

# A Case of Advanced Extramammary Paget's Disease Successfully Controlled by Monthly but Not Weekly Docetaxel Chemotherapy

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## Key Words

Extramammary Paget's disease · Chemotherapy · Docetaxel

## Abstract

Extramammary Paget's disease (EMPD) is an uncommon cutaneous adenocarcinoma arising from the apocrine glands within the epidermis or underlying skin appendages in the anogenital and axillary regions. Surgical excision is basically performed as a treatment for EMPD. However, therapeutic options for EMPD in an advanced stage are limited. Herein, we report the case of a Japanese woman with advanced EMPD successfully controlled by monthly but not weekly docetaxel therapy. We also demonstrate the possibility that a monthly regimen of docetaxel is a more effective and optimal schedule than a weekly one through this case report.

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Published by S. Karger AG, Basel

## Introduction

EMPD is an intraepithelial adenocarcinoma characterized by a chronic eczema-like rash and/or dermatophyte infection-like lesion mainly in the external genital and axillary regions. EMPD in its early stage is usually not invasive and metastatic; therefore, it is simply treated by surgical excision. However, once EMPD progresses to the advanced stage, it often becomes difficult to treat and control despite various therapeutic options such as surgery, radiotherapy and/or chemotherapy. Recently, the clinical efficacy of taxanes, including docetaxel and paclitaxel, a group of antimicrotubule agents, for advanced EMPD has been report-

ed [1–6]. Here, we also report a case of advanced EMPD successfully controlled by monthly docetaxel therapy (MDT), in which the possibility that a monthly administration has an advantage over a weekly one is demonstrated.

## Case Report

An 81-year-old Japanese woman noticed an erythema and erosion on her external genitals. When she was referred to us 7 months later, the erythematous lesion had enlarged with the appearance of a small hemorrhagic tumor on her right labia major (fig. 1a). A skin biopsy specimen revealed multiple Paget's cell nests in the epidermis, and these cells were positive for carcinoembryonic antigen (CEA). At that time, her serum CEA level was in the normal range, and no metastasis was revealed by computed tomography (CT) in spite of a few palpable lymph nodes in the right inguinal region. We performed local excision with a wide margin and removal of the regional lymph nodes of the inguinal area. Histopathology demonstrated tumor cell invasion into the dermis and the inguinal lymph node, and the diagnosis of advanced EMPD (stage III, pT4N1M0) was made. Nine months after surgery, a local recurrence was found around the postoperative scar (fig. 1b). A CT showed some metastatic lesions, including the lymph nodes of the para-aorta, inferior vena cava and pelvis, and the lower abdominal skin (fig. 1c). Although several courses of low-dose FP therapy consisting of 5-fluorouracil (600 mg/m<sup>2</sup>, day 1–5) and cisplatin (5 mg/m<sup>2</sup>, day 1–5) were given [7], the patient had progressive disease in accordance with a persistent trend towards an increase in her serum CEA level. When 6 courses of the low-dose FP regimen were finished 16 months after surgery, she was finally found to have lung, liver and intraperitoneal metastases, causing paralytic ileus, in addition to the formerly found metastatic lesions (fig. 1d).

In order to control the intraperitoneal metastases causing paralytic ileus, MDT at a reduced dose (60 mg/m<sup>2</sup>, once every 4 weeks) was initiated. After 2 courses, the volume of the metastases was reduced by 50% on CT (fig. 2a), and her serum CEA level immediately decreased to 125.0 IU/l from 243.8 IU/l, with a remarkable improvement in ileus as well as in the score of the activities of daily life (ADL) index (Barthel and vitality index), leading to the diagnosis of partial response (fig. 2b). However, due to a drug-induced anaphylactic shock caused by granulocyte colony-stimulating factor administration for the treatment of neutropenia, MDT was discontinued. Consequently, weekly docetaxel therapy (WDT; 25 mg/m<sup>2</sup>, once every week) was started to reduce the single dosage of docetaxel for prevention of neutropenia. Soon after changing to the weekly regimen, her serum CEA level and the size of the metastases increased (fig. 2). Finally, she died 30 months after surgery.

## Discussion

There are several reports indicating the efficacy of taxanes for EMPD, given either as a monotherapy or as a combination therapy with the other anticancer agents and/or radiation. Therefore, we carefully chose docetaxel monotherapy for the treatment of our advanced EMPD case based on the fact that docetaxel has fewer adverse effects than paclitaxel, and it can relatively easily be administered even to elderly individuals without notable impairment of patients' quality of life.

