CASE REPORT

Synchronous anal mucinous adenocarcinoma and anal tuberculosis presenting as chronic anal fistula: Challenging management

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How to cite this article: Benammi S, Bakali Y, Alaoui M, et al. Synchronous anal mucinous adenocarcinoma and anal tuberculosis presenting as chronic anal fistula: Challenging management. Arch Clin Cases. 2023;10(2):74-77. doi: 10.22551/2023.39.1002.10245

ABSTRACT

Metachronous anal tuberculosis to an anal adenocarcinoma is an exceptional condition. The aim of our study was to report management of the first case of synchronized anal canal adenocarcinoma and anal canal tuberculosis and report our multidisciplinary approach. A 71-year-old man was admitted for non-healing anal fistula. Rectal examination at supine position showed an ulcerative growth at the medio-superior quadrant on a radius of 2cm from the anal verge. Digital rectal examination assessed no tumor in the anorectum. Biopsy of fistulae confirmed diagnosis of anal mucinous adenocarcinoma with coexisting anal tuberculosis. Further exploration confirmed diagnosis with no distal metastasis, no active pulmonary tuberculosis and no immunodepression. Adjuvant anti-bacillary chemotherapy was initiated 1 month prior to adjuvant radio-chemotherapy. Patient was re-admitted at the 6th week following the last dose of radio-chemotherapy for surgery. On long-term evaluation at 10 months, the patient reported absence of symptoms with weight gain. Association of both entities is rare. Chronic inflammatory damage may possibly initiate a sequence of metaplasia and dysplasia, resulting in neoplastic transformation. Anal canal adenocarcinoma treatment follows same guidelines as rectal cancer. Extra-pulmonary tuberculosis treatment follows anti-bacillary protocol with consequent side effects. Therefore, our case is a unique clinical challenge for physicians. Management decision was multidisciplinary process. Their pathophysiology relationship is yet to be understood. Moreover, each entity has defined and individual therapeutic protocols and indications. All this taken into consideration, such case presents a clinical and therapeutic challenge for physicians.

KEYWORDS: Anal mucinous adenocarcinoma; Anal tuberculosis; Extrapulmonary tuberculosis; Metachronous; Anal fistula

INTRODUCTION

Anal canal cancer is rare tumor of the digestive tract, counting in recent literature for 3% of all intestinal tumors [1]. Moreover, clinical symptoms of anal cancer are various, non-specific and often chronic with consequent delayed diagnosis.

Tuberculosis is a bacterial infection caused by Koch bacillus strain [2]. And while extra-pulmonary tuberculosis is common, metachronous anal tuberculosis to an anal adenocarcinoma is an exceptional condition [3]. Few cases of anal canal tuberculosis have been described indeed, but no previous case of associated anal cancer and anal tuberculosis has been described in literature to the best of our knowledge. Their pathophysiology relationship is yet to be understood. Moreover, each entity has defined and individual therapeutic protocols and indications. All this taken into consideration, such a case creates a clinical and therapeutic challenge for physicians. The aim of our study was to report the unique case of synchronized anal canal adenocarcinoma and anal canal tuberculosis treated with neo-adjuvant chemo-radiotherapy and anti-bacillary chemotherapy followed by radical surgery.

Received: March 2023; **Accepted after review:** May 2023; **Published:** June 2023.

CASE PRESENTATION

A 71-year-old man was admitted in our structure for perianal discharge. No past medical history was reported. The patient reported no tobacco, alcohol, or illicit drugs intake. His past surgical history included a precedent undocumented surgery of anal fistula over 20 years ago, to which the patient supposedly underwent incision and drainage, according to history assessment. Evolution was uneventful until October 2019 where the patient was treated twice for recurrent anal abscess fistulae at an interval of one month. Twenty-five days later the patient was admitted to our department for non-healing anal fistula. The patient reported upon admission persistent foul-smelling anal discharge with no hematochezia, no blood spotting, and no pain.

Rectal examination at supine position showed an ulcerative growth measuring 1x2cm at the medio-superior quadrant on a radius of 2cm from the anal verge. Clinical examination assessed a healed scar from a fistulous path at the left inferior quadrant (Figure 1.A).

Digital rectal examination showed no growth in the anorectum with a lax anal opening and no inguinal or any generalized lymphadenopathy. The remainder of the examination was standard. Pelvic MRI showed a left perianal abscess creating a complex anal fistula attaining the scrotum, the ischia fossa, and the levator ani muscle.

