

Case Report

Reduction in Tumor Lesions and Exacerbation of Psoriatic Rash after Septic Shock in a Patient with Extramammary Paget's Disease

Takehisa Nakanishi Makoto Kondo Yasuo Nakai Koji Habe
Keiichi Yamanaka

Department of Dermatology, Mie University, Graduate School of Medicine, Tsu, Japan

Keywords

Tumor necrosis factor-alpha · Psoriasis vulgaris · Extramammary Paget's disease · Group G streptococcal infection · Cytokine storm

Abstract

We present a case of extramammary Paget's disease with bilateral inguinal lymph node metastasis treated by monthly docetaxel chemotherapy. He has also well-controlled psoriasis vulgaris for 20 years. One day after completing monthly chemotherapy, cellulitis by Group G *Streptococcus* occurred on both legs, resulting in septic shock and disseminated intravascular coagulation. During the infection, the tumor nodule volume and the exudate from the tumor decreased, and tumor markers carcinoembryonic antigen and cancer antigen 19-9 showed low values. Simultaneously, the psoriatic eruption reoccurred. We proposed that cytokine storm including tumor necrosis factor-alpha (TNF- α) during sepsis might have suppressed tumor lesions, and also TNF- α -dependent psoriatic rash appeared temporarily on his body.

© 2021 The Author(s).
Published by S. Karger AG, Basel

Introduction

Extramammary Paget's disease (EMPD) is an intractable skin cancer. Chemotherapy is necessary for the metastasis cases, and a serious infectious disease sometimes occurs due to low host immunity. Tumor immunity is important to suppress the growth and

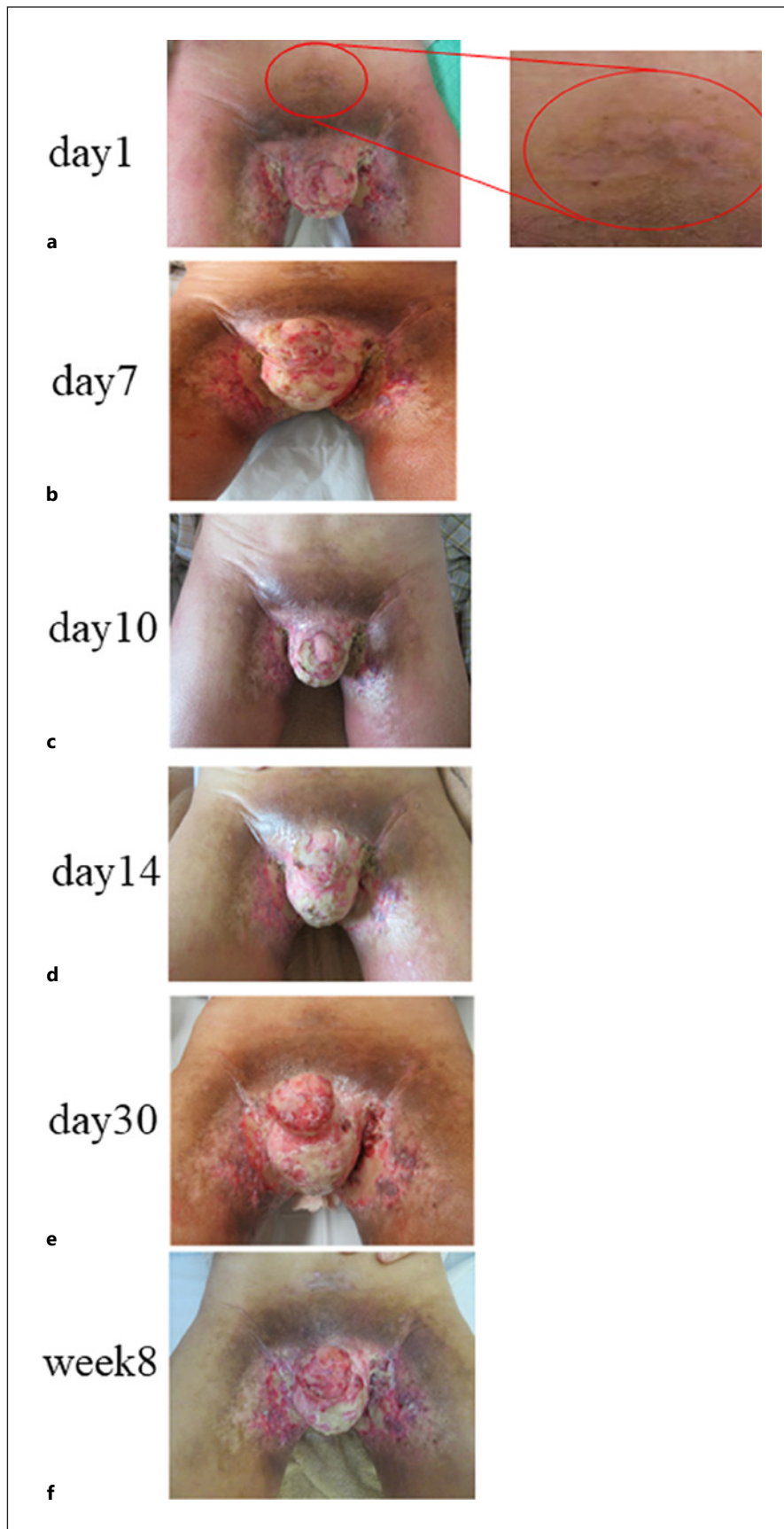
progress of the tumor. Especially tumor necrosis factor-alpha (TNF- α) is an important cytokine for tumor control. On the other hand, psoriasis is an inflammatory cytokine-mediated skin disease, and interleukin -17 plays a critical role, especially at the site of skin lesion, and TNF- α also contributes to the increase and maintenance of dendritic cells such as TNF- α iNOS-producing dendritic cells and contributes to the establishment and exacerbation of psoriatic rash. TNF- α inhibitor is effective as a therapeutic drug for psoriasis. We report the phenomenon by which the diminish in tumor size and tumor markers, and relapse of psoriatic rash occurred during septic shock in a patient with advanced stage EMPD.

