. The Pan CT scan yielded normal results.

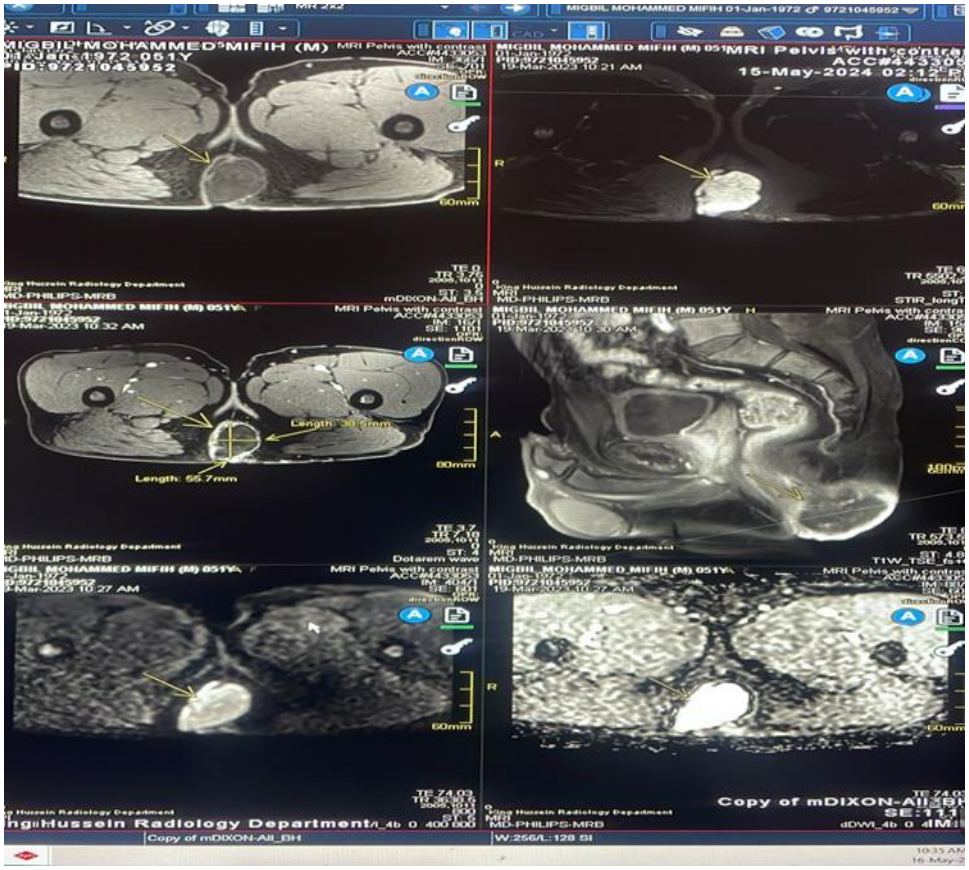

Figure 2: Peri-anal cystic tumor, hypointense at T1wi, hyperintense at T2wi, shows peripheral heterogenous enhancement, with fistulous communication with the anal sphincter. Study date: March 2023.

The examination under anesthesia revealed a mid trans-sphincteric fistula located at the 3 o'clock position. Biopsies were taken from the deep fistula tract and the swollen gluteal region, which indicated the presence of invasive moderately differentiated adenocarcinoma with mucinous differentiation (Figure 3).

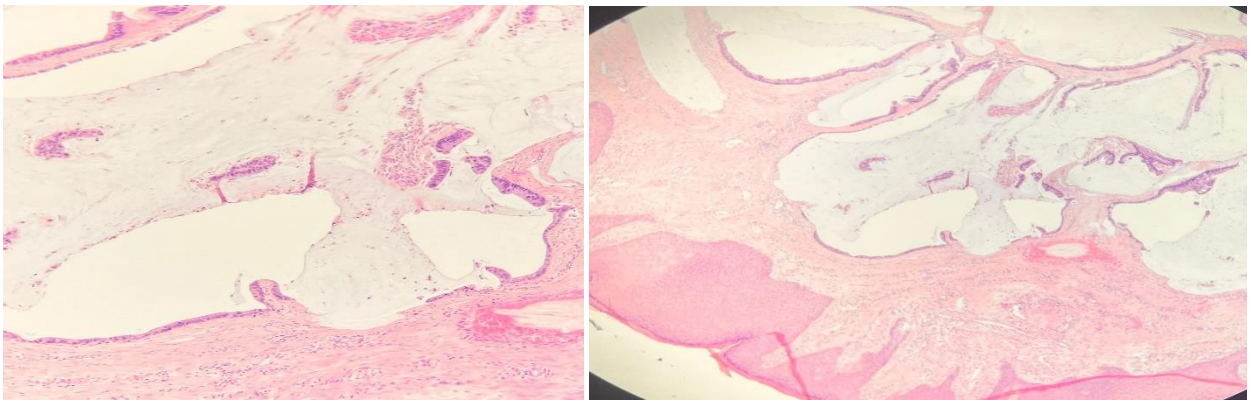

Figure 3: Histopathologic findings of invasive moderately differentiated adenocarcinoma with pools of extracellular mucin.

