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# Adjuvant radiotherapy in the management of porocarcinoma with lymphatic micrometastasis

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### ABSTRACT

**Background.** Porocarcinoma is a rare skin tumor originating from dermal sweat glands. Surgical procedures are the first choice of treatment, but the role of adjuvant therapies, such as chemotherapy and radiotherapy (RT), is not clear. In this case report and review of the literature, we aimed to present a patient who underwent adjuvant RT for the diagnosis of porocarcinoma with lymphatic micrometastasis and a review of the current literature.

**Case summary.** A 61-year-old male was admitted to the dermatology department for a nodular lesion on the left knee skin. An excisional biopsy was performed, and the pathology result was reported as porocarcinoma. The closest surgical margin of the tumor was 0.2 cm. In the inguinal sentinel lymph node sampling, two of the three removed lymph nodes had micrometastases. Then, adjuvant RT was applied to the left inguinofemoral lymphatics and primary tumor bed. No recurrence was observed in the patient with a follow-up period of 24 months. No acute or late toxicity was observed including lymphedema, subcutaneous fibrosis, or stiffness of the knee joint.

**Conclusions.** Although adjuvant RT is not a routinely recommended treatment, it can be applied to increase local and regional control in patients with high-risk factors for recurrence or with lymph node metastases. There is a great need for clinical studies clarifying the role of RT, but for now, all patients should undergo multidisciplinary evaluation when a decision on adjuvant therapies is made.

**Key words:** porocarcinoma, radiotherapy, skin cancer

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## Introduction

Malignant cutaneous adnexal tumors arise from the appendageal apparatus of the skin. Porocarcinoma is an extremely rare malignant appendageal skin tumor. It originates from the intradermal component of dermal sweat gland ducts. The first case was reported in 1963, and since then, only case reports and retrospective studies have been reported [1, 2]. The most common location of malignant cutaneous adnexal tumors is the head and neck region while that of porocarcinoma is the lower extremities, but it can also present at atypical localizations, such as the scalp or breasts [3–5].

It may develop *de-novo* or by malignant transformation of an existing benign poroma [2]. Histopathological examination is essential for a definitive diagnosis. It is generally considered a locally aggressive tumor; however, metastases have also been reported. Surgical excision of the lesion with clear margins is the first choice for treatment. Definitive radiotherapy (RT) may be considered in medically inoperable patients. On the other hand, the role of adjuvant RT is not clear. Sentinel lymph node sampling may be beneficial due to considerably high rates of regional recurrence. The role of systemic therapy is limited to patients with metastatic disease.

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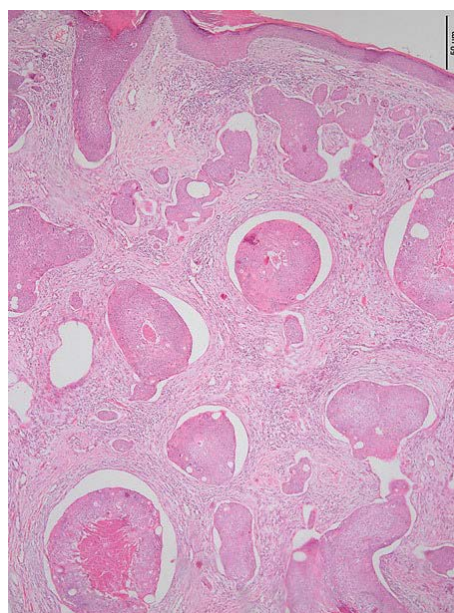
In this case report, we present a patient with the diagnosis of porocarcinoma who underwent adjuvant RT for the primary site and the lymphatic region following sentinel lymph node sampling. We also discuss the role of adjuvant RT.