Biopsy examination confirmed diagnosis of anal mucinous adenocarcinoma with coexisting epithelioid granuloma with caseous necrosis consistent with anal tuberculosis. Pulmonary active tuberculosis was ruled out through TB-biological tests. HIV infection and immunodeficiency state was ruled out as well. Thoraco-abdominal-pelvic CT scan did not demonstrate distal metastasis. Consequent to multidisciplinary deliberation, adjuvant anti-bacillary chemotherapy and long-course chemo-radiotherapy was started. Adjuvant anti-bacillary chemotherapy was initiated 1 month prior to radio-chemotherapy. Surveillance of hepatic liver functions was carried along the treatment course, and the radio-chemotherapy protocol included a total of 50 Gry fractioned over five weeks. The patient was re-admitted at the 6th week following the last dose of radio-chemotherapy aiming to re-evaluate clinically and complete the therapeutic protocol. Latter clinical examination assessed scars of previous peri-anal ulcerative lesions and peri-anal fistulae, and painful digital rectal exam with persistent left abscess (Figure 1.B). The second pelvic MRI showed discreet hemi circumferential focal anal thickening, persistent though reduced perianal abscess, and persistent complex anal fistula attaining the inter-sphincter space (Figure 2).

Decision was made for abdominal perineal resection (APR). Post-operative evolution was uneventful. The patient was discharged on day 10, after completion of hospice-training of surgical wound care, by both the patient and its caretakers including family. Short-term evaluation one month later was satisfying. Further multidisciplinary discussions ruled unnecessary to prescribe adjuvant chemotherapy based on a satisfactory result of operative specimen histology. On long-term evaluation at 6 months, the patient reported absence of symptoms with weight gain with satisfactory wound healing (Figure 3).

DISCUSSION

Anal cancer is a rare entity among the digestive tract representing only 3% [1]. The anal canal region is a complex anatomic structure, with multiple histologic features, leading to the consequently elevated number of anal tumor types. Primary anal adenocarcinoma is the second most common anal tumor, though representing less than 20% of prevalence [1]. Clinical symptoms are various and non-specific. Moreover, it has been described that chronic perianal fistula can masquerade an anal canal adenocarcinoma [4-6]. Indeed, it has been described that the molecular pathogenesis of anal adenocarcinoma may have chronic inflammation as contingent [7]. Treatment of the anal canal adenocarcinoma was described to follow same guidelines as rectal cancer [8].

On the other hand, tuberculosis (TB) is an infection more often chronic and strenuous, caused by the bacteria Koch bacillus. Few cases of anal canal tuberculosis have been described; and to be noted they have been associated to a context of immunodeficiency [9]. Extra-pulmonary tuberculosis is a common entity indeed including anal tuberculosis site, nevertheless metachronous anal tuberculosis and adenocarcinoma is a rare condition. Finally, extra-pulmonary tuberculosis treatment follows a previously well-established guideline [9]. Anti-bacillary guidelines include prolonged periods of adequate anti-bacillary chemotherapy, associated with careful screening for hepatic failure and other side effects [9].

Association of both entities is rare, and their pathophysiology relationship is yet to be understood indeed. It has been described that chronic inflammatory damage may possibly initiate a sequence of metaplasia and dysplasia,

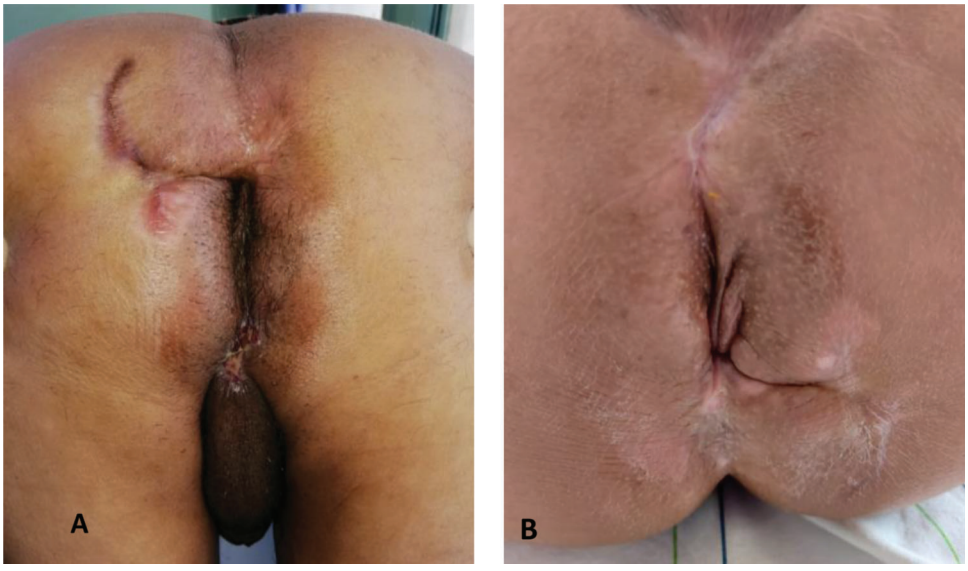

Fig. 1. Clinical examination prior to radio-chemotherapy (A) showing previous peri-anal ulcerative lesions with persistent left abscess, and after radio-chemotherapy (B) showing a healed scar from a fistulous path at the left inferior quadrant.

