Radiotherapy for Perianal Extramammary Paget’s Disease: A case report

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ABSTRACT
Extramammary Paget’s disease (EMPD) is a rare, usually non-invasive intraepithelial skin adenocarcinoma which predominantly involves vulvar, perianal, scrotal and penile skin. Management of EMPD is rather complicated due to multifocal involvement, lack of clear tumor boundaries and clinically occult extensions. High recurrence rates following surgery together with the goal of achieving a better cosmetic and functional outcome have prompted the utilization of non-surgical treatment modalities in the management of EMPD. Radiotherapy may either be used as adjunct to surgery after recurrence or may be employed in the treatment of patients with high risk of local failure after surgery.

76-year-old male patient was admitted to our institution with the complaints of persistent anal itching. He was diagnosed with perianal Paget’s disease after consecutive skin biopsies. The patient was deemed unsuitable for surgery due to external anal sphincter involvement which was detected by endoanal ultrasonography and he was treated with curative radiotherapy in our department. We reviewed the pertinent literature, and discussed treatment options and outcomes.

In conclusion, we recommend radiotherapy as a treatment option for patients with perianal Paget’s disease with curative intent.

Key words: Extramammary Paget’s disease, radiotherapy

ÖZET
Meme dışi Perianal Paget Hastalığına Radyoterapi: Olgu sunumu
Meme dışi Paget hastalığı (EMPD) nadir görülen, ağırlıklı olarak olanlar, perianal, skrotal ve penil bölümler tutan, sliklikla invazyon olmayan intraepidermal cit adenokarsinomasıdır. Multifokal tutulum, tümör sınırlarının belirgin olmayan ve klinik olarak zengin uzamalar nedeniyle EMPD’nin tedavisi komplikasyonlu. Cerrahi sonrası yüksek rekürrens oranları ile birlikte daha iyi kozmetik ve fonksiyonel sonuç elde etme amacıyla EMPD’nin tedavisinde cerrahi sonrası cerrahi sonrası lokal bağırsak riski yüksek olan hastaların tedavisinde kullanılabilir.

76 yaşındaki erkek hasta persistan anal kaşıntısı nedeniyle başvurdu. Moteaksip cilt biyopsileri sonrasında perianal Paget hastalığı tanısı konuldu. Endoanal ultrasonografi eksternal anal sınıfık tutulumu olmasından dolayı cerrahi uygulanımedi ve cerrahi sonrası kozmetik ve fonksiyonel sonuçlar değerlendirildi. Sınırda görülen lokal bağırsak riski yüksek olan hastaydı.

Analtar kelimeler: Meme dışı Paget hastalığı, Radyoterapi

Introduction
Sir James Paget was first to describe Paget’s disease of the breast involving the nipple-areola complex and the surrounding skin associated with underlying ductal carcinoma in 1874 (1). Perianal Paget’s disease was first described in 1893 (2). EMPD predominantly affects white women between 50 and 80 years old (3). EMPD commonly involves vulvar, perianal, scrotal and penile skin as a non-invasive skin adenocarcinoma (4).

Clinically, EMPD presents with itchy erythematous or white patch-plaques (3). Clinical findings are usually inadequate to establish the specific diagnosis. Psoriasis, dermatophytosis, contact dermatitis, lichen sclerosis, squamous cell carcinoma in situ and melanoma are to be ruled out, thus delayed diagnosis of EMPD is common (5,6). Diagnosis is established by performing a biopsy and histologic features are similar to Paget’s disease of the breast.

Standard treatment of EMPD is surgery. Wide local excision is the preferred treatment for non-invasive and local disease (7). In the presence of an underlying anorectal carcinoma, EMPD is treated with abdominoperineal resection including wide excision of the cutaneous lesion (8). Recurrence rates after surgery range between 33% and 60%, therefore other treatment modalities including radiotherapy, CO₂ laser ablation, topical and systemic chemotherapy, photodynamic therapy are considered (9). Radiotherapy has been used in patients with non-invasive EMPD and may be indicated for patients who are not amenable to surgery, for recurrence following surgery or as an adjunct to surgery in patients with a high risk of local recurrences (3,5).

In the present report, we describe a case of perianal Paget’s disease successfully treated using...
radiotherapy with curative intent. We reviewed the pertinent literature, and discussed treatment options and outcomes.

**Case Report**

76-year-old male patient was admitted to our institution with complaints of perianal itching and erythema. Physical examination revealed perianal erythematous, weeping lesions extending to the anal canal (Figure 1). There was no palpable mass under the lesion and lymphadenopathy in the inguinal region. The patient didn’t have a history of familial Paget’s disease and no systemic findings of any malignancy or gastrointestinal symptoms were present. Sample showed mucin producing atypical cell in the epidermis. Neoplastic cells were stained with Mucicarmin, Cytokeratin 7 (CK7), Gross cystic disease fluid protein 15 (GCDFP-15) and not stained with CK20. The patient was diagnosed with perianal Paget’s disease (Figure 2). Thoracic, upper abdominal CT, pelvic MRI, sigmoidoscopy, routine biochemistry and tumor markers showed no specific abnormality. Superficial external anal sphincter fiber involvement was detected by endoanal ultrasonography in June 2011.

