Malignant Hidradenoma: A Report of Two Cases and Review of the Literature

I.E. LIAPAKIS1, D.P. KORKOLIS2, A. KOUTSOUMBI3, A. FIDA3, G. KOKKALIS1 and P.P. VASSILOPOULOS2

1Department of Plastic and Reconstructive Surgery, 2First Department of Surgical Oncology and 3Department of Surgical Pathology, Hellenic Anticancer Institute, 'Saint Savvas' Hospital, Athens, Greece

Abstract. Introduction: Malignant tumors of the sweat glands are very rare. Clear cell hidradenoma is a lesion with histopathological features resembling those of eccrine poroma and eccrine spiradenoma. The biological behavior of the tumor is aggressive, with local recurrences reported in more than 50% of the surgically-treated cases. Materials and Methods: Two patients are presented, the first with tumor in the right axillary region, the second with a recurrent tumor of the abdominal wall. The first patient underwent wide excision with clear margins and axillary lymph node dissection and the second patient underwent wide excision of the primary lesion and bilateral inguinal node dissection due to palpable nodes. Results: The patients had uneventful postoperative courses. No additional treatment was administered. However, sixteen months after surgery, patient 2 developed extensive and massive recurrence involving almost the whole abdominal wall. Although he had received several chemotherapeutic agents, the disease had a relentless course and the patient succumbed two and a half years following surgery. Conclusion: Malignant tumors of the sweat glands are very rare neoplasms with no discrete clinical characteristics. It is necessary to suspect any lesion which shows evidence of enlargement and to verify its status by histological evaluation. Additional resection is generally required, with at least 2-cm clear margins, since surgery is the only effective treatment.

Malignant tumors of the sweat glands represent rare oncological entities, characterized by non-specific clinical presentation and equivocal pathological features. Their precise diagnosis and histological classification can be very difficult (1). Clear cell hidradenoma is an extremely rare tumor with less than 50 cases reported (2, 3).

The cases of two patients, suffering from aggressive dermal lesions invading the abdominal wall and the axillary region, are described here. Surgical resection and histopathological examination ascertained the presence of malignant clear cell hidradenoma. In addition to these cases, a review of the literature is also presented.

Case Reports

Patient 1. Patient 1 was a 68-year-old Caucasian male who had undergone excision of a rapidly growing, ulcerous lesion of the anterior surface of the abdominal wall in another hospital. Histology revealed an eccrine spiradenoma of the sweat glands with squamous differentiation and intense desmoplastic reaction. The tumor had invaded the dermal lymphatic vessels and the subcutaneous fat. The margins of resection were free of disease. During the following six months, the patient developed multiple satellite nodules and was admitted to our institution for further diagnosis and treatment. The complete blood work up, as well as a CT scan of the abdomen and chest, were normal. Lymphoscintigraphy, however, was positive for bilateral inguinal nodal disease. Fine-needle aspiration biopsy of both the skin lesions and enlarged inguinal nodes was positive for malignancy, suggesting a poorly-differentiated, metastatic adenocarcinoma. The patient underwent wide local excision of the abdominal wall nodules with 2-cm margins of resection, as well as formal bilateral inguinal lymphadenectomy. From the pathology report the presence of a clear cell hidradenoma arising from the sweat glands, with multiple nodal metastases, was ascertained (Figure 1). No adjuvant treatment was given. The patient died nine months later from disseminated disease.

Patient 2. The second patient was a 45-year-old Caucasian male who had undergone excisional biopsy of a whitish lump, 2 cm in size, arising in the right axillary region. The histopathological examination was suggestive of a nodular...
hidradenoma with clear cells and a low grade of malignancy (Figure 2). The patient was then admitted to the hospital for a complete wide resection and radical axillary lymphadenectomy. The pathology report revealed no residual disease or nodal metastases. Six months after resection, the patient is doing well with no evidence of recurrence.

Discussion

The recognition of hidradenoma as a distinct entity was first reported in 1941 by Mayer, whereas the term “clear cell hidradenoma” was proposed in 1954 by Keasby and Hadley (4). The malignant form of hidradenoma is extremely rare, with less than 50 cases ever reported in the literature. All these cases were characterized by a significant rate of locoregional recurrence. Some patients developed distant metastatic spread as well (3, 5). The disease is usually expressed as a small intradermal mass which remains inactive for a long period of time before increasing in size. Its aggressive behavior is more apparent after each local relapse with faster growth and invasion of the surrounding tissues. In most cases, no epidermal participation is encountered. Hidradenoma usually affects middle-aged women, although its malignant form shows no age or gender predilection (6-8).

