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ANAL CANAL ADENOCARCINOMA LOCALLY TREATED WITH ABDOMINOPERINEAL RESECTION AFTER CHEMORADIOTHERAPY: CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

Background: Primary adenocarcinoma of the anal canal is rare, representing less than 20% of anal canal cancers. Given the limited data regarding treatment and outcomes, the management of this type of cancer is focused on a combined modality therapy involving radical surgery and neoadjuvant/adjuvant chemoradiotherapy.

Case study: A 74-year-old woman presented with pruritus and anal pain with 6 months duration. MRI showed a semi-concentric mass in anal canal posterior wall. After an incisional biopsy that revealed an adenocarcinoma, the patient underwent neoadjuvant chemoradiotherapy followed by laparoscopic abdominoperineal resection.

Conclusion: There is limited research into anal adenocarcinoma since the rarity of this condition. The prognosis of anal adenocarcinoma is poor and the management remains controversial. Therapy strategies are not well established, however, general agreement states that a combined multimodality (combination of radical surgical resection and pre or postoperative chemoradiotherapy) achieves the best outcome.

Keywords: adenocarcinoma; anal; abdominoperineal resection; chemoradiotherapy

INTRODUCTION

Anal canal tumors account for approximately 2% of all cancers [1]. It is more common in woman and its incidence increases with age [2]. More than 60% of tumors of canal anal are histologically squamous cell carcinomas. Primary adenocarcinoma of the anal canal is a rare malignancy representing less than 20% of all anal canal cancers and many of these tumors represent rectal cancer with downward spread [1, 3]. The overall prognosis is poor. This type of cancer is thought to arise from the columnar epithelium of the anal canal including the mucosal surface, the anal glands, and the lining of fistulous tracts [4, 5].

Anal canal adenocarcinoma has a higher prevalence in the sixth decade and is similar in both genders. It is associated with human papillomavirus infection; a history of receptive anal intercourse or sexually transmitted disease; a history of cervical, vulvar, or vaginal cancer; immunosuppression after solid organ transplantation or HIV infection; hematologic malignancies; certain autoimmune disorders; and smoking. Risk factors also include anal Crohn's disease, and chronic fistula-in-ano [6].

The management and therapeutic approach of this rare type of cancer varies widely. It includes local excision, radiotherapy, chemotherapy, chemoradiotherapy, sphincter-sparing salvage therapy and abdominoperineal excision. Distant metastases are more common in adenocarcinoma of the anal canal than with other primary anal tumors. Superficial inguinal, deep pelvic and abdominal lymph nodes may be involved and could limit surgical indication [7]. This decision should entail a multidisciplinary discussion and clinical course of the patient and lesion.

MATERIAL AND METHODS

Clinical file review at our Hospital Center and concordant literature through PubMed/Medline database. We used the keywords: "adenocarcinoma", "anal canal", "abdominoperineal resection" and "chemoradiotherapy".

CASE STUDY

A 74-year-old woman presented with pruritus and anal pain with 6 months duration. There were no complaints of rectal bleeding during defecation. On anoscopic examination, a mass was felt occupying half of the circumference (posterior) in the canal anal, with extension to anal margin, measuring 3 cm in length. Pelvic Magnetic Resonance Imaging (MRI) showed a mass lesion with 31x27x24 mm, between 3 and 9 o´clock, occupying nearly 180º in the posterior wall of the anal canal, involving both internal and external sphincters (Figure 1). No signs of extension into ischiorectal or ischioanal fossae were evidenced. The rectum did not show any tumor.

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A thoraco-abdominopelvic Computerized Tomography (CT) was performed to complete staging and no distant metastasis were found. According to 8th edition of the AJCC cancer staging manual, the tumor was staged as a cT2 N0 M0 (stage IIA). Her hemogram, liver, and kidney function tests were within normal limits, with tumor markers slightly above normal parameters. The patient was submitted to an incisional biopsy that revealed to be an adenocarcinoma of the anal canal. After a multidisciplinary discussion of the case, it was proposed a short course of neoadjuvant chemoradiotherapy in order to reduce the mass volume and downstage the carcinoma. The regimen planned included capecitabine plus 45 Gy in 25 fractions, 5 times/week (1 fraction/ day in pelvis and inguinal sites according to Volumetric Modulated Arc Technique). Three months after the end of oncologic medical treatment, a re-staging pelvic MRI was performed, revealing lesion reduction in the posterior wall of rectal-ano transition, with extension to the internal but not the external sphincter (Figure 2). Tumor regression was classified as grade 2 (partial response).