## Case presentation

A 61-year-old male was admitted to the dermatology department in January 2020 due to a nodular lesion on the anterior skin of the left knee that had been present for about three years and had recently grown. His medical history was unremarkable except for laparoscopic prostatectomy without adjuvant treatment for low-risk prostate cancer. Physical examination revealed a nodular lesion measuring approximately 2 cm on the anterior skin of the left knee (Fig. 1). The lesion was excised, and the pathologic finding was reported as porocarcinoma. Histopathological examination revealed nodular masses of epithelial cells in the dermis infiltrating focally into the subcutaneous tissue. Some nodules showed a connection with the epidermis and others necrosis in the center. The stroma was desmoplastic. Nodules were composed of round differentiated poroid cells (Fig. 2). In some areas, pleomorphism, tumor giant cells, and mitoses were remarkable. Carcinoembryonic antigen (CEA) revealed focal luminal staining. CD31 staining did not show lymphovascular invasion. Tumor thickness was 1.35 cm and there were 2 mitoses in 10 high-power fields (2/10 HPF). All surgical margins were clear, but the closest surgical margin of the tumor was the deep surgical margin which was 0.2 cm. Owing to the localization of the tumor bed, wide resection was not performed due to the risk of morbidity related to second-look surgery. Sentinel lymph node sampling was performed via radiopharmaceutical and intraoperative gamma probe for nodal staging, and micrometastases were detected in two of the three removed inguinal lymph nodes. Lymph node dissection was not performed because only micrometastases were detected in the excised lymph nodes of the patient, and the combination of lymph node dissection and adjuvant RT would seriously increase the risk of lymphedema. A positron emission tomography scan (PET-CT) was performed for staging and revealed a parenchymal nodule with the largest diameter of 1 cm in the upper lobe of the right lung. Tru-cut biopsy result of the incidental lung nodule was reported as non-small-cell lung carcinoma. Therefore, the patient underwent lobectomy and mediastinal lymph node dissection for lung cancer. He was staged as pT1N0 according to the eighth edition of the American Joint Commission on Cancer (AJCC) TNM staging system and was followed up without adjuvant chemotherapy or RT.

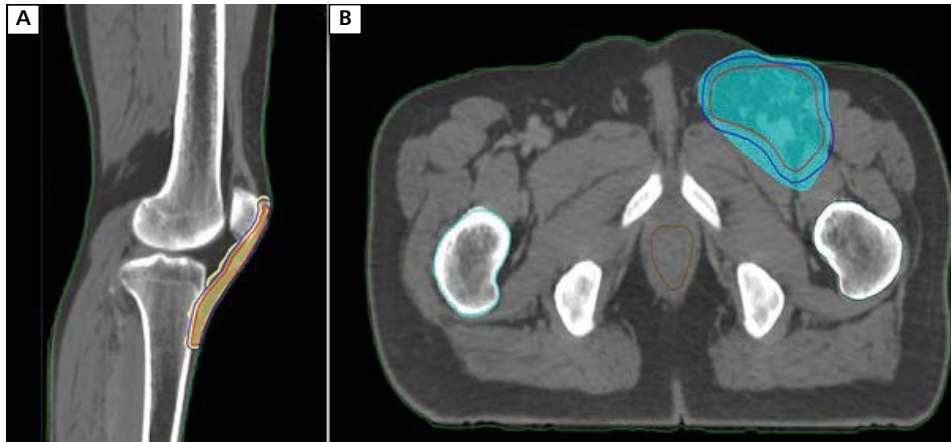


**Figure 1.** Images of the patient's lesion on the skin of the left knee



**Figure 2.** Microscopic image of the tumor. Nodular aggregates of epithelial cells some connected to the epidermis. Separation artifact of nodules from the desmoplastic stroma at the periphery, and necrosis in the center. H.E.  $\times 40$

Because of the incidental diagnosis of early-stage non-small-cell lung cancer, adjuvant RT was planned for the primary tumor bed and to inguinofemoral lymphatics five months after excision of the tumor. Since 5 months had passed since the first excision, knee magnetic resonance imaging (MRI) and inguinal ultrasound were performed again, and no residual or recurrent tumor was detected. Then, simulation computed tomography (sim-CT) was performed in the supine position for RT planning. A radiopaque marker was placed on the surgical scar for better delineation of target volumes. The target volumes were contoured by fusion of preoperative MRI and sim-CT. The clinical target volume (CTV) was contoured by giving a safety margin of 3 cm to the preoperative tumor volume. The planning target volume (PTV) was created by giving a 0.3 cm safety margin to