Curative radiotherapy was planned for the patient. We performed both 2-D and 3-D planning. For 2-dimensional planning, patient was immobilized in prone position in the simulator room. Monitoring of the rectum was performed with rectal barium and wiring of the lesion was performed for assisting in accurate target localization.

For 3-D CT planning (Lightspeed CT, GE Healthcare, Chalfont St. Giles, U.S.) 2.5 mm spaced cross-sectional images were acquired and these images were transferred to the contouring workstation (SimMD, GE, U.S.) via network. Gross tumor volume (GTV) was contoured first and Clinical Target Volume (CTV) and Planned target volume (PTV) was generated by using adequate margins. Organ-at-risk (OAR) volumes (rectum, bladder) were also delineated. After contouring was completed, structure sets were transferred to the treatment planning system (PrecisePlan, Elekta, U.K.)

Since the treatment volume included the neoplastic lesions in the skin and anal canal, radiotherapy was decided to be delivered with Co-60. The patient was immobilized in prone position on the treatment table and both gluteal regions were lateralized with the help of plaster. A total dose of 44 Gy was delivered in 22 fractions over 5 weeks using PA photons.
On the first follow-up visit (12 weeks after radiotherapy) complete remission of Paget’s disease was seen and no acute toxicity except for a mild, grade 2 acute radiation dermatitis (according to the Radiation Therapy Oncology Group acute toxicity scale) developed (Figure 3).

Discussion

EMPD, a rare form of adenocarcinoma in the apocrine gland-rich regions of the skin, is an epithelial malignancy. Diagnosis is made by performing a biopsy. Intraepidermal Paget’s cells with pale-staining cytoplasm and round-wide nuclei are observed in histopathological examination (5).

EMPD is usually confined to the epidermis and rarely involves the lymphatics. Prognosis depends on the depth of invasion. While EMPD in situ has excellent prognosis, invasive EMPD and particularly cases with lymphovascular invasion fare worse (5).

EMPD is a rare malignancy and management is complicated by the presence of occult extensions and multifocal, non-contiguous nature of the disease (3). Wide local excision or Mohs micrographic surgery (MMS) is the standard treatment in EMPD, but recurrence rates are quite high with this procedure. Recurrence rates after standard surgical excision and MMS was found to be 33-60% and 16-28% respectively (9). Median time to recurrence was 2.5 years and long-term follow up is needed (10).

Utilization of non-surgical treatment modalities in the management of EMPD, have emerged given the high recurrence rates after surgery and the desire to achieve a better cosmetic and functional outcome. Localized treatment modalities for non-invasive, well-defined, unicentric EMPD other than radiotherapy are topical chemotherapy and photodynamic therapy (3).

5-fluorouracil and imiquimod as topical chemotherapeutic agents have been used to treat EMPD. However there is not extensive experience with the sole use of topical 5% imiquimod in the treatment of EMPD. Researchers Qian et al. (11) and Wang et al. (12) reported successful use of this agent in limited EMPD. Randomized controlled trials are needed to determine the safety and efficacy of imiquimod compared with the other therapy modalities currently used to manage EMPD.

Topical 5-Fluorouracil (5-FU) chemotherapy is another option that may be useful both for symptomatic pain relief and cytoreduction prior to surgery along with the use in post-operative early disease recurrence detection (13, 14). The mechanism of 5-FU is the penetration of the skin to a depth of only 1-2 mm whereas EMPD involves deeper layers making 5-FU an incomplete curative agent in EMPD therapy compared to effective therapeutic use of radiotherapy with the capability to treat any desired skin depth.

Photodynamic therapy is another treatment option for EMPD (15). In this therapeutic modality, topical photo-reactive 5-aminolevulinic acid (5-ALA) is used in localization of the tumor tissue, eliminating tumor cells through an appropriate wavelength beam (16). Shieh et al. (15) and Li et al. (17) reported their results in their EMPD series. However, recurrence rates are high with this modality and mostly preferred for superficial disease (15).

Radiotherapy can be used in the setting of recurrent disease after surgery and as a primary treatment modality in patients with high risk of local recurrence following surgery or in patients who are not amenable to surgery (3,5).

Besa et al. used radiation doses of 40-60 Gy in patients deemed unsuitable for surgery. Radiation was delivered with AP / PA fields or with a single field using photon, electron and combination of photon-electrons in their study. At 21 months after treatment they found no evidence of recurrent disease (18). Velenik et al. suggested delivering total doses of 40-44 Gy in the radiotherapy of in situ EMPD and they also observed complete treatment response at 28 months after diagnosis (19).

In our study, total radiotherapy dose was 44 Gy in 22 fractions over 4 weeks. On the first follow-up visit (12 weeks after the radiotherapy) complete remission of Paget’s disease was achieved and no acute toxicity except for a mild, grade 2 acute radiation dermatitis (according to the Radiation Therapy Oncology Group acute toxicity scale) developed. Our experience reveals that radiotherapy is a viable treatment option for patients with perianal Paget’s disease with curative intent. However, our single case report clearly needs verification in randomized study with long-term follow up to calculate the role of radiotherapy in EMPD.

References