The treatment was, then, followed by laparoscopic abdominoperineal resection (APR). Radical surgery was carried out with perineum skin resection. The histological analysis of the specimen resected indicated an adenocarcinoma of the anal canal with invasion of the pericolic fat tissue (pT3N0), whereas there was no evidence of disease in local lymph nodes. The postoperative course was uneventful and the patient was discharged on the 8th post-surgery day. Six months after, the patient performed a pelvic MRI and a CT scan that revealed pelvic recurrence with invasion of the vagina and vulva. The patient was proposed for palliative chemotherapy with irinotecan plus cetuximab.

DISCUSSION

The anal region is comprised of the anal canal and the perianal region. The definition of anal canal cancer, based on the 8th edition of the AJCC cancer staging manual states them as tumors that develop from mucosa that cannot be entirely seen when the buttocks is gently pressed[8]. Histologically, the mucosal lining of the anal canal is predominantly formed by squamous epithelium and its margin is lined with skin. The anatomical anal canal begins at the anorectal ring and extends to the anal verge. Functionally, is defined by the sphincter muscles. The superior border is delineated by the palpable upper border of the anal sphincter and puborectalis muscles of the anorectal ring with 3-5 cm in length, and the inferior border starts at the anal orifice [9]. This definition is important when radical surgical treatment is considered. According to World Health Organization, there are 3 types of anal canal adenocarcinoma: those whose origin includes the upper portion of the anal canal, those that derive from anal glands or ducts and those associated with chronic anorectal fistulas [10, 11].

Patients diagnosed with anal canal adenocarcinoma usually present with advanced disease, distant metastasis e, consequently poor survival rates comparing to squamous tumors[12, 13]. Clinical presentation of anal cancers varies between fistulas, abscesses, rectal bleeding, in approximately 45% of patients and anal pain or sensation of a rectal mass in 30% of the cases. National Comprehensive Cancer Network (NCCN) guidelines recommend a careful clinical history and physical observation including anoscopic examination, palpation of the inguinal lymph nodes, fine needle aspiration and/or excisional biopsy of enlarged nodes. Before treatment, a PET/CT scan and pelvic MRI is needed to provide information about tumor staging. Final diagnosis is, only, stablished with a biopsy or histological analysis [14]. Most adenocarcinomas in the anal canal are rectal carcinomas that have spread distally or arise above the dentate line through the rectal mucosa. The distinction between an anal canal or rectal adenocarcinoma with distal spread is very difficult. It involves the pattern of local growth and its dual lymphatic drainage, carrying a high risk of metastasis in inguinal and femoral lymph nodes than adenocarcinomas of the rectum. In our case, the patient did not present with enlarged lymph nodes that could lead to a worse prognosis due to high risk of distant metastasis. Fortunately, the diagnosis was made in an early stage (stage IIA).

There are few studies in what concerns anal canal adenocarcinoma and it shows that does not exist a well stablish treatment protocol [7, 13]. Historically, many authors recommended abdominoperineal resection as the treatment of choice for this type of cancer. Existing retrospective multicentric studies revealed combined therapy with chemoradiotherapy and local excision as the best choice for these patients, reserving APR as a salvage treatment. There is no standard protocol for anal canal adenocarcinoma treatment nor European guidelines for its management [15]. Nevertheless, currently, the advisable therapy for T2/3 N0 M0 carcinomas is neoadjuvant chemoradiotherapy followed by radical surgery, considering adjuvant treatment in micrometastases prevention. Chemoradiotherapy alone should be reserved for patients not fit to surgery or regional metastatic lymphadenopathy. Novel techniques such as robotic and microsurgery are promising since they enable a precise dissection in the pelvis and can minimize morbidity. However, these have a wide learning curve and are still under development [16].

Therapeutic management of our patient was conducted according to existing literature [11]. In our case, a multidisciplinary team involving surgeons, oncologists and radiologists decided our patients' treatment should associate primary chemoradiotherapy and surgical resection. The discussion of all possible options, mainly

in initial stages, is essential to guarantee the best quality of life. APR was performed without complications. Unfortunately, the patient showed pelvic recurrence in 6-months follow-up exams. The overall prognosis is poor. Adenocarcinoma of the anal canal often requires multimodality therapy to achieve better overall survival rates (disease-free and 5-year overall survival rates of 54% and 58%, respectively) [17]. Recurrence rates after combined treatment are observed in nearly 20% and depend on several factors such as tumor grade [15].

Further research and publication of more clinical cases of this rare entity is required for development and uniformity of treatment strategies.

CONCLUSION

The prognosis of anal carcinoma is based on the size of the primary tumor and the presence of lymph node metastases. It is usually poor, and research into this type of cancer is limited by its rarity. Therefore, there is little information on the optimal management. Relevant studies show that a multimodality approach combining radical surgical resection and neoadjuvant/adjuvant chemoradiotherapy offers the best chance of survival.

CONFLICT OF INTEREST:

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