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Case Report

A Rare Case of Hidradenocarcinoma and a Literature Review

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Abstract

Introduction: Hidradenocarcinoma is a malignant lesion arising from the intradermal duct of eccrine or apocrine sweat glands. Extremely rare, the incidence of this lesion in the United States is 0.45 per million persons per year. Due to its rarity, treatment in advanced stages is not standardized. The prognosis remains unclear, with recent optimistic data reporting a 10-year Overall Survival (OS) until 80%.

Case report: A 38-year-old woman presented with an axillary mass evolving for at least one year with no underlying skin lesion. Mammography was negative; on the CT scan, no evidence of clear cell renal carcinoma or other primary lesion was found. The PET-CT scan revealed multiple, one-sided axillary lymph nodes. Fine needle, US-guided biopsy showed a lymph node infiltrated by a high-grade clear cell malignancy. An extensive axillary lymph node dissection was suggested. Anatomopathological examination of the surgical specimen found 14 infiltrated lymph nodes by a high-grade, nodular, clear cell malignancy with risk factors for advanced disease. Immunohistochemistry study favored a malignant clear cell hidradenocarcinoma. Based on current scientific literature, concomitant chemotherapy with paclitaxel/carboplatin and high-dose radiotherapy of 70 Gy in the axillary region, followed by two more cycles of carboplatin/paclitaxel, was administered. Treatment was tolerated without complications. Six months after surgery, at the end of systemic treatment, there are no signs of recurrence.

Conclusion: The report and follow-up of rare cases, such as the one presented in this study, may serve as a ground for establishing treatment guidelines. A multicentric clinical trial should be considered in order to obtain high-quality recommendations.

Keywords: Acrospiroma; Neoplasms; Adnexal and skin appendage; Poroid hidradenoma; Tubular sweat gland adenomas

Introduction

Hidradenocarcinoma is a rare malignant lesion arising from the intradermal duct of eccrine or apocrine sweat glands, belonging to cutaneous adnexal tumors. It was first described in 1954 by Keasby and Hadley [1], after observing lesions with the characteristic features of a hidradenoma but aggressive behavior and widespread metastases. At this time, it was thought that hidradenocarcinoma was a malignant transformation of preexisting hidradenoma. Recent studies showed that hidradenocarcinoma could also arise de novo [2]. The incidence of this lesion, also found in the literature under clear cell eccrine carcinoma, apocrine hidradenocarcinoma, nodular malignant hidradenoma, or malignant acrospiroma is 0.45 per million persons per year. It represents less than 1% of all skin tumors. It is observed more frequently between the ages of 50 and 70, with a range from birth until 90 years, without sex predisposition. It develops predominantly on the head and neck, anterior trunk, or upper extremities, where sweat glands are distributed [3,4]. Due to the rarity of these tumors, the prognosis remains difficult to determine. It was considered extremely poor, with a five-year OS at 30%, a local recurrence rate of 50%, and a rate of distant metastasis of 60% in the first two years [5,6]. However, the recent epidemiological analysis of Gao et al. [3] finds a 10-year OS of 60.2% and a 10-year Cancer-Specific Survival (CSS) of 90.5%, challenging preview results. For the same reason, there is no clear consensus on managing hidradenocarcinoma, and our practice is based on case reports, institutional experience, and expert opinion. We report a case of a high-grade clear cell hidradenocarcinoma in a woman presenting with an axillary mass.

Case Presentation

We report the case of a 38-year-old woman, an active smoker (13 pack-years), known for a previous history of hidradenitis suppurativa and more recent psoriasis treated with topical steroids. She consulted for a right axillary mass that appeared a year ago, growing more rapidly over the last three months, with intermittent swelling, responsible for occasional pain. The overlying skin was normal, without ulceration, discoloration, or discharge. A complete dermatological examination revealed no skin lesions, and the rest of the clinical and senological exam was normal.

A US-guided biopsy of the right axillary mass was performed. The biopsy showed a lymph node infiltrated by a high-grade malignant proliferation consisting of cohesive cells with marked nuclear pleomorphism and clear cytoplasm, and some eosinophilic areas. On immunohistochemical study, the tumor cells were positive for keratins, EMA, CK7, AE1/AE3, and negatives for CK20, ER, PR, S100, SOX 10, TTF1, WT1, and HER2 receptors. A weak expression of PD-L1 was observed with a TPS of 5% and CPS of 15. A morphologic and immunohistochemical profile suggesting a clear cell hidradenocarcinoma [6].

