# Neoadjuvant radiation to facilitate surgical treatment of a microcystic adnexal carcinoma with perineural invasion of the vulvar region

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***Key words:*** microcystic adnexal carcinoma; neoadjuvant radiation; tissue conservation; treatment strategy; vulvar carcinoma.

## INTRODUCTION

Microcystic adnexal carcinoma (MAC) is a rare, locally aggressive carcinoma that presents with glandular and follicular differentiation and proclivity for perineural invasion.[1] Most MACs are found in the head and neck region; rarely are they reported in the vulva.[2] Mohs micrographic surgery is the treatment of choice for MACs; however, wide local excision (WLE), radiotherapy (RT), and chemotherapy have also been employed.[3] RT, as a primary treatment, has been used successfully in some cases of MAC but is considered insufficient for treatment in most cases. For the treatment of MAC, adjuvant or postoperative RT after excisional surgery has yielded control rates comparable to those of Mohs micrographic surgery.[4] Because of their aggressive nature, high-recurrence rates, proclivity for perineural involvement, and need for tissue conservation, MACs are commonly treated with adjuvant radiation after excisional surgery.[5] Although there are numerous cases of MAC treated with adjuvant radiation, there are no reports of MAC treated with neoadjuvant radiation before surgery. Here, we report a patient who had successful treatment of a rare vulvar MAC with neoadjuvant RT and excisional surgery.

*Abbreviations used:*

MAC: microcystic adnexal carcinoma
RT: radiotherapy
WLE: wide local excision

## CASE REPORT

An 86-year-old woman presented with a cystic mass (4.2 cm in width × 6.3 cm vertically, measured with ruler) in the lower pole of the right vulva region. The lesion was an indistinct nodular erythematous mass with multiple punctate cystic papules covering the surface (Fig 1, *A*). She stated that the lesion had been slowly growing for 2 years, was bothersome, and occasionally bled. An incisional biopsy with subsequent pathology and hematoxylin-eosin staining demonstrated numerous cysts lined by squamous epithelium with foci of calcification in the papillary dermis. In the reticular dermis, there were similar small nests and stands of homomorphous ovoid and rounded cells that permeated between reticular collagen bundles (Fig 1, *B*). In several foci confined to the dermis, there was perineural invasion (nerve diameter 0.07 mm) (Fig 1, *C*). Her history included having 2 separate basal cell carcinomas on the nose treated with Mohs micrographic surgery and a course of ionizing radiation, respectively. The patient was not immunosuppressed and had no history of ionizing radiation to the vulva area. A pelvic magnetic resonance imaging demonstrated no deep invasion or metastases. She was staged at stage 1 (cT1, cN0, cM0; American Joint Committee on Cancer 8th Edition). After discussing risks and benefits of surgical treatments, the patient expressed overt concern regarding the peri-surgical morbidity with WLE, difficult margin

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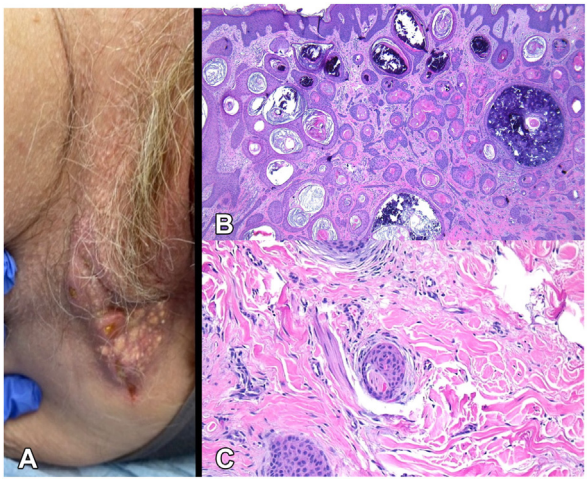


**Fig 1.** Microcystic adnexal carcinoma clinical and histopathologic findings. **A,** Clinical image of microcystic adnexal carcinoma on the right vulva. **B,** Hematoxylin-eosin stain showing dermal cysts lined by squamous epithelium and calcification foci. **C,** Perineural invasion is shown.

control of MACs, and adversity in caring for a relatively large surgical wound in the vulvar location. Moreover, the patient did not agree to Mohs micrographic surgery under local anesthesia because of an extreme aversion to the discomfort of multiple lidocaine injections. She even suggested to have solely RT to the vulvar area because she stated that she had a good experience with RT for a basal cell carcinoma on the nose. After tumor board (dermatology, surgical oncology, gynecology, gastroenterology, and radiation oncology) discussion and recommendation, she was presented with an option and agreed to undergo neoadjuvant radiation to shrink the MAC in the vulvar area before excision under general anesthesia.

She underwent electron beam radiotherapy (total dose 4500 cGy given with 25 fractions) to the vulvar region over 58 days. Three months after the completion of electron beam radiotherapy, a follow-up positron emission tomography/computerised tomography scan was performed, which revealed no abnormal 18F-fluorodeoxyglucose avidity in the vulva or lymph nodes but 18F-fluorodeoxyglucose avidity within the anorectal region. She subsequently had an elliptical excision (2-cm margins, under general anesthesia) with anoscopy in the right vulvar region. The *en bloc* specimen with bread-loaf sectioning (hematoxylin-eosin stain) displayed a residual MAC measuring 6.0 mm in horizontal spread × 2.5 mm in depth, with margins appearing free of carcinoma (pathologic staging pT1b, pNX, American Joint Committee on Cancer 8th Edition). The defect was closed with a primary repair by gynecologic oncology surgeons. After surgery, gynecologic examination revealed a normal urethral meatus, perineum, and anus and no appreciable adnexal masses. The patient had intermittent clinical examinations for up to 18 months with dermatology and demonstrated no signs of recurrence.

## DISCUSSION

The use of RT alone for the treatment of a MAC was not recommended because reports demonstrated that it was not an effective treatment and may cause clinically aggressive transformation of MACs.[4,6] Moreover, the heterogeneity of cases using RT in MAC makes the exact role of RT in treating MAC challenging to interpret. Surgical resection of the neoplastic region was planned after neoadjuvant RT, recognizing not only the insufficiency of RT alone but also to assess potential morphologic changes or reductions in neoplastic volume. RT has the advantage that it can induce both direct and indirect double-strand DNA breaks in tumor cells, thereby impeding their function.[7] It also leads to the ionization of water within the cell cytoplasm, creating reactive oxygen species and causing further unrepairable DNA damage. In the neoadjuvant setting, this can lead to the destruction and shrinkage of tumors. Another potential advantage of neoadjuvant RT is the abscopal effect, which signifies the immune system-mediated regression of distant metastatic cancer postirradiation.[8] This effect results from RT-induced immunogenic cell death, releasing neoantigens into the tumor microenvironment. This effect has been reported for other skin cancers with RT, but not necessarily for MACs and RT.[9] As mentioned before, there were early reports of aggressive transformation of MACs with RTs,[4,6] but several studies and the present study do not show this. In fact, we observed a substantial reduction in tumor size from 4.2 cm × 6.3 cm to 6.0 mm × 2.5 mm with neoadjuvant RT.

Treatment of MACs with surgery, because of their extension and indistinct margins, leads to extensive morbidity. Employing neoadjuvant RT is novel for treating MACs but not for treating other tumors.[10] Neoadjuvant RT, which has the advantages of shrinking a tumor or inducing the abscopal effect, with subsequent WLE or Mohs micrographic surgery, should be considered for large MACs in areas where tissue conservation is needed or desired.

### Conflicts of interest

None disclosed.

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