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Chemoradiation Therapy as the Treatment of the Adenoide Cystic Cancer of the Bartholin Gland : About One Case Report and Review of the Literature

[1]S. El Baz; [2]O. Eddarif; [3]I. Lahlali ; [4]K. Nouni; [5]A. Lachgar; [6]H. El Kacemi; [7]T. Kebdani; [8]K. Hassouni
National Institut of Oncology RABAT –MOROCCO

Abstract:- Adenoid cystic carcinoma (ACC) of the Bartholin's gland is a rare yet clinically significant malignancy Originating from the Bartholin's gland, situated in the vulvar region, ACC exhibits unique histopathological features and clinical behaviors. In our article, we describe a clinical case involving a 28-year-old female patient who initially presented with a painful swelling on the left labia majora. Initially misdiagnosed as simple Bartholin's gland inflammation, biopsy revealed cystic adenoid carcinoma of the Bartholin gland upon histopathological examination. Radiological evaluation revealed a locally advanced left vulvar lesion with no evidence of distant metastasis. Given the impracticability of surgical intervention, concurrent chemoradiation therapy was administered, resulting in favorable outcomes.

ACC has been a diagnostic therapeutic challenge, there is currently no established therapeutic standard. Despite its infrequent occurrence, ACC warrants attention due to its potential for aggressive local invasion, distant metastasis, and propensity for recurrence.

Keywords :- *Adenoid Cystic Cancer; Bartholin Gland; Radiation Therapy; Chemotherapy.*

I. INTRODUCTION

Adenoid cystic carcinoma (ACC) of the Bartholin's gland is a rare but aggressive tumor, representing a small fraction of 0.1 to 7% of malignant tumors in the vulvar region and less than 1% of gynecological cancers in women[1, 2] Despite its rarity, ACC of the Bartholin's gland presents significant diagnostic and therapeutic challenges due to its subtle clinical presentation and unique biological behavior[3]. In this article, we report a case of adenoid cystic carcinoma of the Bartholin's gland treated exclusively with concurrent radiochemotherapy at the Radiotherapy Department of the National Institute of Oncology in Rabat. Additionally, we provide a review focusing on the clinical characteristics, diagnosis, treatment, especially the role of radiotherapy, and prognostic perspectives of this rare yet important tumor.

II. CASE REPORT

A 28-year-old patient, mother of two children, with no significant medical history, consulted one year after self-palpating a painful vulvar formation on the left labia majora associated with vulvar itching. Clinical examination revealed a painful swelling of the left labia majora measuring 3 cm. Bartholinitis was suspected, and treatment with protected amoxicillin and anti-inflammatory drugs was administered. Due to the non-resolution of symptoms, a biopsy was performed, which returned in favor of an adenoid cystic carcinoma with predominantly compact features, infiltrating the adjacent striated muscle with positive vascular emboli and positive perineural invasion. Immunohistochemistry data revealed positive staining for CK7, P63, AML, and PS100 antibodies.

An MRI revealed a left vulvar process measuring 64x52x40 mm, locally advanced and extending to the right, invading the clitoris, external urethral orifice, levator ani muscle, and lower third of the vagina, but sparing the uterine cervix without lymph node involvement, classified as stage II according to FIGO criteria. Thoraco-abdomino-pelvic CT scan did not reveal any metastatic lesions.

The patient received conformal 3D radiotherapy using photon beams at a dose of 66 Gy (50 Gy to the pelvis and vulva, and 16 Gy as a boost to the tumor lesion), delivered in 2 Gy fractions. During treatment sessions, the patient experienced grade 1 radiodermatitis and radiomucositis. Concurrent chemotherapy was also administered (6 sessions of cisplatin at a dose of 40 mg/m²) with good tolerance. After a mean follow-up of 9 months, the patient is in complete remission with no signs of recurrence.

III. DISCUSSION

The cancer of Bartholin gland (BCG) was first documented by Klob in 1864 [4]. Bartholin's gland cancer is not well understood, and its diagnosis poses challenges.

Among all the reported cases, 10-15% had adenoid cystic carcinoma (ACC), which is histologically similar to the adenocarcinoma of the salivary glands [5].

The symptoms are nonspecific, often resembling those of Bartholin's gland infection or cysts. Consequently, many patients undergo initial treatment with marsupialization

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and/or antibiotics before the cancer is diagnosed[4]. The most commonly reported symptoms in patients with a slowly progressing palpable mass near the Bartholin's gland area include pain, itching, or bleeding [6]. Our patient presented a pain and itching. The duration of symptoms before diagnosis is longer in patients with ACC than with other histological types, as was the case with our patient, since the diagnosis was made only 1 year after the onset of symptoms.

The positive diagnosis of ACC is histological : Adenoid cystic carcinoma (ACC) is defined by the presence of two distinct cell populations: basal/myoepithelial and luminal cells. Its growth patterns typically include cribriform, solid (basaloid), and tubular arrangements [7] Perineural invasion is common, described in 84.4% of published cases [8]and is a hallmark feature of ACC. Immunohistochemically, ACC often shows expression of CK8/18, CK7, CK14, epithelial membrane antigen, and CD117 (cKit) , P53 and S100 [9, 10]

The radiological assessment is not standardized, but thoracoabdominopelvic CT scan is most commonly used. Its purpose is to rule out a primary tumor, search for inguinal and pelvic metastases, or distant metastases. Pelvic MRI may be indicated to assess local extension.[3]

The rarity of this histological entity explains the lack of consensus regarding the optimal therapeutic management.