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PET-CT scan confirmed the presence of multiple hypermetabolic lymphadenopathies of the right axillary and sub-pectoral region but did not reveal any other secondary lesion or a primary site (Figure 1). Mammography was normal. The case was discussed in our tumor board, which proposed a wide surgical excision (Figure 2 and 3). A complete lymph node dissection was performed without complications during the postoperative period, and the patient was discharged on day four.

The final pathological examination of the 15 removed nodes, Figure 4 showed 14 infiltrated nodes by a high-grade nodular malignancy of poor differentiation, round pleomorphic cells with clear cytoplasm, and PAS-positivity. The immunohistochemistry analysis was the same as on the biopsy. There was a high number of mitoses and areas of necrosis. Other high-risk factors included node capsular effraction, adjacent adipose tissue infiltration, and angio-lymphatic and perineural invasion. At the molecular level, genetic sequencing showed a TP53 and TSC2 mutations; no evidence of a fusion transcript, in particular, no MAML2 fusion was demonstrated. The retained diagnosis was a high-grade clear hidradenocarcinoma. Because of the histological high-risk features described above, an adjuvant radio-chemotherapy with carboplatin/paclitaxel was proposed to the patient.

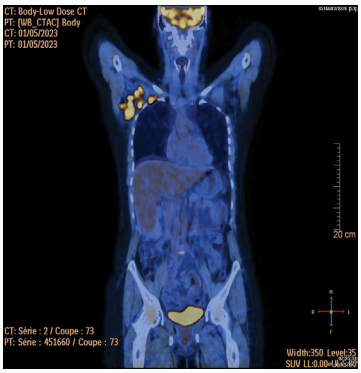

Figure 1: PET-CT showing multiple hypermetabolic lymphadenopathies of the right axillary and sub-pectoral region.

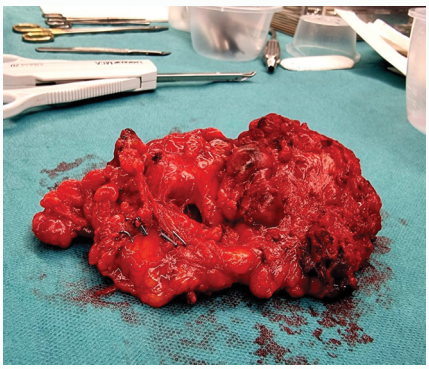

Figure 2: The surgical specimen of the 15 infiltrated axillary lymph nodes.

Discussion

Cutaneous adnexal malignancies are rare skin cancers. The overall incidence rate estimated in the United States is 5.86 per million persons per year [4]. Their classification is based on the cellular origin of the malignancy: sudoral (eccrine or apocrine glands), hair follicle, and sebaceous origin [7,8]. They are multiple, depending on where they originate with their benign and malignant forms, leading to different clinical presentations. Due to these cancers' rarity and morphological overlap, the diagnosis remains challenging. In the scientific literature, studies refer to hidradenocarcinoma as clear cell eccrine carcinoma or acrospiroma [9] and historically as malignant hidradenoma to describe the malignant transformation of its benign counterpart [1]. Firstly, Kaesby and Handley [1] reported lesions that appeared mainly as benign skin tumors of self-limited growth (clear cell hidradenomas) but sometimes recurrent, locally invasive, with ulcerations and muco-serosanguinous discharges and rarely, with widespread metastasis to lymph nodes and bone (metastasizing clear cell hidradenomas). In an old review, Hernandez et al. [10] reported 6 cases of whom a one-year-old child who died from metastatic disease and one 46-year-old woman whose foot lesion regressed spontaneously. Since then, the development of immunohistochemical and molecular markers [4,11] has helped better understand each lesion's nature and behavior, separating benign hidradenoma from its malignant counterpart hidradenocarcinoma. Hidradenocarcinoma expresses cytokeratin, EMA, CEA, and has a variable positivity for Androgen Receptor (AR), estrogen and progesterone receptors (ER/PR), EGFR and HER-2. It is characterized by high mitotic activities and angiolymphatic invasion. At the molecular level, hidradenoma demonstrates *MAML2* fusion gene in 50% to 75% of cases. This rearrangement is less frequently found in hidradenocarcinoma than in its benign counterpart, while a subset carries TP53, AKT1 and PI3KCA mutations [11,12]. In our patient, the molecular analysis showed a TP53 mutation but no MAML2 rearrangement. The challenge of the case was the absence of a primary skin lesion. Tingaud et al. [11] have already described a case of a hidradenoma located on the inguinal lymph nodes, which can rarely occur. However, there are no references to a lymph node location of hidradenocarcinoma in the current literature. One

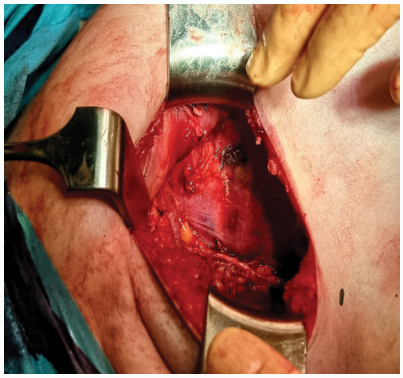

Figure 3: The surgical site after the extended lymph node dissection. Normal overlying skin.