**Figure 3.** Dose distribution images of the radiotherapy plan; **A.** Sagittal images of the primary tumor bed. Yellow dose color-wash received 59.4 Gy. The red contour is clinical target volume, and the blue contour is planning target volume; **B.** Axial images of the inguofemoral lymphatic area. Blue dose color-wash received 50.4 Gy. The red contour is clinical target volume, and the blue contour is the planning target volume

the CTV due to the image-guided radiotherapy (IGRT) facility in our department. Volumetric modulated arc therapy (VMAT) of 50.4 Gy in 28 fractions was applied to the primary tumor bed and inguofemoral lymphatics of the patient with daily cone-beam computed tomography (CBCT). Due to the close surgical margin, five more fractions of RT were applied to the primary tumor bed, increasing the total dose to 59.4 Gy (Fig. 3). The patient used topical moisturizer for dermatitis prophylaxis during RT. Grade 1 dermatitis was observed on the irradiated skin according to common terminology criteria for adverse events version 5.0 (CTCAE v5.0) during RT. No severe acute toxicity was observed during RT.

After adjuvant RT, the patient was followed up every three months with a complete dermatological examination, inguofemoral ultrasound, and knee MRI for porocarcinoma, thorax CT every 6 months for lung carcinoma, and blood tests including prostate-specific antigen for prostate adenocarcinoma. No local, regional, or distant recurrence was observed at a follow-up of 24 months. The patient is still under follow-up and is in remission for all three separate malignancies. In addition, no late toxicity was observed in the patient during the follow-up. There was no clinical subcutaneous fibrosis, joint stiffness, or difference in diameters between the lower extremities.

## Discussion

Malignant cutaneous adnexal tumors arise from hair follicles and sebaceous, apocrine, or eccrine glands of the skin. Porocarcinoma, also known as eccrine porocarcinoma or malignant hydroacanthoma simplex, is an extremely rare histological variant of these tumors. It

originates from the intradermal component of dermal sweat gland ducts. The term of eccrine porocarcinoma was first introduced by Pinkus and Mehregan in 1963 [1]. It constitutes approximately 0.003% to 3.5% of all skin malignancies [6]. Its incidence increases with age and is most common in the 7–8<sup>th</sup> decades of life. There is no sex predominance. While it is most commonly observed on the skin of the lower extremities, as in our patient, atypical localizations such as the scalp, breasts, and vulva have also been reported [3–5, 7]. Although immunosuppression and some genetic syndromes are blamed in the etiology, there is no clearly defined etiological factor. It may develop as *de-novo* or by malignant transformation of an already existing benign poroma [2].

The rates of local recurrence, regional recurrence, and distant metastasis are around 17%, 19%, and 11% after primary therapy, respectively [8]. Wide local excision is the preferred approach for definitive treatment, but Mohs micrographic surgery is also used with increasing frequency, especially in the head and neck region [9, 10]. In definitive surgery, the primary objective is to obtain a negative surgical margin. There is no clear consensus about the optimal surgical margins for porocarcinoma. Surgical margins between 3 mm and 10 mm have been reported to be effective [11, 12]. In a review of 1968 patients with different subtypes of adnexal carcinomas, it was suggested that the surgical margins should be at least 2 cm after wide local excision. However, due to rarity of the porocarcinoma, it is difficult to conduct studies to generate optimal histology-specific recommendations for surgical margins. Based on these results in the literature, our patient was considered at high risk for local recurrence because the tumor was 0.2 cm away from the closest surgical margin.

