Anal tumors with infrequent histology: Analysis of a series of cases and literature review

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CASE SERIES AND LITERATURE REVIEW

Abstract

Background: The most frequent tumor of the anal region is epidermoid carcinoma; however, other types of tumors such as melanomas, sarcomas, and lymphomas can also develop. Most of them present similar symptoms although diagnosis and prognosis might be radically different. Objective: The objective of this study was to report the clinical and histopathological characteristics of a group of patients diagnosed with non-epidermoid anal neoplasm in a third-level hospital. Materials and Methods: Eight patients with non-epidermoid anal neoplastic biopsy samples were evaluated from March 2013 to January 2017. Demographic data and histopathological results were obtained from the clinical records. Results: Mean age of the patients was 48.9 years (23-84); 37.5% of women and 62.5% of men. Patients presented with rectal bleeding in 25%, anal pain 87.5%, anal tumor 75%, and fever 25%. Among the patients, 37.5% presented with melanoma and 62.5% lymphoma. Regarding patients with lymphoma, 60% had plasmablastic lymphoma and 40% non-Hodgkin’s lymphoma. The diagnostic time was 4 months on average (1-8 months) and 25% of the patients had been previously misdiagnosed with hemorrhoidal disease. Conclusion: Non-epidermoid anal neoplasm cases are infrequent and its accurate diagnosis can take months, therefore, changing prognosis.

Key words: Melanoma. Plasmablastic lymphoma. Anal neoplasm abdominoperineal resection. Anal pain. Colonoscopy. Endoanal ultrasound.

Introduction

The most common malignant tumor in the anal region is epidermoid carcinoma located in the anal canal and in the perianal region1. The American Cancer Society estimated an incidence of 7060 cases in the United States during 20131. Other types of anal tumors are less frequent or rare, which represent a diagnostic and therapeutic challenge because information available is very scarce2. Less frequent histological types include melanoma, carcinoid tumor, sarcomas, lymphomas, hemangiomas, bowel endometriosis, and fibroids. Symptomatology is similar to benign diseases, which delays diagnosis and prognosis as a consequence2. In addition, information reported internationally is scarce, and in our country, we have not found any reports in such regard. The objective of this study is to report the clinical and histopathological characteristics of a series of patients treated for non-epidermoid neoplasm in a tertiary health-care center.
Materials and Methods

A retrospective evaluation and collection of the demographic, clinical, and histopathological data were conducted in patients who were treated at the Coloproctologist Service of the General Hospital of Mexico (Hospital General de México) from March 2014 to January 2017 with a diagnosis of non-epidermoid malignant anal neoplasm. The data obtained by means of descriptive statistics were analyzed for mean quantitative variables and standard deviation (SD) and nominal variables expressed in percentages.

Results

Eight patients were included in the study, of which 5 were men (62.5%) and 3 women (37.5%). Three patients were diagnosed with melanoma, 2 of which (66.6%) were women and 1 (33.4%) a man, five patients were diagnosed with lymphoma, 4 of which (80%) were men and 1 (20%) woman. The lymphoid lineages were three plasmablastic lymphomas and two non-Hodgkin’s lymphomas.

The average age of the patients was 48.9 years (SD 23.19). In relation to patients with melanoma, average age was 73 years (SD 16.52), with a median of 81; of the patients with lymphoma, average age was 34.4 years (SD 10.31), with a median of 39.

In relation to clinical manifestations, anal pain occurred in 5 (100%) patients with lymphoma and 2 (66%) patients with melanoma. Rectal bleeding occurred in 2 (66%) patients with melanoma and no cases were reported for patients with lymphoma. Increased rectal volume was presented in 1 (33.3%) patient with melanoma and in 5 (100%) patients with lymphoma and changes in bowel habits were presented in 1 (33.3%) patient with melanoma and 1 (20%) patient with lymphoma. Table 1 summarizes the patient’s characteristics (Table 1).

To reach a definitive diagnosis, the average time was 4 months (SD 2.82), with 4.3 months for melanoma and 3.8 months for lymphoma.

All patients (100%) with anal lymphoma were positive for human immunodeficiency virus (HIV). Two of these patients received treatment with chemotherapy and radiotherapy plus antiretroviral therapy. The other three patients presented the following evolution: one died before receiving chemotherapy, two patients did not receive treatment, and their outcome is unknown.

As for the three patients with anal melanoma, two of them were classified as clinical stage (CS) IV and one patient with CS II. One patient (CS IV) was treated with abdominoperineal resection (APR) and post-operative radiotherapy. One of the patients (CS IV) was diagnosed with an unresectable cancer, which during its evolution presented severe digestive tract bleeding that was managed with derivative colostomy, tumor embolization, hemostatic radiotherapy, and internal iliac artery ligation, to control hemorrhagic events. The third patient (CS II) was referred to chemotherapy and radiotherapy. However, the patient did not follow treatment.