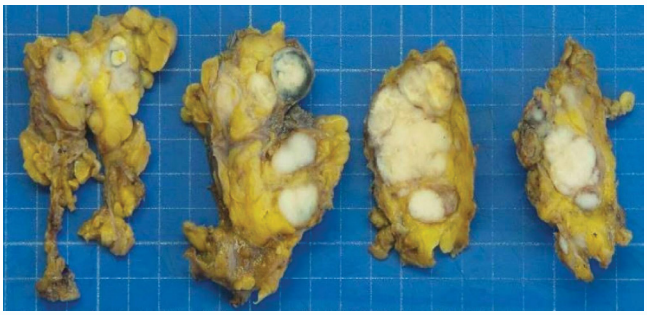

Figure 4: The anatomopathomical macroscopic aspect of the lesion excised.

hypothesis could be the transformation of a benign lesion located on the lymph nodes, but without any evidence on histology of a benign lesion preexisting, it is difficult to reach this confirmation.

Concerning the treatment, clinical trials are lacking. Our current practice is based on case reports and some series due to the rarity of this disease. In our research, we found some reviews of the literature [9,13,14], the one of Soni et al. [9] published in 2015 being the most recent. Surgery of the primary consists of a wide local excision with negative margins up to 3 cm and sentinel node removal [9]. In our patient, since the primary was not certainly found and the biopsy of the axillary mass showed infiltrated nodes, we proposed an extensive lymph node dissection to provide the safest margin. The final pathology report showed the presence of multiple risk factors for recurrence, such as poor differentiation, lymph node capsular effraction, angiolymphatic, and perineural invasion. We considered the risk of local and distant recurrence high, and administration of adjuvant therapy necessary [14]. Postoperative radiotherapy has shown survival advantages and treatment of recurrence after surgery in several case reports [15,16]. We considered adding systemic treatment because of the high risk of distant recurrence. Different chemotherapeutic agents have been used in metastatic disease, including fluoropirimidine, platinum, anhracycline, cyclophosphamide, vincristine, bleomycin, and paclitaxel [9,17,18]. The effectiveness of these treatments may vary from case to case; decisions should be made in a multidisciplinary approach and individualized based on the tumor's immunobiological profile, patient's age, and performance status [13,19,20]. Since our young patient was in good performance status, and even if there is no data on concomitant chemoradiotherapy in this situation, we proposed it as to avoid delaying systemic treatment during radiotherapy. Concomitant chemotherapy with weekly paclitaxel carboplatin with high dose radiotherapy of 70 Gy in the axillary region followed by two more three-week cycles of carboplatin/paclitaxel was administered. Six months after surgery, at the end of systemic treatment, there is no evidence of recurrence on the CT scan. Since most cases of recurrence happen on the first two years, a 2-year follow-up, at least, is necessary to demonstrate the effectiveness of the treatment strategy.

Historically, hidradenocarcinoma was associated with a bad prognosis, a 5-year OS after surgery of less than 30%, and a recurrence rate between 10% and 50% [6,9]. In one more recent database analysis of 103 patients, including all types of adnexal carcinomas, 10-year OS was found to be 80% [17], which correlates with the analysis of Gao et al. [3], who found especially for hidradenocarcinoma, a 10-year OS and CSS of 60.2% and 90.5%, respectively. Both studies associate a worse prognosis with tumor size. Carlos also associates age greater than 70 years and positive Sentinel Lymph Node Biopsy (SLNB) or clinically positive nodes with recurrence, contrasting with Gao's findings. In the latter analysis, data are lacking concerning tumor AJCC stage and lymph node involvement in many patients, 50.5% and 18.7%, respectively.

Conclusion

We report a unique case of clear cell hidradenocarcinoma, which presented as an axillary mass in a young female patient and its management. Since such tumors are rare, it is essential to share our experience, hoping it will contribute to further research and help other physicians. Follow-up will let us know more about the prognosis of this pathology, which until today believed to be extremely poor. Unfortunately, the lack of cases and sufficient data remain an obstacle to establishing guidelines for treatment. A register or a multicenter study can lead to better management of these patients.

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