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Case Report

Anal Cancer with Atypical Brain and Cranial Bones Metastasis: About 2 Cases and Literature Review

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Canal anal tumor · Cranial metastasis · Brain metastasis

Abstract
Canal anal cancer is a rare tumor that accounts for 2% of all colorectal neoplasms, with a low propensity for metastasis. The spread of anal squamous cell carcinoma to the brain is exceedingly rare and has been previously reported only 5 times in the medical literature. However, the first and only case of cranial bone metastasis from anal canal carcinoma was described in 2019. The purpose of this article is to add our cases to the limited literature for the management of metastatic anal cancer. The current study presents 2 cases of patients diagnosed with squamous cell carcinoma of the anal canal how underwent chemo and radiotherapy. Despite the treatment our patients developed neurological symptoms, cerebral magnetic resonance imaging showed brain lesions for the first case, and cranial bones metastasis for the second one, histopathology confirmed these lesions to be a poorly differentiated squamous cell carcinoma, consistent with the known primary tumor of the anal canal. Unfortunately, both patients succumbed quickly to systemic complications of the disease during these treatments. Despite its rarity, brain metastasis should be considered in any patient with a history of anal cancer presented neurological symptoms.

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Introduction

Anal cancer is a rare tumor among gastrointestinal tract neoplasms, distinct from cancers of the colon and rectum. The most common subtype is squamous cell carcinoma. It is also notable for a relatively low incidence of metastasis [1]. When metastases are identified, the liver is the most likely location. Brain metastasis is a rare entity, with only 5 cases that have been described in the literature. For cranial bone metastasis, it is a very uncommon location accounting for <5% of all secondary bone locations [2].

To the best of our knowledge, we report 2 cases of metastatic anal carcinoma. The first one, it is a female patient, 44 years old, with a cranial bone lesion. The second one, it is a male patient with intracranial lesions above and below the tentorium.

Cases Presentation

Case 1

A 44-year-old female patient, whose medical history included Crohn's disease since 2003, was admitted to our hospital for squamous cell carcinoma of the anal canal which was accidentally discovered during a consultation to control her Crohn's disease. The patient's management was delayed due to the confinement of the COVID-19 pandemic. A physical examination showed a painful mass in the external anal sphincter and extended to the gluteal muscle. The performance status was at 2–3.

Pelvic magnetic resonance imaging (MRI) showed an ulcerated anoperineal tumor process in hypo signal on T1-weighted sequences, a hyper signal on T2-weighted sequences, and intensely enhanced after injection of gadolinium. This process is locally extended in gluteal soft tissue with mesorectal nodules, cutaneous nodules of the sacral region, and bone lesions of the left greater trochanter. Total body computerized tomography was performed and no systemic involvement was noted. Colonoscopy revealed no synchronous tumor.

The case was discussed in a multidisciplinary consultation meeting. A concomitant radiochemotherapy treatment has been retained. Treatment was then initiated with combined chemoradiation therapy with Capecitabine 825 mg/m^2 twice daily, 5 days per week, 2 piles of 500 mg in the morning and 2 piles in the evening for a body surface of 1.28, cisplatin 80 mg/m^2 with a dose reduction of 20% given the performance status at 2, and a total dose of 80 mg every 28 days. And external radiotherapy total dose of 60 Gy, 2 Gy/fraction, and 5 fractions/week.

During the treatment, the patient presented with a 3 days history of headaches. Cerebral MRI was performed and revealed an important heterogeneous metastatic lesion in the left parietal and frontal bone extended to the adjacent soft tissue of the scalp (shown in Fig. 1). Histopathology confirmed the cerebral lesion to be a poorly differentiated squamous cell carcinoma, consistent with the known primary tumor of the anal canal. The patient underwent total brain external radiotherapy, a total dose of 20 Gy, 4 Gy per fraction, and 5 fractions per week. The patient succumbed to systemic complications of the disease during her treatment.

Case 2

A 60-year-old male presented to our hospital with a 12-month history of anal abscess that has been complicated by fistula. Performance status was at 1–2.

Colonoscopy found a mass within 3 cm of the anal margin; the patient underwent a dissected biopsy, a histological report identifying basaloid-type squamous cell carcinoma. Staging computed tomography scans of the chest, and abdomen showed secondary lung localization, external iliac, and left inguinal adenopathy.