Discussion

Lymphomas and melanomas of the anal region are rarely diagnosed in our service and no patient is really referred to our unit with such a diagnosis. Most patients were initially evaluated and treated as benign diseases of the anal region, but later developed a tumor lesion with bleeding and complex symptoms that required multidisciplinary management.
As for gastrointestinal melanomas, anorectal melanoma is the most common and represents 0.1-4.6% of anal tumors and represents 0.5-1.6% of melanomas. Less than 500 cases have been reported in literature. About 60% of patients present with metastatic disease when their diagnosis is made. Two of our patients were diagnosed with CS IV; what evidently grants a bad prognosis. The most frequent metastatic sites are the liver, lungs, and bones.

The 5-year survival rate of patients with anal melanoma is 6%. The most common presenting symptom is rectal bleeding, which in some cases can compromise life. One of our patients required multiple treatments to control bleeding. Anal pain and changes in bowel movements are frequent symptoms reported by patients. Anal melanomas are usually confused with hemorrhoidal disease as presented in our series, which delays diagnosis. Anorectal melanomas can be amelanotic in up to 30% of cases; however, dissemination and prognosis are similar to skin cancer; that is, the most important prognostic factor is the depth of the invasion. Likewise, lymphatic invasion is a bad prognosis factor.

The disease usually spreads directly into the rectal mucosa. The most common lymphatic metastases are in the inguinal region and the mesorectal and iliac lymph nodes. It has been reported that mesorectal lymph nodes are positive in up to 40-60% of cases in APR specimens.

The most used treatment is radical surgery APR. However, a less-aggressive surgical procedure has been proposed in the past decade, aimed at the preservation of the anal sphincter complex. In retrospective studies, wide local excision (WLE) is favored over APR due to the morbidity that this entails. In a retrospective study conducted at the MD Anderson Cancer Center, local recurrence was 58% in the WLE group versus 29% in those patients treated with APR. In this same study, the survival rate was 19.5 months for patients treated with APR versus 18.9 months for patients treated with WLE. The authors concluded that it is better to perform WLE when possible, as there is no significant difference in survival rates and systemic dissemination occurs regardless of the procedure to which the patient is subjected.

Regarding adjuvant treatment, there is no evidence that chemotherapy or immunotherapy is curative or reduces the risk of recurrence; in patients with metastatic disease, it has been used although without great benefits. In a retrospective study that evaluated treatment with biochemotherapy, the overall response rate was 44% and a total response rate of 11%, which is similar to the rates reported in the treatment of advanced cutaneous melanoma.

Gastrointestinal lymphomas account for 5% of all lymphomas and primary lymphomas of the colon, rectum, and anus represent < 1% of colonic and rectal neoplasms, perhaps, the least frequent in the region. Most cases of primary colorectal lymphomas are non-Hodgkin’s lymphomas. They can be found in patients with HIV, those associated with this virus such as plasmablastic lymphoma.

Patients present with gastrointestinal lymphomas during their sixties, but, currently, it appears in younger patients, related to HIV infection or immunocompromise. In this case series, all patients were young and had HIV infection. In the study by Castillo et al., it was shown that the average age of plasmablastic lymphoma diagnosis was 38.8 years, more common in men with a ratio of 4:1. Plasmablastic lymphoma and diffuse B-cell lymphoma are among the lymphoma subtypes related to HIV. About 70% of patients with this lymphoma subtype have HIV infection.

The clinical presentation of these tumors is similar to that of squamous cell carcinomas of the anus or rectal adenocarcinomas, with rectal bleeding as the main symptom mostly associated with fever, abdominal pain, nausea, vomiting, and weight loss.

During the proctologic examination, an external tumor can be observed during the digital rectal examination. There may be a palpable lesion, but, sometimes, it is only visible by anoscopy. It is not uncommon for the tumor to be abscessed; therefore, it can be easily confused with other benign pathologies. Clinically and by imaging analysis, it is very difficult to differentiate an anorectal lymphoma from an adenocarcinoma; thus, biopsy is fundamental, as patients’ prognosis and treatment rely on it. It is important to differentiate lymphoma subtypes because some lymphomas such as the plasmablastic type grant a worse prognosis, with a 3-year survival rate of 25%, an overall survival rate of 15 months, and a 2-year survival rate of 10% for HIV-positive patients.

Treatment of anal lymphomas depends, as in all neoplasms, on their CS, although due to their low frequency, there is no known best algorithm to follow in the treatment. Unlike lymphomas in other sites, some studies suggest that in cases where resection is viable, surgical resection should be performed, as patients with residual disease have a worse prognosis; although surgical treatment is rarely indicated and is controversial. Treatment with chemoradiotherapy is indicated for all patients and should be administered taking into
account the disease extension and other factors such as CD4 count in immunocompromised patients².

The survival rate for patients with non-Hodgkin's lymphoma of the colon is low. Patients with localized disease have a significant difference in relation to those patients with nodal involvement at 5 years, 50% versus 24%, respectively.

There are no adequate reports in literature on the survival of patients with rectal plasmablastic lymphoma. However, there are some studies of oral plasmablastic lymphoma, which have shown that the use of antiretroviral drugs associated with chemotherapy is the most effective treatment with a normal survival rate of 5-14 months¹³,¹⁷,¹⁸.

Conclusion

Non-epidermoid anal neoplasms are rare in our service and it may take several months to reach an accurate diagnosis. Anal lymphoma occurs more frequently in conjunction with HIV infection. Anal melanoma has a poor prognosis in relation to survival.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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