Malignant hidradenoma is usually found in the scalp, face or anterior surface of the trunk. Regional lymphadenopathy, with or without serous discharge, may develop years after initial treatment. Wong et al. (5) described three patients suffering from clear cell hidradenoma who developed metastatic disease in the regional lymphatic basins 8-22 years after initial surgical extirpation. Histologically, clear cell hidradenoma seems to originate from the ductal epithelium of the sweat glands, whereas histogenetically it appears to represent a transitional tumor, sharing features of eccrine poroma and eccrine spiradenoma (6).
Currently, there is no clear distinction between eccrine and apocrine glands, or between their malignant counterparts. The characterization of a sweat gland tumor, however, as of eccrine or apocrine origin, still remains useful (9, 10). In general, clear cell hidradenoma is considered to have an eccrine background, although quite recently Gianotti and Alessi (11) supported an apocrine histology based on their own series of five consecutive cases. Clear cell hidradenoma consists of two main cell subpopulations. The first one is composed of round or polygonic cells with round nuclei and clear cytoplasm, which is the result of abundant glycogen storage. The second subpopulation consists of multifacetted cells comprised of oval nuclei and basophilic cytoplasm evenly arranged at the periphery of the first cellular line (12). Clear cells may be also seen in other, more frequent malignancies of the head and neck, such as squamous and basaloid tumors, as well as in metastatic deposits of renal cell carcinoma (6).

The recognition of the eccrine origin of a malignant hidradenoma may be accomplished through specific immunohistochemical techniques, a positive PAS stain, as well as with the presence of lobules with epidermal differentiation (5, 13-15).

Clear cell hidradenoma may contain keratinocytes forming keratin congregates (13). In addition, some cystic configurations noted on the specimen most probably represent empty spaces between degenerated cells rather than ductal formations of the tumor itself (6).

Malignant clear cell hidradenoma usually develops de novo and invades the dermis and subcutaneous tissue. Surprisingly, it might share significant histopathological features with its benign form. The mitotic index may not be representative or may affect only a small cellular subpopulation. Thereafter, the diagnosis of malignancy through standard pathological examination may prove extremely difficult (16).

In our small series, it was interesting to note that, in contrast to the final diagnosis, previous pathology reports had ascertained the presence of an eccrine spiradenoma. The latter is a benign tumor of the sweat glands with similar clinical presentation and equivocal enzyme reactions, which pose tremendous diagnostic dilemmas (12). Because of the rarity of these oncological entities, as well as their histopathological similarity, it is almost impossible to define whether a malignant clear cell hidradenoma had been developed from a benign eccrine spiradenoma or was the correct diagnosis from the beginning.

The most recent reports support the fact that malignant clear cell hidradenoma should be considered as a distinct entity rather than the result of a malignant transformation of its benign type, underlining the importance of a precise initial diagnosis (7, 17). Rosen et al. (19) presented a case of a clear cell hidradenoma of the eyelid complicated by multiple recurrences and invasion of nearby structures. Histologically, no atypia or increased nuclear mitoses were found. The precise identification of a benign or malignant hidradenoma, based on pathological examination, was not possible. Similar findings were noted in other case reports of clear cell hidradenoma (20-25).

Surgical excision remains the therapeutic modality of choice. Wong et al. (5) supported wide surgical resection with a least 2 cm of clear margins for both primary disease and local recurrences. Elective regional lymphadenectomy after lymphoscintigraphy should also be performed. The role of sentinel lymph node biopsy in the treatment of malignant hidradenoma is controversial. Locoregional recurrence even after wide surgical excision has been reported in more than 50% of cases, although overall and disease-free survival rates are hard to determine as the result of the very limited number of reported cases (18). Adjuvant chemotherapy and radiotherapy have no impact in local control or survival (26).

In conclusion, malignant clear cell hidradenoma is a rare oncological entity, with no particular clinical or histopathological features. It should be included in the differential diagnosis of dermal lesions with an aggressive behavior and multiple recurrences, despite aggressive surgical treatment.

References


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