

An advanced case of extramammary Paget disease: Safe and effective treatment in an inoperable elderly patient using extensive en face electron irradiation



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INTRODUCTION

Extramammary Paget disease (EMPD) is an intra-epithelial adenocarcinoma characterized by epithelial infiltration of large atypical cells with prominent nuclei.¹ The disease process is hypothesized to originate in the apocrine sweat glands in the anogenital region. It is often diagnosed in postmenopausal women and most commonly affects the vulva, perianal skin, and axilla but can sometimes be associated with invasive visceral or adnexal adenocarcinoma.²

Standard therapy for EMPD is wide local excision. However, many of the elderly patients affected by EMPD may be medically unfit for aggressive surgery. Radiotherapy is rarely used, and there is a paucity of reports detailing the efficacy of electron beam radiotherapy for exceptionally large EMPD lesions.

CASE REPORT

A 92-year-old white woman with a history of hypertension and congestive heart failure presented with an erythematous and scaling plaque that enlarged over 15 years. Although not painful, the plaque itched. Topical moisturizing creams and antifungals did not improve the lesion.

Physical examination revealed a 27- × 16-cm suprapubic lesion, extending superiorly onto the abdomen and inferiorly onto the right thigh. There was a 12-cm central macerated area. In other areas, there was hyperpigmentation (Fig 1).

Abbreviation used:

EMPD: extramammary Paget disease

Shave biopsy revealed a confluent proliferation of pagetoid cells in the epidermis with pleomorphism, hyperchromasia, and irregular nuclear contour. Mitotic activity among the pagetoid cells was observed. No dermal invasion was identified. The pagetoid cells expressed cytokeratin 7, carcinoembryonic antigen, and epithelial membrane antigen but did not mark with Mart1 (Fig 2). Basic laboratory studies were unremarkable, and a positron emission tomography scan identified no other foci of disease.

Exceptionally large extramammary Paget disease was assessed. A dermatologic surgeon and general surgeon evaluated the patient, but she was not a candidate for any extensive surgical resection. Topical medications were impractical, at which point radiation therapy was pursued. The patient received 6000 cGy in 30 fractions, delivered as a single en face electron cone field to the lower abdomen and perineum, using 6 MeV electrons and a ½-cm bolus (Fig 3). Aquaphor ointment was used to treat the short-term erythema and hyperpigmentation of the skin.

After 12 months of follow-up, the patient had an excellent response to radiation therapy (Fig 4). The skin over the treatment area is mildly

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Fig 1. EMPD before irradiation. The patient presented with an exceptionally large plaque measuring 27 × 16 cm with a 12-cm region of central maceration and surrounding hyperpigmentation. The lesion originated in the vulva and extended superiorly into the abdomen and laterally onto the bilateral thighs. The lesion did not cross over onto the poster perineum.

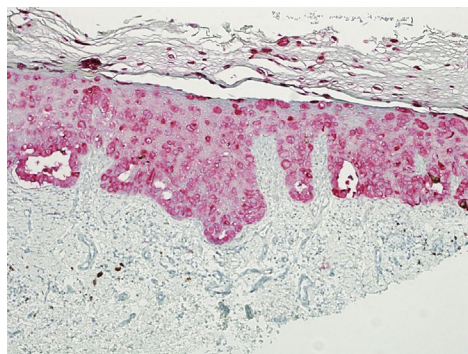


Fig 2. Carcinoembryonic antigen staining of EMPD before irradiation. Carcinoembryonic antigen marks positive in all the epidermal pagetoid cells. Pagetoid cells in the stratum corneum are also evident.

hyperpigmented, but it is otherwise unaffected. Areas of desquamation, erosion, and bleeding resolved entirely. There is no evidence of treatment failure manifesting as recurrent skin erosions, lymphadenopathy, or visceral metastases, and the patient is asymptomatic and pleased with the result.

DISCUSSION

We describe a rare North American case of EMPD in an elderly white woman characterized by an unusually large size of the primary vulvar lesion. The primary lesion was not associated with synchronous or metachronous neoplasm and demonstrated a positive response to electron beam radiotherapy as monotherapy.

Literature review did not identify prior use of radiotherapy (and electron beam radiotherapy in particular) to treat lesions of this size.² Despite a recent Cochrane review³ citing insufficient evidence

to direct a given therapy for EMPD, surgical excision has largely been accepted as the treatment of choice. However, owing to the multifocal nature of the disease and margin irregularity, even wide local excision results in positive margins at a rate of between 40% and 75%.⁴ Furthermore, many elderly patients may be unwilling or unable to tolerate an extensive surgery given the risk of functional impairment and cosmetic disfigurement. In these common scenarios, we aim to underscore our positive experience with electron beam radiotherapy.

Several reasons point to why radiotherapy may be an ideal modality to treat extensive lesions such as the one in our patient. As mentioned above, the multicentric biology underlying EMPD can result in treatment challenges that may be overcome with a more widely targetable local therapy. Additionally, local irradiation was recently found to have systemic antitumor immune effects via enhanced expression of MHC class I, local dendritic cell priming, and upregulation of proimmunologic cell signaling.⁵ Thus, radiation may be appropriate in more extensive lesions with greater risk of invasion, given that immunosuppressive tumor microenvironments in EMPD have been directly linked to more extensive cases of vulvar EMPD and disease recurrence.⁶

Although some reports detail treatment efficacy with radiotherapy as an adjunct to surgery, fewer reports detail the use of primary radiotherapy for EMPD. Of those reports, standard orthovoltage x-ray therapy² is most often cited, with still fewer reports describing therapeutic efficacy of electron beam radiotherapy alone.

Electron beam therapy targets superficial tissues while sparing deeper structures, and thus is an appropriate therapy for cutaneous malignancies such as EMPD. Given reports of second malignancies following radiotherapy,⁷ we favored a therapy that would reduce unnecessary dosing of underlying visceral structures. Electron beam radiation therapy, either alone or as an adjunct to x-ray therapy, is found to result in histopathologic clearance without evidence of any tumor cells on repeat skin biopsies.⁸ Our report further supports the notion that deeper penetration of ionizing radiation is not required to achieve cure in patients with large lesions that have not infiltrated into the dermis. Similarly, prophylactic pelvic radiation, although effective,⁹ does not seem to be necessary for in situ disease even when extensive.

With regard to radiation dose, although the optimal dose has yet to be established, doses higher than 5000 cGy have been suggested,⁷ and we found that 6000 cGy adequately treated the disease without undue toxicity. Our patient demonstrated positive



Fig 3. Electron beam plan. External electron beam radiation plan for extensive EMPD shows isodose lines of superficially deposited radiation. Ninety-five percent of the prescribed total dose of 6000 cGy in 200 cGy fractions was delivered to the area bounded by the magenta lines.



Fig 4. Resolution of EMPD after irradiation. After electron beam irradiation, the skin over the treatment area is mildly hyperpigmented, areas of desquamation and bleeding have resolved, and the skin is re-epithelized and smooth without ulcerations.

responses, and the treatment was well tolerated. Our patient experienced a durable response to therapy, with no evidence of disease at 12 months of follow-up, consistent with prior reports.⁷ Furthermore, no early or late grade ≥ 3 toxicities were appreciated, and the postradiation skin changes experienced by our patient were transient and easily manageable, also consistent with other studies.⁹

The rarity of EMPD and wide variation among medical specialties diagnosing EMPD have problematized the standardization of treatment and resulted in significant delays in diagnosis and treatment,¹⁰ as

was the case for our patient. In the absence of randomized data, we hope this case illustrates that the extensive lesions that result may be safely and effectively treated with electron beam radiotherapy.

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