



## Case Report

## Paclitaxel-related dermatological problems: Not only alopecia occurs

Ming-Hsuan Su <sup>a, b</sup>, Guan-Yeu Chen <sup>a, b</sup>, Jun-Hung Lin <sup>a, b</sup>, Howard Hao Lee <sup>a, b</sup>,  
Kai-Cheng Chung <sup>a, b</sup>, Peng-Hui Wang <sup>a, b, c, d, e, \*</sup>

<sup>a</sup> Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan

<sup>b</sup> Department of Obstetrics and Gynecology, National Yang-Ming University, Taipei, Taiwan

<sup>c</sup> Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan

<sup>d</sup> Department of Medical Research, China Medical University Hospital, Taichung, Taiwan

<sup>e</sup> Female Cancer Foundation, Taipei, Taiwan

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## ABSTRACT

**Objective:** Dermatological problems after chemotherapy are often neglected with gynecological oncologists. Since paclitaxel is one of most popular agents for gynecology organ-related cancers, dermatologic change after paclitaxel treatment is seldom reported before.

**Case report:** Two patients with gynecological organ malignancy who underwent the postoperative dose-dense weekly schedule of paclitaxel 80 mg/m<sup>2</sup> plus carboplatin (area of curve 5) every three weeks had repeat dermatological problems (skull, facial and upper trunk areas) during the treatment. They included dermatitis, eczema, and folliculitis. Topical use of anti-fungal cream and oral anti-histamine agents stopped the disease progression and all had completed their chemotherapy without interruption.

**Conclusion:** Clinicians should be aware of paclitaxel-induced skin toxicities, especially on the skull, face and upper trunk areas to minimize the occurrence of severe morbidity and to provide the better quality of life when cure is our primary priority in the management of gynecological organs-related malignancies.

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## Introduction

Paclitaxel is one of the most popular agents for the advanced epithelial ovarian cancer (EOC), fallopian tube cancer (FTC) and primary peritoneal serous carcinomas (PPSC), not only given as neoadjuvant therapy, but also used as adjuvant therapy after surgery [1–3]. The standard treatment protocol of paclitaxel (175 mg/m<sup>2</sup>) has been prescribed every three weeks with the combination of carboplatin (dose equivalent to an area under the curve [AUC] 6 or cisplatin 75 mg/m<sup>2</sup>) [4–7]. The other dose-dense therapy (weekly schedule of paclitaxel 80 mg/m<sup>2</sup>) combining with carboplatin AUC 6 every 3 weeks from the Japanese Gynecologic Oncology Group study number 3016 (JGOG 3016) has been frequently used in recent years [6–8]. The well-known adverse events of paclitaxel include major hypersensitivity reaction (anaphylaxis), disturbances in

cardiac rhythm, alopecia, peripheral neuropathy, gastrointestinal and hematological toxicities [9,10], and the development of these adverse events are dependent on regimen (weekly versus three-weekly), dose, duration, previously received treatment, or combination with other cytotoxic agents [11]. Besides the above-mentioned adverse events, dermatological adverse events happen frequently during chemotherapy, although they are often missed. In our previous publication [12], we reported the nail changes after paclitaxel treatment. In addition, alopecia is a well-known adverse event of taxane-based treatment. However, other taxane-related skin changes are often missed or neglected. In the current article, we report the dermatological problems during taxane-based chemotherapy treatment in two patients.

## Case presentation

## Case 1

A 49-year-old woman with endometriosis-associated with endometrioid type EOC, the supposed International Federation of Gynecology and Obstetrics (FIGO) stage IA because she only

\* Corresponding author. Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, National Yang-Ming University, 201 Section 2, Shih-Pai Road, Taipei 11217, Taiwan. Fax: +886 255702788.