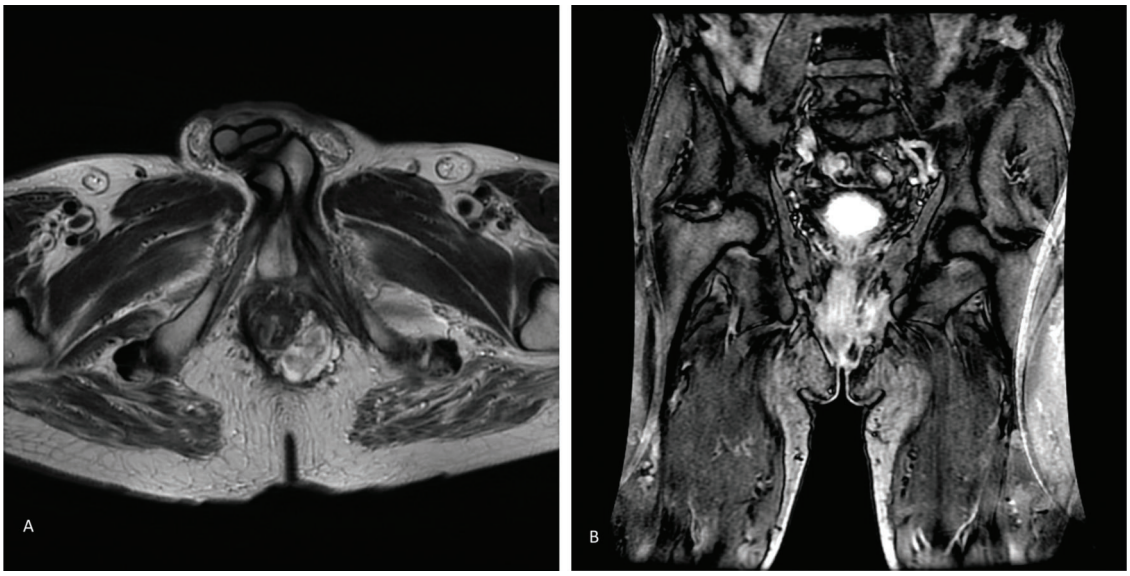

Fig. 2. Transversal (A) and sagittal (A) view of the second pelvic MRI showing discreet hemi circumferential focal anal thickening, persistent perianal abscess, and persistent complex anal fistula attaining the inter-sphincter space.

Fig. 3. Perineal wound healing at follow-up.

resulting in neoplastic transformation [10]. Furthermore, anorectal tuberculosis often presents as chronic non-healing anal lesions, frequently mimicking Crohn's disease, or neoplastic disease [9].

All this taken into consideration, our clinical case represents a unique and interesting clinical challenge for physicians. In fact, we report a highly rare case of synchronized anal canal adenocarcinoma and anal canal tuberculosis with considerable interest in the challenging therapeutic strategy to be adopted. The treatment course was approved upon institutional multidisciplinary tumor board meeting. We decided to manage our case with a neo-adjuvant anti-bacillary chemotherapy course of induction exclusively over 1 month, followed by association with neo-adjuvant radio-chemotherapy standard protocol after achieving macroscopic containment of inflammatory ongoing process. And finally, radical resection surgery was conducted at standard timing.

To the best of our knowledge, we found restricted available data regarding the association between anti-bacillary and systemic neoplastic chemotherapy and radiotherapy in the literature. We sought to first start the anti-tuberculosis regimen therapy prior to chemoradiation as it places the patient in a myelosuppressive condition with an increased risk of microbial infection [11]. Therefore, it is believed that early use of antimicrobials may play a role in restraining microbial infections [11]. Moreover, current anti-bacillary chemotherapy protocol is a two-phased chemotherapy consisting of an initial intensive phase with multiple drugs and a continuation phase that has been largely approved to be efficient in successful tuberculosis curation [12].

The multidrug initial intensive phase aim is to achieve control of drug-resistant organisms as well as reduction of the bacillary load and risk of dormant reactivation [12]. Hence, we sought to start upfront with anti-tuberculosis therapy prior to radio-chemotherapy restricted to one month in order to limit any delay in cancer management.

However chemotherapeutic agents and antimicrobial agents in general may be responsible for serious complications due to various possible mechanisms [11]. For instance, studies have demonstrated the essential role of normal gut microbiota in the anticancer immune response [11]. Antimicrobial use can therefore possibly alter aimed interactions with immunotherapy, and consequently the outcomes [11]. This emphasizes the importance for close follow-up with the patient, as well as the vital role of multidisciplinary collaborations throughout the treatment protocol and follow-up.

CONCLUSION

We believe that this rare case report would contribute to the literature reporting the management of a rare synchronized anal canal adenocarcinoma and anal canal tuberculosis.

Acknowledgement

This clinical case was presented and published as abstract during the The 14th European Colorectal Congress, 29 November–2 December 2020, St. Gallen, Switzerland.

Conflict of Interest

No conflict of interest to declare.

Ethical Consideration & Disclosure

Patient's informed consent for publication of this case report was obtained.

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