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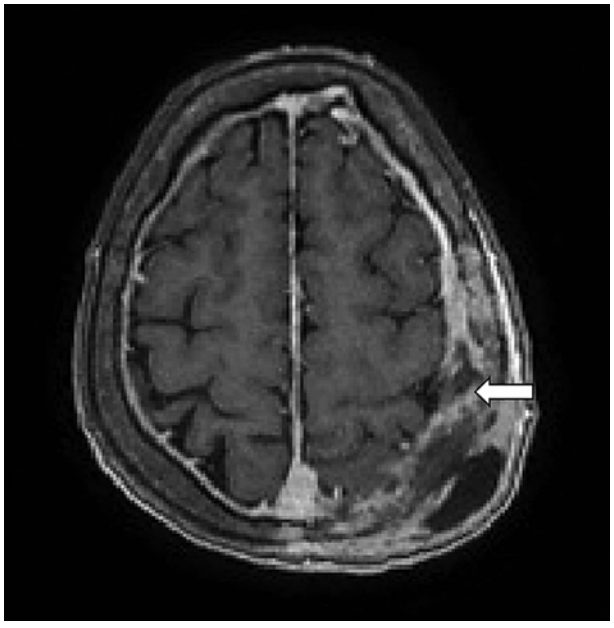

Fig. 1. White arrow: Cerebral MRI in the axial section after injection of Gadolinium: Left frontoparietal lesion, heterogeneous, invading the soft parts of the scalp. MRI, magnetic resonance imaging.

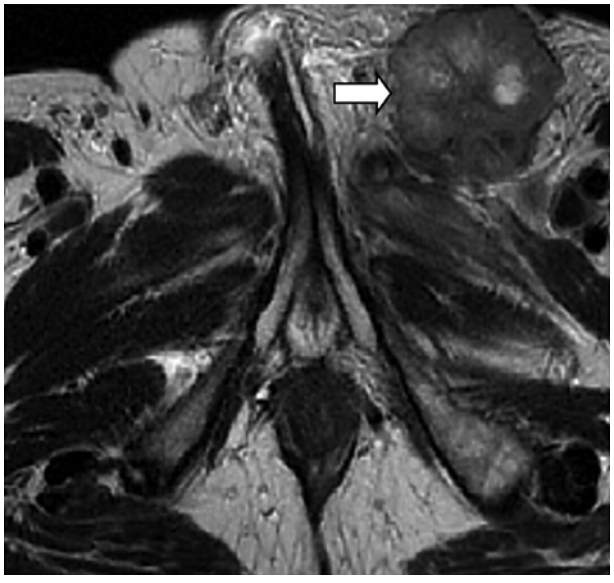

Fig. 2. Pelvic MRI showed a left metastatic inguinal lymphadenopathy (white arrow) in heterogeneous signal in T2. MRI, magnetic resonance imaging.

Pelvic MRI showed left pelvic and inguinal metastatic lymphadenopathy without tumor wall thickening of the anal canal or mass syndrome (shown in Fig. 2). Skeletal scintigraphy was also performed, and lesions were revealed in the right sacrum, pubis, and coccyx. Biopsy of lung lesion was carried out; the anatomopathological results and immunohistochemistry profile suggesting moderately differentiated squamous cell carcinoma with positive Anti P40.

Patients receive the first cure of palliative chemotherapy docetaxel, cisplatin, 5 – fluorouracil with granulocyte colony-stimulating factor, docetaxel 40 mg/m^2 and, 5 fluorouracil 2,400 mg/m^2 in 48 h every 2 weeks for 6 cures then evaluation. Treatment was complicated by persistent neutropenia which forced to stop the chemotherapy.

A follow-up positron emission tomography scan showed moderate anal hypermetabolism, metabolically active external iliac and left inguinal adenopathies, and nonhypermeta-

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bolic bilateral pulmonary micronodules, without other hypermetabolic lesions. Programmed death-ligand 1 (PD-L1) and microsatellite instability status studies were negative.

The case was discussed in a multidisciplinary consultation meeting. The patient was treated with concomitant radiochemotherapy including external radiotherapy a total dose of 60 Gy, 2 Gy/fraction, 5 fraction per week, capecitabine 825 mg/m^2 twice daily, 5 days per week, 3 piles of 500 mg in the morning and 3 piles in the evening, and cisplatin with a total dose of 100 mg every 28 days. The patient presented a good clinical evolution with subsequent disappearance of the anal margin tumor and a 50% reduction of the left inguinal ADP. A few months after, he presented to the emergency with an epileptic seizure, confusion, and memory disorders with a 15-day history of decreased tactile sensation and motor control.

MRI was performed and showed multiple metastatic intracranial lesions above and below the tentorium. These lesions were rounded, well limited, with annular enhancement, and surrounded by edema (shown in Fig. 3). At this point, total brain radiotherapy was planned however the patient succumbed to his disease before starting this therapy.

Discussion

Carcinomas of the anal canal are rarely observed in practice, accounting for <2% of all gastrointestinal malignancies. The disease usually occurs in the sixth decade of life. The pathogenesis of this malignancy is not entirely clear. Some risk factors such as Crohn's disease, chronic inflammation, and preexisting fistula have been hypothesized and studied [3–5]. Immunosuppression associated with human immunodeficiency virus or transplantation and smoking is also incriminated [6, 7]. Human papillomavirus infection, especially type 16, has been highly associated with the development of anal cancer, and human papillomavirus DNA has been found in up to 88% of tumors. Besides, recent work with vaccines targeting these viral serotypes has shown some reduction in the risk of developing previous lesions [8].