Although there is no study comparing definitive RT and surgery, primary RT can be a treatment option in patients medically unfit for surgery or in case of cosmetic concerns. There is limited evidence regarding the role of adjuvant RT in the literature and usually consists of case reports or retrospective reviews. Adjuvant RT in cutaneous adnexal carcinomas is recommended in the presence of high-risk factors such as perineural invasion, lymph node metastasis, extracapsular nodal extension, positive surgical margins, high tumor grade, and recurrent disease [13]. In a study evaluating the clinicopathological characteristics of 69 patients with porocarcinoma, high mitotic index ( $\geq 14$  mitoses per HPF), presence of lymphovascular invasion, tumor depth  $> 7$  mm, and infiltrating type of margins which is defined by malignant clusters infiltrating, and the dermis or hypodermis, instead of pushing type, were reported as negative prognostic factors which are predictive of local recurrence [2]. There are also case reports in which adjuvant RT prevented local recurrence in patients with positive surgical margins [5]. Adjuvant RT doses in the previous reports range from 24 Gy in 12 fractions to 70 Gy in 35 fractions [14]. In our department, we prefer two different fractionation schemes in adjuvant RT for cutaneous adnexal tumors, 50–50.4 Gy in 20–28 fractions or 59.4–60 Gy in 30–33 fractions for patients with R0 resection. In cases with R1 or R2 resection, we apply total doses of 64–70 Gy in conventional fractions.

Regional lymph node dissection (LND) is a common treatment when clinical lymph node metastasis is confirmed, but no survival benefit has been demonstrated. On the other hand, the role of sentinel lymph node sampling (SLNS), which has become a standard procedure in thick malignant melanomas, remains unclear for porocarcinoma. Because of the relatively high rates of lymphatic metastases with porocarcinoma, some authors propose that SLNS should be standardized in the first-line management for optimal staging and decisions on appropriate adjuvant treatments [15, 16]. However, when a micrometastasis is detected in the sentinel lymph nodes the second step in treatment is not clear. LND can be performed; however, the survival benefit is not certain. Besides the lack of survival benefit, LND also increases the risk of lymphedema, particularly in the inguinal region. Considering that regional control can also be achieved with RT in patients with microscopic nodal disease, with breast cancer and malignant melanoma, unnecessary LND and related toxicity can also be prevented with SLNS plus RT in patients with malignant cutaneous adnexal tumors [17, 18]. We achieved good loco-regional control with this approach in our patient, and lymphedema was not observed. However, we think that the decision on treatment for lymph nodes should be made from a multidisciplinary perspective since there is not enough evidence about

the effectiveness of RT in patients with particularly macroscopical nodal disease.

The current evidence for adjuvant systemic treatment is based on case reports or retrospective studies, and they are limited only to metastatic patients. Although cutaneous adnexal tumors are considered relatively chemoresistant, there are case reports in the literature showing that satisfactory treatment results are obtained with single-agent or multi-agent systemic treatments, targeted therapies, or hormone therapy agents such as tamoxifen [19, 20]. On the other hand, there are also centers where adjuvant chemotherapy after excision of the primary tumor, is the standard protocol in cases with lymph node metastasis and without distant metastasis [15]. Since our patient had only micrometastatic lymph nodes, adjuvant chemotherapy was not applied, and no distant or regional recurrence was observed at the end of the 24-month follow-up.

## Conclusions

Adjuvant RT may have high local control rates in patients with risk factors for recurrence after primary surgery, with minimal toxicity. However, current data are insufficient to support a routine recommendation for the use of adjuvant RT in patients with porocarcinoma, and there is a great need for prospective studies that examine the role of adjuvant RT. Sentinel lymph node sampling may be useful in detecting occult lymph node micrometastases and preventing unnecessary LND. RT alone may be sufficient in patients with occult lymph node micrometastasis detected by SLNS. The adjuvant treatment options in patients with malignant cutaneous adnexal tumors should be discussed in multidisciplinary meetings.

## Ethical consideration

Written informed consent was obtained from the patient for the use of his medical information and photographs in an academic article.

## Conflict of interest

Authors declare no conflict of interest.

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