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A Case Report of Recurrent Metastatic Sebaceous Carcinoma Which Showed Favorable Response Tt Non-Fluorouracil Based Chemotherapy

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 59
Final Diagnosis: Metastatic sebaceous carcinoma
Symptoms: Palpable mass
Medication: —
Clinical Procedure: Chemotherapy
Specialty: Oncology

Objective: Unusual setting of medical care

Background: Sebaceous carcinoma is a rare malignant tumor of the skin adnexa. While surgical resection is a treatment of choice in localized disease, frequent recurrence and distant metastasis make treatment difficult. Moreover, due to its rarity, optimal systemic treatment has not been determined.

Case Report: A 59-year-old female presented with disseminated subcutaneous nodules. Past history indicated she received repeated surgery, radiation therapy, and fluorouracil-based systemic chemotherapy for recurrent sebaceous carcinoma. Following a subcutaneous nodule biopsy, histopathologic examination confirmed recurrent metastasis of sebaceous carcinoma. Because there was no established regimen as salvage chemotherapy, we decided to administer paclitaxel plus Adriamycin as a combination regimen after a thorough search of previous reports on PubMed. After the patient received 6 cycles of chemotherapy, all masses dramatically regressed. Unfortunately, several new lesions appeared 3 months after cessation of chemotherapy. Therefore, she was treated with anti-HGF antibody through a clinical trial. After that, she received nivolumab. But treatment with all the new agents did not show any response. Furthermore, her disease progressed rapidly. We re-challenged with the paclitaxel and Adriamycin regimen, 2 cycles of chemotherapy, and the follow-up positron emission tomography - computed tomography revealed marked decrement of multiple metastatic nodules.

Conclusions: Although several clinical reports have shown the effectiveness of fluorouracil, especially 5-fluorouracil-based chemotherapy, there has been a paucity of reports on other chemotherapeutic agents. We report a case of metastatic sebaceous carcinoma which showed favorable response to non-fluorouracil-based chemotherapy.

MeSH Keywords: Adenocarcinoma, Sebaceous • Antineoplastic Agents • Doxorubicin • Paclitaxel

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Background

Sebaceous carcinoma is a rare malignant neoplasm which originates from the sebaceous gland. Although sebaceous carcinoma can occur in any sebaceous gland containing skin-covered areas, such as eyelid, faces, scalp, trunk, external genitalia, and neck areas, the peri-ocular area has the highest incidence. As for treatment, surgical resection following radiation therapy achieves favorable treatment outcome in localized disease. However, frequent recurrence and metastatic preferences make treatment difficult and necessitate effective systemic treatment during the entire treatment course [1].

However, there is a lack of information regarding the optimal systemic chemotherapy for metastatic sebaceous carcinoma, although there have been many clinical studies surrounding surgical management of localized disease [1]. Herein, we report a case of metastatic sebaceous carcinoma which showed excellent response to various systemic chemotherapy regimens including a non-fluorouracil-based regimen. Furthermore, we discuss effective systemic treatment of sebaceous carcinoma based on previously published clinical studies and our case.

Case Report

A 59-year-old female presented to our department with multiple palpable subcutaneous nodules. A review of her medical history found that she received right eyelid mass excision in 1998 at Yeouido St. Mary's Hospital. Her disease recurred at the right parotid gland for the first time in 2001. Therefore, she received total parotidectomy with neck node dissection followed by radiation therapy (55.8 Gy). In 2012, she presented with multiple subcutaneous nodules. Excisional biopsy of one of the nodules confirmed recurrence of sebaceous carcinoma. Because of extensive distribution and relatively rapid progression, she received 5-fluorouracil (5-FU) (750 mg/m^2 on day 1 to day 5) and cisplatin (75 mg/m^2 on day 1) combination chemotherapy (every 3 weeks) from June 2012 to December 2012. After 6 cycles of systemic chemotherapy, all masses regressed [3]. But 6 months later, remnant masses enlarged. At this time, capecitabine (1250 mg/m^2 bid for 2 weeks every 3 weeks) plus carboplatin (AUC 5) (XP regimen) was administered (June 2013 to October 2013). The response was better than observed with the previous regimen (Figure 1A, 1B). Twelve months after 6 cycles of XP chemotherapy, only a few nodules progressed.