Anal tumors can be divided into 2 categories depending on their anatomical location, anal canal, and anal margin. Anal canal tumors are predominantly squamous cell carcinomas [9]. Although tumors have traditionally been divided into well-differentiated keratinizing and nonkeratinizing types (cloacogenic/basaloid and transitional), both types share a similar natural history. Therefore, no distinction was made in their management [10]. Other less common types are adenocarcinoma, anaplastic carcinoma, undifferentiated tumors, and melanomas. Squamous cell carcinoma also predominates in the anal margin subtype, which

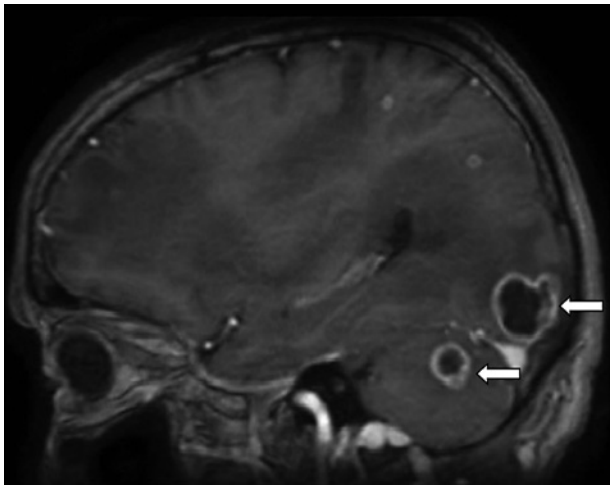

Fig. 3. Brain MRI of a 60-year-old patient with brain metastases from an anal canal tumor: The sagittal section after injection of gadolinium: annular enhancement of over and under tentorial lesions (arrow). MRI, magnetic resonance imaging.

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is usually well-differentiated and keratinizing. Overall, squamous carcinomas account for 75% of anal cancers [10].

Benign anal disease is very common and can be the first sign of anal cancer [11]. In one of our cases, a persistent perianal abscess was the first manifestation of the disease. Such a situation should always raise the possibility of malignancy. Patients with recurrent or unhealed perianal abscesses and fistulas should be sampled for anal cancer and be closely monitored.

The most important clinical sign is rectal bleeding (45%) and anorectal pain, 10–20% of patients' exhibit extrapelvic disseminated disease at the time of diagnosis. The most frequently observed metastatic site is the liver [9]. The 5-year stage IV survival rate is greater in epidermoid than nonepidermoid carcinoma and represents 20.9 versus 7.4%, respectively [10].

Exceptionally rare incidence of brain metastases from primary anal cancer can be explained by the low incidence of the disease, and the low propensity toward distant metastasis. Only a few cases of anal cancer with brain metastasis have been previously reported in the literature. The first was identified in a review of 373 cases of anorectal "transitional cloacogenic carcinomas" (now considered squamous cell carcinomas) by Klotz et al. [12], they report that 19% of patients in their series had metastatic disease, with 1 patient reported having a brain metastasis, without further detail given.

In 1991, Davidson and Yong [13] reported the case of a 61-year-old female how had initially nonmetastatic anal carcinoma treated by abdominoperineal amputation, and 8 years later, the patient develops a single brain lesion at the cerebellopontine angle. She was treated with surgery and adjuvant fractionated radiotherapy with posterior recurrence of the primary tumor [13]. Squamous cell carcinoma of the anus is also of interest because, in recent decades, the therapeutic management has changed, as it has become a nonsurgical disease, and the main treatment now consists of combined chemotherapy and radiotherapy [14].

Cisplatin-based chemotherapy in combination with 5FU and paclitaxel is the standard treatment for metastatic anal carcinoma, with radiotherapy being planned for local treatment. Cetuximab as anti-epidermal growth factor receptor therapy in anal carcinoma can be proposed in case of overexpression of the epidermal growth factor receptor [15].

One of our cases had the peculiarity of being a basaloid undifferentiated carcinoma, unlike the previous cases which were the squamous type (although poorly differentiated). But unfortunately, regardless of the histological type, the rare cases described in the literature have shown that canal anal cancer with cerebral metastasis has a very poor prognosis and patients succumb shortly to the disease.

Conclusion

Cerebral metastasis from anal SCC is extremely rare, and these cases are now present to enrich the literature. Based on all reported cases, it is clear that brain metastases are associated with poor prognosis, even aggressive medical, and surgical treatment. In these cases, palliative care alone may be the most justified. Also, brain metastases can occur late, even years after successful primary treatment. Therefore, the diagnosis should be considered when patients with a history of this malignancy present new neurological symptoms.

Statement of Ethics

Written informed consent was obtained from the families of both patients for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All the authors participated in the writing of the article and the bibliographical research concerning the case described. They also declare having read and approved the final version of the manuscript.

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