Case Presentation

A man in his 70s was diagnosed with psoriasis vulgaris 20 years ago, which was well-controlled by the use of topical ointment (combination of vitamin D3 and steroid). The patient had become aware of a genital rash 10 years ago. Four years ago, he was referred to our department for a genital tumor. We made a diagnosis of EMPD with bilateral inguinal lymph node metastasis: T1N2M0, stage IV by skin biopsy and computed tomography scan. He was initiated on radiation therapy and monthly docetaxel chemotherapy for EMPD. For 3 years, he was stable with no distant metastasis through the penis, scrotum, both inguinal areas, or anus; however, the ulcers and nodules had not been cured. No significant adverse effects were observed during the course of treatment.

One day after completing the 37th course of monthly docetaxel, he experienced pain and warmth on both lower limbs. He was transferred to our department by ambulance the next morning. He had low blood pressure (80/48 mm Hg) and high temperature (39.4°C), and both lower limbs were erythematous and warm to touch (Fig. 1a). Group G thymosin-type lysin bacteria was detected in blood culture, and Group G *Streptococcus* was identified. He required emergency admission for septic shock from cellulitis of the lower limbs. Blood tests showed elevated inflammatory markers (C-reactive protein, 22.0 mg/dL; white blood cells, 22,000 cells/mm³) and disseminated intravascular coagulation (DIC) (Japanese Association for Acute Medicine acute-phase DIC diagnosis score, 4). Seven days after the infection, the psoriatic rash recurred, but the tumor nodule volume and the exudate from the tumor decreased (Fig. 1b). Ten days after the infection, the exudate from the tumor lesion decreased further, and the erosion area also shrank (Fig. 1c). Fourteen days after the infection, the tumor area further improved (Fig. 1d). Thirty days after the infection, the psoriatic rash in the lower abdomen had resolved, and the nodules with necrosis in the left inguinal region grew gradually (Fig. 1e). He recovered through therapy for DIC, although he had severe hemophagocytic syndrome due to Group G *Streptococcus*. We postponed the monthly docetaxel to 8 weeks after the last therapy for EMPD until his infectious condition improved (Fig. 1f). The tumor markers carcinoembryonic antigen and cancer antigen 19-9 showed low values during the infection (Fig. 2).

Fig. 1. **a** At the time of infection, the psoriatic rash with a red circle became apparent. **b** Seven days after the infection, the nodule size of the tumor had reduced. **c** Ten days after the infection, the exudate from the tumor area had decreased. **d** Fourteen days after the infection, there was further improvement of the tumor area. **e** Thirty days after the infection, the psoriatic rash had disappeared. **f** Eight weeks after the infection, the tumor lesion after restarting therapy for EMPD is shown. EMPD, extramammary Paget's disease.
(For figure see next page.)



