Radiotherapy in eccrine porocarcinoma: literature review

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Abstract

Introduction: The eccrine porocarcinoma is a pathology originated in the ductal intradermic portion of the sweat gland, with an incidence of 0.2 per million of habitants. It is more frequently in women above 70 years old and mostly lower extremities. The etiology is not known precisely, nevertheless it is been associated to several pathologies. **Clinical Case:** Female, 79 years old, with a dermal injury on the outer side of the left leg, from which a biopsy was performed (11/21/14) resulting an eccrine porocarcinoma, surgical treatment was offered as first option, but it was rejected by the patient, so she was treated with external beam radiotherapy (April–May 2015), during the treatment, skin toxicity grade 1 was shown. Follow up of 24 months with adequate evolution. **Discussion:** This is a pathology that can be presented de novo or secondary to an eccrine poroma. There is no consensus for their treatment in the whole world, however the most used treatment is by surgical resection as a single modality. In the clinical case presented, the treatment with radical external beam radiotherapy is explored as a management option, with similar results in disease control compared to the surgical treatment. **Conclusions:** Radical external beam radiotherapy can be a option to treat this pathology, achieving local and remote control of the disease, however further studies are required to support what we have previously discussed.

Key words: Radiotherapy. Eccrine porocarcinoma. Malignant eccrine poroma.

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Introduction

Eccrine porocarcinoma is a malignant tumor of the skin originating in the intradermal ductal portion of eccrine sweat glands. This pathology is also known as malignant hydroacanthoma simplex, dysplastic poroma, malignant syringoacanthoma or malignant intraepidermal eccrine poroma, among other terms¹. It was described by Pinkus and Mehran in the ankle of an 82-year old woman in 1963, and there has been a very reduced number of reports around the world ever since^{2,3}. Its incidence is slightly higher in the female gender, with 40% being localized in the lower limbs and 20% in the head and neck region⁴. It has been associated with extramammary Paget's disease, sarcoidosis, chronic lymphocytic leukemia, pernicious anemia, Hodgkin's lymphoma, chronic exposure to superficial ionizing radiation and trauma⁵.

There is little experience in the management of eccrine porocarcinoma, and therefore there is no therapeutic consensus on this condition, which is typically surgically managed. We present one case of eccrine porocarcinoma, localized in the lateral portion of the middle third of a female patient's leg, which was treated with external beam radiotherapy since the patient refused the surgical procedure as first management option. The case is presented and a medical literature review is made.

Clinical case

The patient is a 79-year old woman with no relevant history to the presenting complaint, which started in 2015 with dermatosis at left leg external face, characterized by hyperchromia, indolent and progressive growth, accompanied by itching and desquamation of approximately 5 x 6 cm. The patient attended the Hospital General de México, where she was evaluated by the Dermatology Department. A biopsy was taken (November 21, 2014), with histopathological result of eccrine porocarcinoma, and she was therefore referred to the Oncology Department. She was evaluated by the Department of Mixed Tumors (March 11 and 23, 2015) and offered surgical treatment, which she rejected, and thus she was referred to the Radio-oncology Department for external beam radiotherapy treatment (April 02, 2015), where a 5 x 6 cm keratotic dermal lesion was found at the left leg middle third posterolateral face, with presence of hematic scab and elevated nodulations within the area (Fig. 1). Chest X-ray (March 11, 2015) showed no evidence of metastatic disease, and she was therefore

Figure 1. 5 x 6 cm initial lesion localized at left leg posterolateral face, with presence of fiducial markers on borders for conventional simulation.

considered candidate to receive treatment with external beam radiotherapy with a 60 Gy dose in 30 fractions using a 1.25-MV Cobalt-60 machine with one direct field, using a 0.5-cm wax bolus, which was accepted after previous informed consent, with conventional simulation carried out on April 13, 2015 (Fig. 2), and treatment starting on April 30, 2015. The patient was reassessed after 10 treatment sessions, with the lesion being found with smooth borders and increased homogeneity; after 22 treatment sessions she was assessed again, with grade I radiodermatitis being found (Fig. 3), which was resolved with topical treatment one month after the treatment was completed (Fig. 4). Currently, with a 24-month follow-up, the patient shows no clinical data consistent with locoregional recurrence or evidence of distant metastasis (Fig. 5).

Discussion

Eccrine porocarcinoma was originally described by Pinkus and Mehregan in 1963. It has an incidence of 0.2 per million population and 0.005% among epithelial tumors^{2,3}. Even though there are reports described in patients since 37 years of age, it is more common in adults older than 70 years, with 70% of cases corresponding to females, as in the presented case^{6,7}. Anatomical localization of this pathology is more commonly reported to be the lower limbs, as in the case of our patient, which is reported in up to 40%, with 20% being found in the head and neck area; however, in some series it is equitably reported^{4,6}.

Figure 2. Skin lesion covered by 0.5 cm-thick wax bolus during conventional simulation.

Figure 4. Radiodermatitis resolution.

Figure 3. Grade I radiodermatitis sicca at treatment session 22.

Figure 5. At 24 months' follow-up, without toxicity or tumor lesion.

This condition is thought to be able to occur de novo or secondary to the presence of a long-standing eccrine poroma (30-50%), with progression in approximately 25% of cases at 20 years^{4,8}. Eccrine porocarcinoma arises from the intra-epidermal ductal portion of the sweat gland, specifically from acrosyringium cells⁹.