The primary standard treatment remains surgery, with a management approach inspired by the treatment of midline vulvar cancers [11]. Two approaches have been described in the literature: posterior hemivulvectomy for small tumors, and radical total vulvectomy for tumors larger than 3 cm or multifocal tumors [3]. The aim of surgery is to achieve clear margins to prevent the risk of recurrence and the need for further surgery. However, some authors have shown that the status of surgical margins may not have a significant impact on the recurrence rate and advocate for conservative surgery, especially for small unilateral tumors [12]. Surgical excision of ACC is associated with sentinel lymph node biopsy for small tumors, or deep inguinal lymphadenectomy for large tumors or pN1 disease [13]. According to the literature, the status of inguinal lymph nodes strongly affects patient survival[14]. Furthermore, in the absence of clinical and radiological lymph node involvement, other authors suggest unilateral lymph node dissection combined with adjuvant radiotherapy[15].

Regarding adjuvant treatment, it has been reported that a less radical surgery combined with inguinal-femoral external radiotherapy is considered the best treatment for ACC. This approach allows for good long-term survival and helps prevent complications [16].

Radiation therapy (RT) is typically administered when positive or close margins are present, perineural invasion is detected, or lymph nodes are positive.[6] Total dose to the tumor bed ranged from 40 Gy [14]to 74 Gy [17] and to the lymph node areas (homo or bilateral pelvis and inguinal area) from 20 Gy [14] to 70 Gy [18]. Tumor bed boost is delivered most often by external radiation therapy with photons or less frequently with electrons [14], carbon ions [17] or brachytherapy [19, 20]. Carbon ion boost was used in several centers with promising results. Bernhardt D et al. reported no recurrence 16 months after ion therapy without severe toxicity (1 patient)[17]. Brachytherapy was also reported as a boost modality or exclusively without external RT with a prolonged local control [19-21]. In literature, 6 of 44 patients (13.6%) who received postoperative RT had local recurrence and 20 of 56 (35.7%) who did not receive RT[8]. The risk of relapse of any type (local, nodal or metastatic) was 40.9% of patients who receive adjuvant RT and 48.2% of patients who did not[8]. RT could reduce the risk of local recurrence regardless of margin status, which is consistent with the results reported by Alsan et al [22].

Fo our case , a chemoradiation therapy was the only treatment administrated , In a previous study, primary radiotherapy or chemoradiation therapy was performed in 10 patients with BG carcinoma [21]. Treatment options included teletherapy combined with a boost to the primary site, regional nodes and/or interstitial brachytherapy. The median follow-up period was 87.2 months (range, 45-142 months). Three- and five-year survival rates were 71.5% and 66%, respectively, comparable to outcomes after surgery and postoperative radiotherapy [21]. This indicates that primary nonsurgical treatment might provide an effective alternative to surgery with preservation of genital function and low morbidity [6, 21].

For chemotherapy ,its role in the treatment of metastatic extra-gynecological adenoid cystic carcinomas has been proven, even with slow and short responses. However, no protocol has been established regarding localization at the Bartholin's gland apart from metastases [6, 21].

Neoadjuvant chemotherapy has been utilized in some cases, particularly to avoid radical surgery, using cyclophosphamide, adriamycin, and cisplatin [20]. Concomitant chemoradiotherapy, not commonly administered, has been reported using cisplatin or irinotecan [23, 24]. Recently, irinotecan has been indicated as an adjuvant treatment in a patient who underwent tumor resection with invaded margins [23]. After a two-year follow-up, the patient did not experience recurrence. In cases of recurrence or multiple metastases, various combinations including Adriamycin, Cyclophosphamide, Dactinomycin, and Methotrexate have been attempted.[12]

Adenoid cystic carcinoma (ACC) is characterized by its slow growth, boasting a high 10-year survival rate ranging from 59 to 100%. Despite this favorable long-term prognosis, local and metastatic recurrences are common and can occur many years after the initial treatment. In a recent review, the median time to relapse was found to be 24 months (ranging from 6 to 156 months), with 45% experiencing any type of relapse (local and/or metastatic), and 26% experiencing local relapse specifically. Among patients experiencing metastatic relapse, the lungs were the most frequent site (76.7% of metastatic relapses), followed by bones, and more rarely, the liver and brain[8].

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IV. CONCLUSION

Adenoid cystic carcinoma originating from the Bartholin's gland is an uncommon malignancy characterized by slow progression yet aggressive behavior, often associated with frequent recurrences, occasionally manifesting years following initial diagnosis.

Because of the limited reported cases, there is currently no established therapeutic standard. The optimal treatment, including surgical techniques and radiotherapy regimens, remains undetermined. Primary radiation or chemoradiation therapy seems to be a suitable treatment approach. However, a prospective randomized study would provide the most robust evidence for selecting the appropriate treatment modality.

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