However, the optimal type of taxanes and the optimal schedule of administration for EMPD are still controversial. Sparano et al. [8] examined the disease-free and overall survival of breast cancer patients after weekly paclitaxel therapy and MDT and WDT, respectively,

compared to those after monthly paclitaxel therapy (MPT) in adjuvant treatment. This study revealed that weekly paclitaxel therapy and MDT were significantly better than MPT, while WDT was not significantly better than MPT, demonstrating the indirect evidence that MDT is better than WDT in the adjuvant treatment for breast cancer [4]. However, there is no study which directly compares the effect of docetaxel therapy given weekly and monthly in any type of neoplasm. Our case coincidentally proved the possible advantage of MDT over WDT based on the rapid enlargement of the metastatic lesions and the increase in the serum CEA level immediately following a conversion from the monthly to the weekly regimen, although the possibility of acquisition of resistance to docetaxel by tumor cells cannot be completely denied.

In conclusion, we demonstrated the efficacy of docetaxel therapy, especially a monthly regimen, for advanced EMPD compared to a traditional low-dose FP therapy. Taxanes have a great potential as one of the major anticancer drugs for the treatment of advanced EMPD, provided that the administration schedule is optimized.

### Statement of Ethics

The case report was conducted according to the Declaration of Helsinki principles. The patient gave written informed consent.

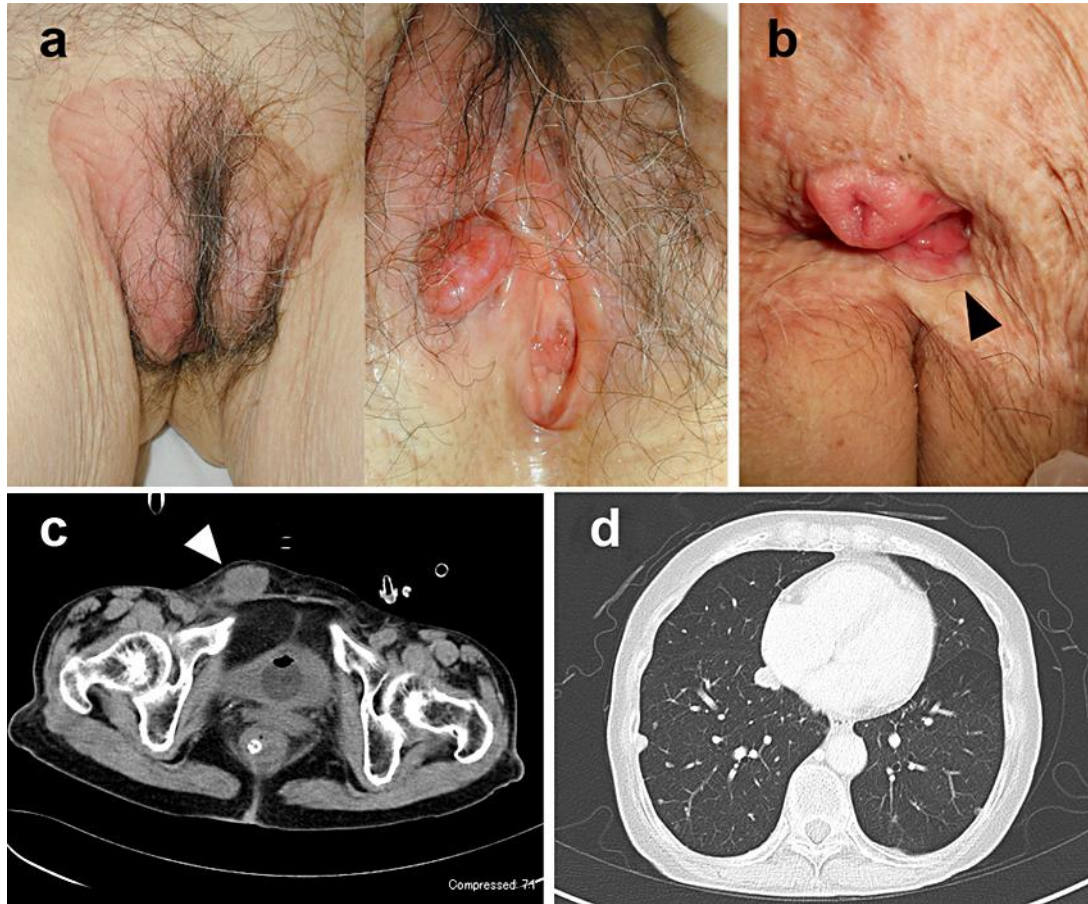
### Disclosure Statement

The authors report no conflicts of interest.