Clinically, it occurs as a nodular (46% of cases) or multi-nodular (40%) lesion and, to a lesser extent, in form of plaques, which can be accompanied by warty, atrophic and exophytic lesions in 21% of cases, in addition to ulcers⁷. Other clinical presentation is as a single, slowly growing, pearly papular lesion that reminds of basal-cell carcinoma, which is a mandatory differential diagnosis¹⁰. Other clinical data can include

local pruritus (33% of cases), pain (40%) and spontaneous bleeding of the lesion (13%). In the presented case, it was as a pruritic, painless multi-nodular lesion and presence of hematic scab, which is consistent with features described in the medical literature⁷.

Histologically, eccrine porocarcinoma appears irregular with poromatous basaloid epithelial cell population with ductal differentiation and cellular atypia⁶. Characterized by pleomorphic cells with nuclear hyperchromia and important mitotic activity, surrounded by ductal lumens, an intraepidermal variant (in situ) can be found in 10-15% of cases, which has horizontal growth and pagetoid infiltration⁷. Invasive eccrine porocarcinoma occurs in 90% of cases, and it is characterized by

extensive growth of bands of tumor cells with nuclear pleomorphism, asymmetric intradermal proliferation, important mitotic activity and presence of necrotic areas with multiple ductal structures⁷. There are three tumor border patterns: infiltrative border, which has a poorly-defined inferior margin with cell groups infiltrating the dermis (similar to an infiltrative basal-cell carcinoma); pushing border, where a polypoid tumor with different dermal limit is observed, and pagetoid border, with intraepidermal spread mimicking Paget's disease¹¹. Different histopathological patterns have been observed: comedonecrosis (32-45%), squamous differentiation (42%), diffuse necrosis (64%), mature ductal formation (36%), melanocytic colonization (21%) and Bowenoid pattern (20-30% of cases); therefore, from the histological point of view, differential diagnosis is mandatory, with squamous cell carcinoma standing out due to the presence of squamous differentiation⁷. For this, special immunohistochemistry staining is performed, including testing with epithelial membrane antigen, which positively stains eccrine porocarcinoma poroid cells. Carcinoembryonic antigen, anti-cytokeratin 5.2 and cytokeratin 19 can also be used, with the latter being useful for differentiation from squamous cell carcinoma. In the case of S100-staining, it highlights the ducts contour in eccrine porocarcinoma and stains myoepithelial cells of glandular portions, while fissures are negative^{3,8}.

There is a brief description available on eccrine porocarcinoma prognostic factors. In general, around 20% of these tumors are known to recur, 20% have regional lymph node metastases and 10%, distant metastases^{12,13}.

Tumor-associated factors include the presence of primary tumors > 5 cm, as in the case of our patient; there is a tendency towards higher incidence of regional lymph node disease, which did not occur in this case. In addition, some clinical features, such as the presence of ulceration, sudden and rapid growth, spontaneous bleeding, presence of pain, pruritus and lesion multi-nodularity, are associated with poorer prognosis^{7,14,15}.

Some histologic features have been reported as predictive factors of aggressive behavior, such as the presence of 14 or more mitoses per high-power field, lymphovascular invasion, primary tumor with > 7-mm depth and presence of infiltrative margins⁶. The presence of metastatic disease at diagnosis, either visceral or to regional lymph nodes, indicates high mortality rate with life expectancy ranging from 5 to 24 months⁸. Performing the differentiation between a de novo tumor

and one originating in a poroma has no prognostic impact, since both are known to have high rates of recurrence and metastasis¹⁰.

As for treatment-associated prognostic factors, Mohs microsurgery is known to produce cure rates of up to 70% and a recurrence rate of 38%, and risk of lymph node disease of 20%. Specific mortality associated with this disease is reported to range from 7 to 67% in spite of wide surgical margins being obtained^{4,8,14}.

Up to this moment, owing to the limited information there is about this condition and to the lack of patient follow-up, there is no standard therapeutics as such. Over time, different approaches have been tried, with the performance of a wide local excision and Mohs microsurgery standing out, by means of which the best results have been obtained so far; however, there are important technical difficulties for adequate resections in tumors > 5 cm, which is the therapeutics initially proposed to our patient and that she expressed her refusal to^{8,14,16}. In view of such an important rate of regional lymph node metastatic disease present at diagnosis, systematic prophylactic lymphadenectomy has been proposed, although no disease-free and overall survival has been demonstrated so far, and the sentinel lymph node approach should therefore be considered in the presence of risk factors such as tumor invasion > 7 mm in depth, high mitotic index and presence of lymphovascular invasion⁸. Considering the important rate of recurrence, using external beam radiotherapy has been preferred as adjuvant management in case of positive or close margins and in those patients with regional lymph node metastatic disease with extracapsular extension. In the medical literature, we were able to find only one case report with a 12-month follow-up without recurrence or disease progression, and other cases where similar management was provided and where no difference was demonstrated in those treated only with surgery^{8,14}. With regard to systemic treatment, there are only few reports about the management of metastatic disease, with no advantage been provided in the obtained results¹⁷.

Conclusions

Owing to the limited number of patients, there are no sufficiently large series to determine the ideal therapeutics for these patients. Up to this moment, it is accepted that surgical treatment provides the best results, in spite of important rates of recurrence, and hence we consider radiotherapy should be included in the therapeutics for patients with poor prognosis factors.

Furthermore, our patient, treated with radical radiotherapy, has so far shown a comparable response to that observed in surgically-treated patients and, therefore, treatment with this modality should not be ruled out in those patients with any contraindication for the performance of surgery.

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Conflict of interests

The authors of this work declare not having any conflicts of interest.

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