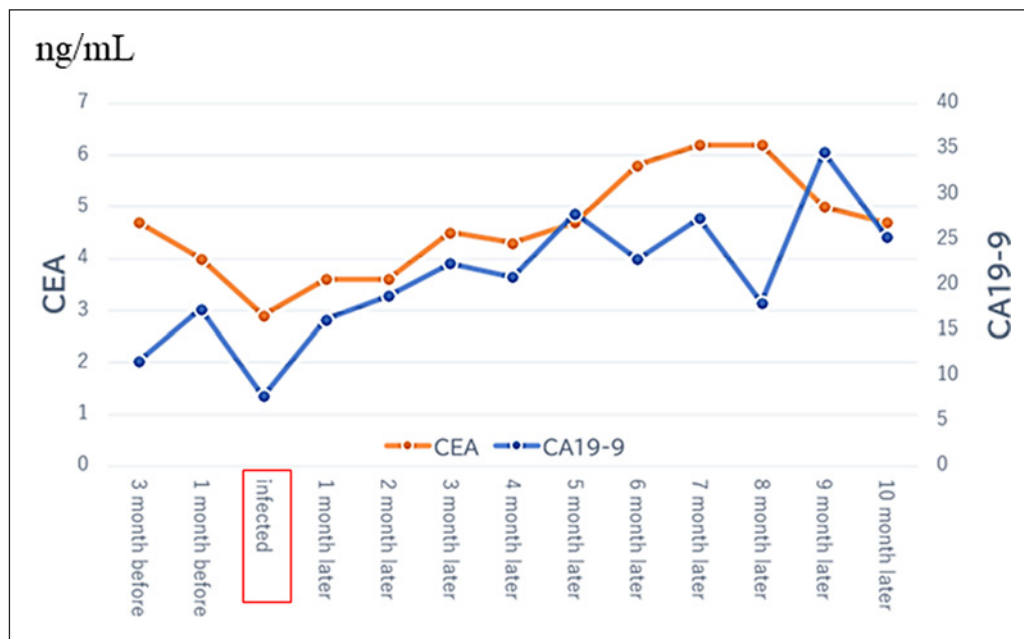


Fig. 2. Changes in tumor makers. CEA and CA19-9 levels decreased temporarily during the infection. After treatment of the infection, the markers increased gradually. CEA, carcinoembryonic antigen; CA19-9, cancer antigen 19-9.

Discussion

We focused on the transition of tumor lesions, psoriatic rash, and tumor markers before and after septic shock and the connection of TNF- α [1] in the current patient. Carcinoembryonic antigen and cancer antigen 19-9 levels were lower than previous data at the time of severe infection, and the tumor lesions also simultaneously improved. A psoriatic rash recurred at the onset of infection. Although the concentration of TNF- α was not measured either in the blood or skin lesions, increased TNF- α during the interaction between bacteria and the immune system might cause local and systemic antitumor inflammatory reactions [2, 3]. We propose that TNF- α released in large quantities during cytokine storm due to sepsis would have suppressed the tumor lesions and improved them temporarily, following which the TNF- α -dependent psoriatic rash appeared on his body.

Statement of Ethics

The research was conducted in accordance with the Declaration of Helsinki. The patients provided written informed consent to publish their case studies, including publication of images. The results of the blood sampling and imaging studies and the treatments presented in this case were necessary for the patient's care. Therefore, this article is exempted from the approval of the Ethics Committee.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

None of the authors received any financial support for the present study.

Author Contributions

T.N., M.K., Y.N., K.H., and K.Y. treated the patient. T.N., M.K., and K.Y. wrote the manuscript.

Data Availability Statement

Data are available on request to the authors.

References

- 1 Kuno H, Kotani T, Takeuchi T, Wakura D, Wakura R, Yu A, et al. Psoriasis like eruption induced by adalimumab in a patient with rheumatoid arthritis: a case report and review of literature. *Jan J Clin Immunol*. 2012 Dec; 35(6):520–5.
- 2 Perez-Ruiz E, Minute L, Otano I, Alvarez M, Ochoa MC, Belsue V, et al. Prophylactic TNF blockade uncouples efficacy and toxicity in dual CTLA-4 and PD-1 immunotherapy. *Nature*. 2019 May;569(7756):428–32.
- 3 Nyboe Andersen N, Pasternak B, Basit S, Andersson M, Svanström H, Caspersen S, et al. Association between tumor necrosis factor- α antagonists and risk of cancer in patients with inflammatory bowel disease. *JAMA*. 2014 Jun;311(23):2406–13.