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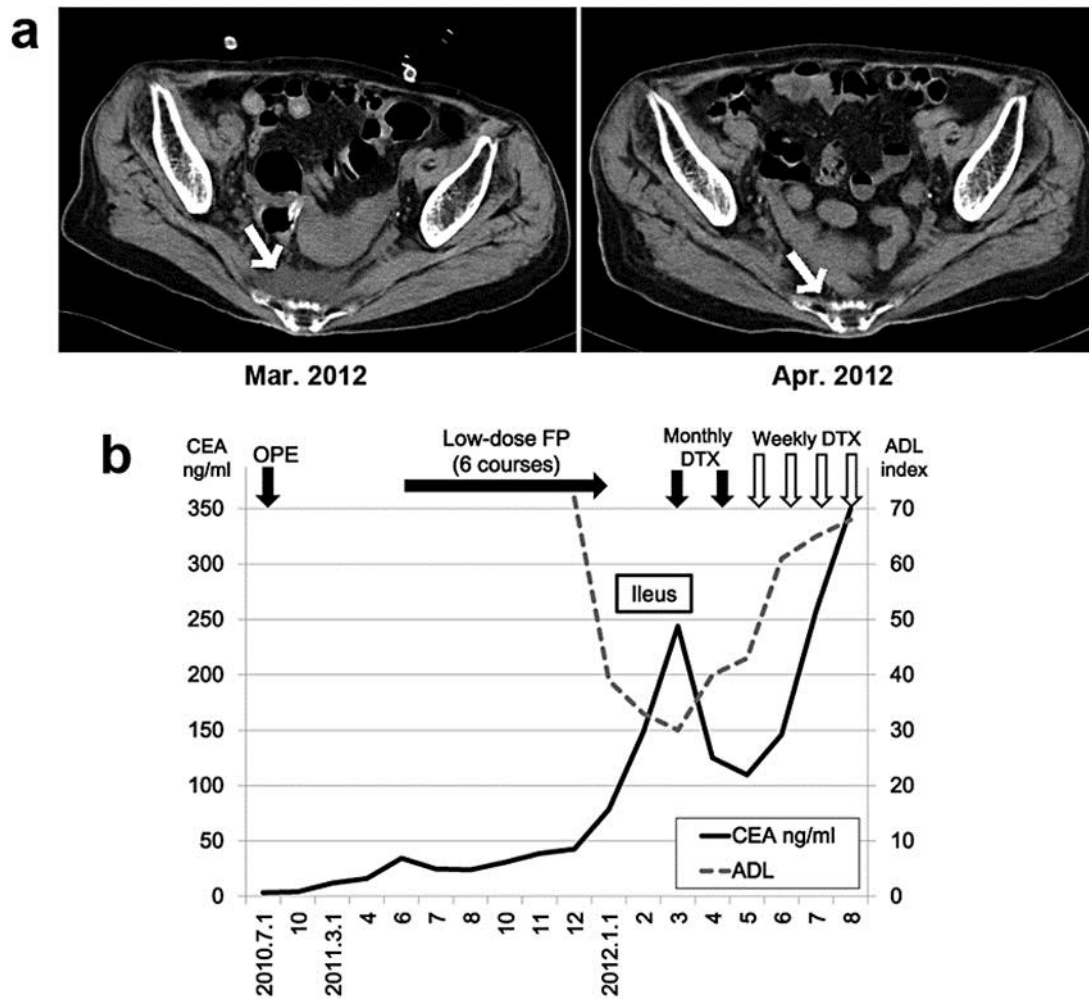
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**Fig. 1.** **a** Clinical findings before surgery. Erythematous lesion on the patient's genital and hemorrhagic tumor on the right labia major. **b** Local recurrence around the postoperative scar (black arrowhead). **c** Skin metastasis before docetaxel therapy (white arrowhead). **d** CT revealed multiple lung metastases.

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**Fig. 2.** Response to docetaxel therapy. **a** The patient demonstrated partial response, since the volume of the metastases was reduced by 50% on CT (white arrows). **b** Changes in serum CEA levels and ADL index. The serum CEA level and ADL index improved after 2 courses of MDT. However, the serum CEA level immediately increased after changing to a weekly regimen. OPE = Operation; DTX = docetaxel.