Squamous Cell Carcinoma Arising from Perianal Fistula in HIV Positive Patient

Pedro Silva¹,* , Rita Vitorino², Catarina Travancinha¹, João Freire²

ABSTRACT
Anal carcinomas account for 1-2% of all digestive tract cancers. They may occur in the anal canal, perianal region (up to 5cm) and surrounding skin. Squamous cell carcinoma (SCC) is the most frequent type (80%). In the last two decades, the incidence of anal SCC has increased in relation with the human immunodeficiency virus (HIV) infection, especially in men who have sex with men (MSM). Individuals with impaired immunity, such HIV positive, are at higher risk of perianal diseases, which has not been altered by the introduction of highly active antiretroviral therapy. SCC arising from a perianal fistula is rare. We report a rare case of a large squamous cell carcinoma arising from a perianal fistula, in a HIV positive patient, successfully treated with chemo-radiotherapy alone with no late toxicity. Long standing perianal fistula often causes late diagnosis of perianal carcinoma. A previous history of HIV positive may increase the index of suspicion for malignancy.

Key words: Perianal carcinoma, Fistula, HIV, Chemo-radiotherapy.

INTRODUCTION
Anal carcinomas are uncommon malignancies that represent 1-2% of all digestive tract cancers.¹ They may occur in the anal canal, perianal region (up to 5cm) and surrounding skin. Squamous cell carcinoma (SCC) is the most frequent type (80%). In the last two decades, the incidence of anal SCC has increased in relation with the human immunodeficiency virus (HIV) infection, especially in men who have sex with men (MSM).² Individuals with impaired immunity, such HIV positive, are at higher risk of perianal diseases, which has not been altered by the introduction of highly active antiretroviral therapy.³ SCC arising from a perianal fistula is rare.

Long standing perianal fistula often causes late diagnosis of perianal carcinoma. A previous history of HIV positive may increase the index of suspicion for malignancy.⁴ We report a rare case of large squamous cell carcinoma arising from a perianal fistula, in a HIV positive patient, successfully treated with chemo-radiotherapy (CRT) alone.

CASE REPORT
A 69 year-old-man started with perianal suppuration associated with pain about 9 months before being referred to our hospital. The patient had a 25-year history of perianal fistula and was on surveillance for his fistula after undergoing three surgical procedures. He had also history of Non-Hodgkin Lymphoma managed with chemotherapy about 10 years ago, on complete remission. He is HIV positive on antiretroviral therapy and HCV positive. He had no history of inflammatory bowel disease.

On physical examination he presented with a vegetative and ulcerated lesion on the left perianal region, measuring about 8cm and infiltrating subcutaneous tissue around fistula trough left gluteus; hypotonic anal sphincter, with an orifice in the anal posterior pole (Figure 1); there were not palpable enlarged inguinal lymph nodes. Biopsy of perianal fistula revealed a squamous cell carcinoma (SCC).

Pelvic magnetic resonance imaging (MRI) and computed tomography (CT) scan demonstrated tumour in the left ischioanal fossa and intergluteal cleft, measuring about 66mm in long axis diameter and associated with previous trans-sphincteric fistula; there were not enlarged pelvic or inguinal lymph nodes. Thoraco-abdominal CT scan showed no distant metastasis.

His case has been referred to our hospital and discussed on multidisciplinary team meeting and proposed for CRT treatment with curative intent. The patient had Mitomycin C / 5-Fluorouracil (5FU) chemotherapy (5FU 1000mg/m²/24hr IV D1 - D4 and D29 – D32; Mitomycin C 10mg/m² (max 20mg) IV D1 of week 1). Regarding radiotherapy (RT), he underwent external beam radiotherapy (EBRT), using intensity-modulated radiation therapy (IMRT) in a total radiation dose of 59.4Gy in 33 fractions (45Gy to pelvis and inguinal lymph nodes, followed by boost to pelvis up to 50.4Gy and then boost to tumour up 59.4Gy) (Figure 2,3,4). There were 2 days...
The technical challenge was to ensure correct coverage in the intergluteal cleft and left perianal region with minimum side effects. Both treatments were well tolerated with low toxicity (maximum grade 2 cutaneous) (Figure 5,6).

Three years after treatment the patient remains with clinically and MRI complete remission (Figure 7). He has no gastro-intestinal symptoms, no fecal incontinence and no other late side effects.
DISCUSSION

Anal SCC is a rare disease accounting for about 1-2% of digestive tract tumours. Its incidence is increasing throughout the world and is particularly high in the HIV positive population. In Europe, about 2000 males and 2300 females are diagnosed with anal cancer every year; 5-year survival varied between 66% (Central Europe) and 44% (Eastern Europe). Anal cancer may arise from the anal canal (85%) or from the anal margin (15%).

Anal carcinoma is strongly associated with persistent infection with a high-risk form of HPV (eg, HPV-16; HPV-18). Other risk factors include HIV infection, history of cervical, vulvar or vaginal cancer (HPV-related), immunosuppression after organ transplant, smoking, history of receptive anal intercourse. Prolonged survival with highly active anti-retroviral treatment (HAART) is likely to lead to further increase in incidence among HIV-positive subjects.

Patients with diseases that reduce the body’s immunity - such as AIDS/ HIV positive - are at a higher risk of anorectal pathology, such fistulas. The prevalence and distribution of both HIV-related and non-HIV-related anorectal pathology do not seem to be altered by the introduction of HAART.

Routine screening in high-risk individuals, such as HIV positive for anal cancer precursor lesions is controversial, because despite the potential benefit reducing morbidity and mortality, large randomized controlled trials showing that are lacking.

Historically, primary treatment was abdomino perineal resection. Use of preoperative CRT in Nigro et al demonstrated excellent rates of complete response suggesting that it might be possible to cure anal carcinoma without surgery and permanent colostomy. Although no Phase III study has directly compared surgery versus CRT, evidence supporting the effectiveness of CRT as a radical treatment has been provided by multiple phase II and case-series studies. Multiple randomized studies have shown that addition of MMC to 5-FU based CRT improves outcomes. RTOG 0529 demonstrated significant reduction in hematologic, gastro-intestinal and skin toxicity by using IMRT for anal cancer compared to historic 3D-Conformal RT, as in our case. IMRT is preferred over 3D-conformal RT.

SEO et al reported that the combination of HAART and CRT is as safe and effective for immunodeficient for immunocompetent patients. VATRA et al compared 20 HIV-positive patients with diagnosis of anal SCC with 24 HIV-negative subjects. The remission rate with anal conservation at 1 year follow-up and the mortality at 3 years were better in HIV negative patients. Alfa-Wali et al showed that CRT of HIV-associated anal cancer is associated with significant prolonged CD4 suppression that may contribute to late deaths of patients in remission, regardless of HAART use.

In conclusion, long standing perianal fistula often causes late diagnosis of perianal carcinoma. A previous history of HIV positive should increase the index of suspicion for malignancy for early detection. A better prognosis is related with an early diagnosis and the combined treatment of HAART plus CRT.

REFERENCE