The patient's condition was extensively discussed by a team of experts from various disciplines, and it was decided that the next steps would be to undergo neo-adjuvant chemo-radiotherapy, followed by a reevaluation and potential surgery.

The patient commenced his neo-adjuvant treatment (combined chemo-radiotherapy, 8 courses of 5FU+ Radiotherapy 45 Gy, NACRT) in March 2023, and completed the last dose in September 2023. Subsequently, a follow-up pelvic MRI was conducted, revealing a marked decrease in the size of the tumor and surrounding edema due to the radiotherapy effect (Figure 4).

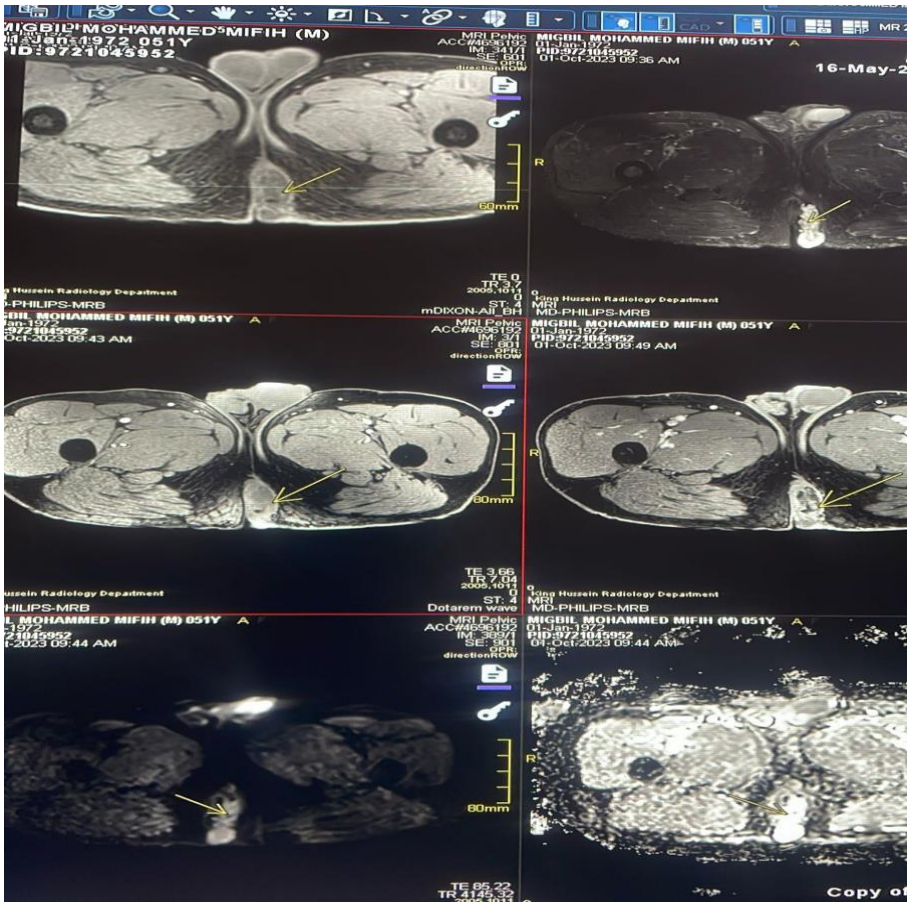

Figure 4: The peri-anal mass still present with same relation to anal sphincters but with significant size reduction. Study date: 1 October.

The patient had a laparoscopic Abdominoperineal Resection with primary closure of the perineal wound in November 2023, as shown in Figure 5. The patient recovered well and was discharged home on the second day after the operation.

Figure 5: post APR image.

Fourteen days following the patient's visit to the clinic, during which he reported no issues and adjusted well to his stoma, the histopathology of the removed specimen indicated the absence of any remaining viable tumor, with ypT0 ypN0 and thirteen reactive lymph nodes (see Figure 6). Upon the recommendation of the Multidisciplinary Team member (the hematologist), the patient commenced adjuvant chemotherapy (consisting of 6 cycles of FOLFOX). Subsequent follow-up appointments, both in person and by phone, confirmed that the patient was tolerating his stoma well and had no complaints.