E-mail addresses: [phwang@vghtpe.gov.tw](mailto:phwang@vghtpe.gov.tw), [pongpongwang@gmail.com](mailto:pongpongwang@gmail.com) (P.-H. Wang).

received laparoscopy surgery for right salpingo-oophorectomy for the above-mentioned disease, was treated with a modified JGOG 3016 regimen of carboplatin (AUC 5) every 3 weeks plus paclitaxel 80 mg/m<sup>2</sup> weekly. During the first cycle day 8, the patient presented with pustular, exfoliating over the entire skull area, posterior neck and upper back. Physical examination revealed a diffuse erythematous rash with pustules and scaling, involving her upper trunk and neck, and skull area (Figs. 1 and 2). However, laboratory studies were all within the normal limits. The prescription included anti-fungal cream and anti-histamine agents. Although the dermatological problems persisted during chemotherapy, which did not interfere her from the treatment, and symptoms were subsided one month later when chemotherapy was completed.

### Case 2

A 46-year-old woman with a locally advanced squamous cell carcinoma of the cervix, FIGO stage IIB, had been treated with neoadjuvant chemotherapy with a dose-dense chemotherapy, containing with cisplatin 20 mg/m<sup>2</sup> plus paclitaxel 80 mg/m<sup>2</sup> weekly. At the 3 weeks of treatment, the patient had an occipital erythema with scarring alopecia and sparse follicular pustules at the edge of the lesion. Some red skin, small red bumps, inflamed skin, even pus-like sores were also noted at the forehead, cheeks, chin, and upper chest. The patient received the combination of the oral anti-histamine drug and topical use of anti-fungal cream with well-controlled disease status. The chemotherapy could be continued without interruption.

### Discussion

Since taxanes have proved to be effective in the management of various kinds of gynecological organ-related cancers, including EOC, FTC, PPSC, endometrial cancer, and cervical cancer [13–16]. Therefore, many of paclitaxel-related adverse events have been



Fig. 1. Multiple irregular erythematous patches on the occipital area of the scalp.

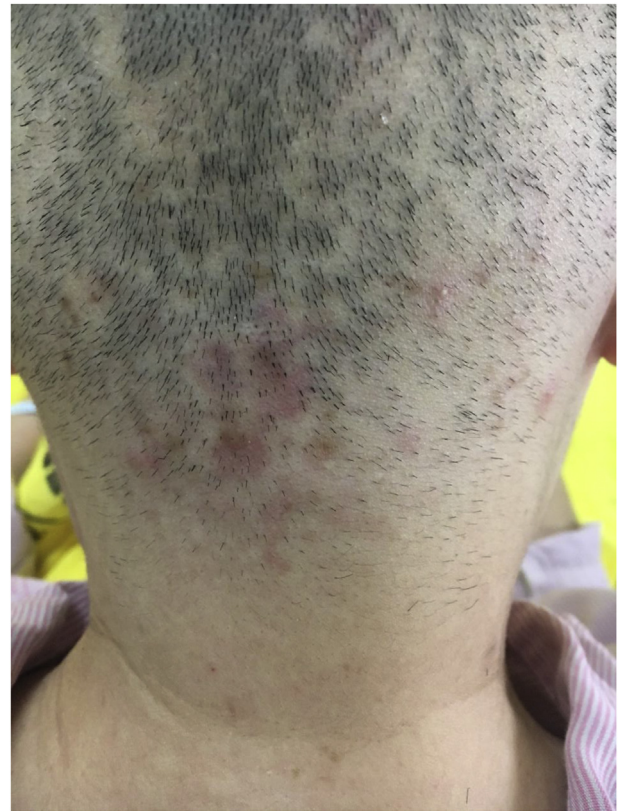


Fig. 2. The confluent lesions are shown on the occipital area of the scalp and some small acne vagaries-like lesions scattered distribution are also noted.

well known. However, some minor adverse events are often neglected in the clinical practice. Dermatological problems are the best example. In our previous report, we have reported one of commonly detected dermatological problems-nail changes [12], which occurred in near to half of patients [17]. In this report, another type of dermatological problems-skin change has been discussed.