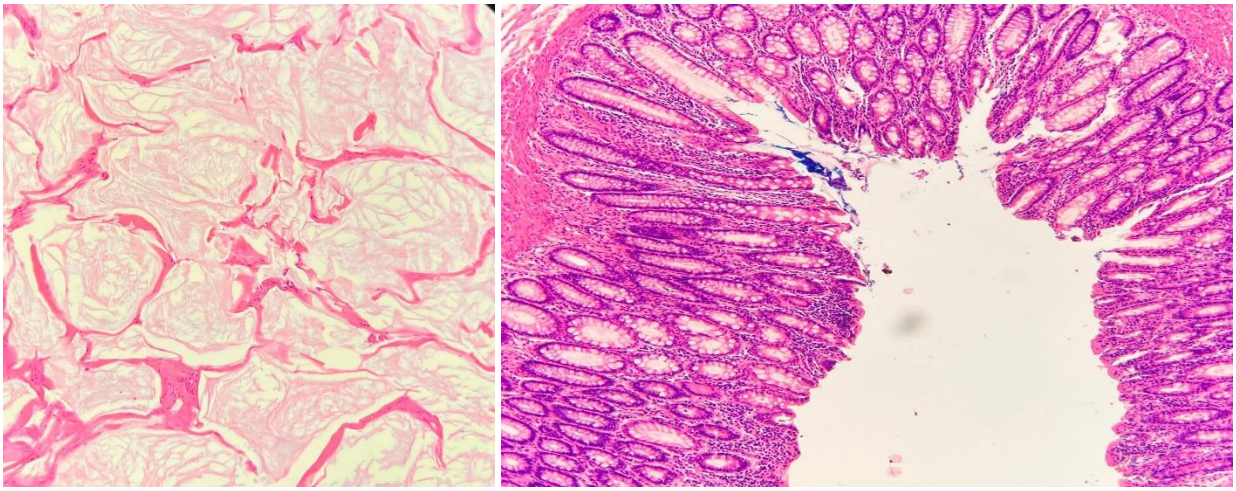

Figure 6: APR Histopathology: no residual viable tumor, ypT0 ypN0.

DISCUSSION

In presenting this case, we seek to highlight the rare diagnosis of MA occurring in the setting of chronic fistula-in-ano. Inflammatory bowel disease and diabetes are additional established risk factors for the occurrence of MA in the perianal area.[11]

The extended duration of perianal fistula and anal discomfort during defecation, along with the occasional gelatinous discharge, are the main defining features of perianal mucinous carcinoma. Conversely, 15% of patients do not report any symptoms associated with this tumor.[12]

Diagnosing this tumor is challenging because early symptoms can be similar to those of a fistula with abscess formation. Therefore, it is crucial to conduct a deep biopsy of the fistulous tract and opening in order to accurately diagnose the condition.[5]

In order to diagnose perianal adenocarcinoma associated with anal fistula, Rosser established specific determining factors, including a fistula that existed at least 10 years before the carcinoma, the fistula opening internally into the anal canal and outside the tumor, and the tumor being evident in the anal canal and extending directly from the fistula.[13] Subsequent case reports and series have been documented in the literature, but no clearly defined diagnostic standards have been established.

Serum CEA testing has been proposed as a way to detect the potential for chronic perianal fistulas to develop into malignancies.[14] Despite the high CEA levels observed in our case study (CEA 78) and in approximately 73% of

patients in existing literature, it cannot be relied upon as a definitive tumor marker for malignancy in fistula-in-ano.[15]

With respect to the utilization of MRI results for anticipating the diagnosis of carcinoma in chronic fistula, it appears that MRI may be advantageous but requires additional research to validate its effectiveness.[16]

In this particular case, the patient underwent a colonoscopy that yielded normal results. This was performed to screen for colorectal cancers that could potentially develop in a chronic fistula, as has been documented in medical literature, despite the infrequency of such occurrences.[17]

The typical method of spread for these tumors is through the lymphatic system, often leading to metastasis in the inguinal lymph nodes. Similar to the majority of cases documented in literature, our patient had locally advanced disease upon presentation, but no metastasis to the inguinal lymph nodes.[5]

The recommended treatment for these tumors is Abdominoperineal resection. In this case study, the treatment approach involved a Multidisciplinary Team considering this locally advanced fistula-in-ano associated with MA in a manner similar to locally advanced rectal cancer. The patient was therefore provided with neoadjuvant chemoradiotherapy and then offered laparoscopic APR, followed by adjuvant chemotherapy. The significance of neoadjuvant chemoradiotherapy in the management of perianal MA is not yet well established.[18]

However, in our case report, NACRT led to tumor downsizing and downstaging, as evidenced by the post neo-adjuvant MRI images (Figure 4). This allowed us to move forward with a laparoscopic standard APR + wide local excision and primary closure of the perineal wound. Consequently, NACRT eliminated the necessity for extra-levator APR and perineal reconstructive procedures, thereby preventing the short-term complications associated with these surgical options.[19]

Concurrently, the application of the NACRT method to treat the tumor in our patient resulted in achieving R0 and a complete pathological response (ypT0 ypN0 with Thirteen reactive lymph nodes), as demonstrated by the histopathological analysis of the resected specimen. This outcome will aid in preventing local recurrences.[20]

CONCLUSION

Fistula-in-ano associated MA is a rare tumor that can be diagnose with difficulty as it mirrors other benign inflammatory conditions resulting in a delayed diagnosis and more advanced stage at initial presentation. The primary considerations in reaching a diagnosis for this tumor involve maintaining a high level of clinical suspicion and conducting several deep biopsies of the affected area.

A Multidisciplinary team discussion is of extreme importance in approaching these tumors. The management strategy of NACRT + APR + Adjuvant chemotherapy seems to be suitable in a locally advanced fistula-in-ano associated MA and can achieve the resection rates of R0 and reduce the risk of local recurrence. Further studies are actually needed to validate this management approach.

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