Dermatological problems, including allergic reaction have been reported with the use of paclitaxel [10,18]. It has been proposed that cremophor EL, a nonionic surfactant derived from castor oil that is used as a solubilizer for the insoluble paclitaxel, might be a cause to induce type I hypersensitivity reaction, although taxane-directed cytotoxic effect, such as the cytotoxic action to chemotherapy of keratinocytes, is also possible [10,18,19]. The reactions usually occur after the first dose of treatment and may be dose dependent, with relief of discomfort during relapses when the dosage of drugs was decreased and the administration of drugs was ceased. One case report showed that a 35-year-old woman with breast cancer treated by weekly paclitaxel was complicated with severe skin toxicity, including painful swelling of hands, feet and a bilateral symmetrical rash over the extensor surfaces of legs up to the knees, and these skin lesions included ill defined macules, papules, and pustules with surrounding erythema [20].

Skin changes secondary to taxanes varied greatly, including diffuse or facial erythema, acute generalized exanthematous pustulosis (similar to our presented two cases), dysesthesia, lupus erythematosus, photosensitivity, scleroderma-like skin changes, and hand-foot syndrome [10,18–21]. Taxane-induced rash is often found on warm sites prone to trauma, such as the folds, contact areas, or under dressing or pads [22,23]. In the current report of two cases, an inflammatory folliculitis occurs predominantly on the

upper part of the body, particularly the scalp and shoulders. In fact, the similar finding is also reported before [24]. The typical feature of an inflammatory folliculitis is negative if microbial cultures are performed [22].

To prevent the above-mentioned dermatological adverse events, the following strategies, including scalp, hands, and feet cooling down methods could be done to reduce metabolic and biochemical activities in the hair follicle and to induce vasoconstriction, which can decrease blood flow and cellular uptake of taxanes [10]. After discontinuation of taxane-based chemotherapy, the dermatological problems often recover completely and spontaneously.

The current report has a limitation, because we did not provide the incidence of dermatological adverse events in patients who underwent dose-dense or non-dose-dense paclitaxel regimen. However, based on the literature review, dermatological adverse events are frequent and most treated patients are affected, but the real incidence is hard to be estimated and tends to vary greatly (6%–81%) [21–26]. In addition, we did not examine the histopathological change by lesion biopsy, since the dermatological adverse events are classified as mild to moderate in severity in our presented cases. We believed that dermatological adverse events are commonly under-reported and not systematically ascertained, because they are generally mild to moderate (CTCAE Grade 1/2) in severity and self-limiting, as like our cases and based on literature review [21,23–25]. The more severe form (CTCAE Grade 3 or higher) is mainly induced by a toxic and non-immuno-allergic mechanism [26]. We still conclude that generalized skin changes, exanthematous pustulosis, diffuse erythema and dysesthesia, folliculitis and eczema-like or scleroderma-like changes are secondary to paclitaxel treatment, although paclitaxel perhaps portrays a better dermatological adverse event profile than other type of taxanes, such as docetaxel [26]. Finally, we did not exclude the possibility of the dermatology paraneoplastic syndromes associated with gynecological cancers, which include dermatomyositis, palmar fasciitis and polyarthritides syndrome, digital ischemia, malignant acanthosis nigricans, tripe palms, Leser-Trélat sign, hypertrichosis lanuginosa acquisita, paraneoplastic pemphigus [27]. However, clinical course of our presented cases are unlike.

Clinicians should be aware of the above. The substantial psychological sequelae and morbidity might be severely affected by this adverse event, contributing to worse quality of life in cancer patients and for minimizing dose modifications of their antineoplastic regimen. Adequate information and minimization of occurrence is important not only for the success of the cancer treatment but also for the maintenance of quality of life.

## Conflict of interests

The authors declare that they have no competing interests.

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