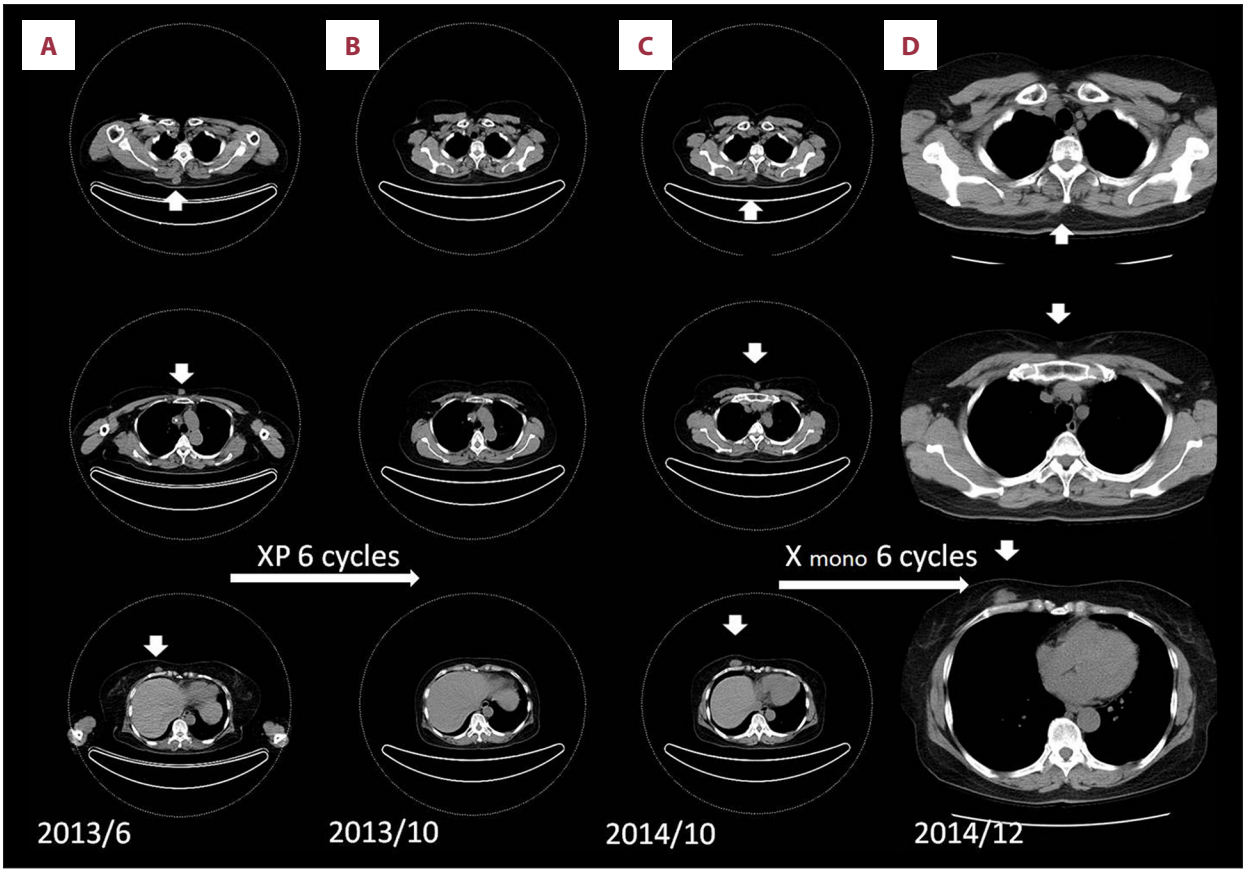

Figure 1. (**A, B**) Chest computed tomography (CT) scans, which followed after 6 cycles of XP (capecitabine and cisplatin) chemotherapy showed disappearance of multiple subcutaneous metastatic nodules (white arrows). (**C, D**) Chest CT following capecitabine monotherapy revealed no interval change of regrown metastatic nodules.

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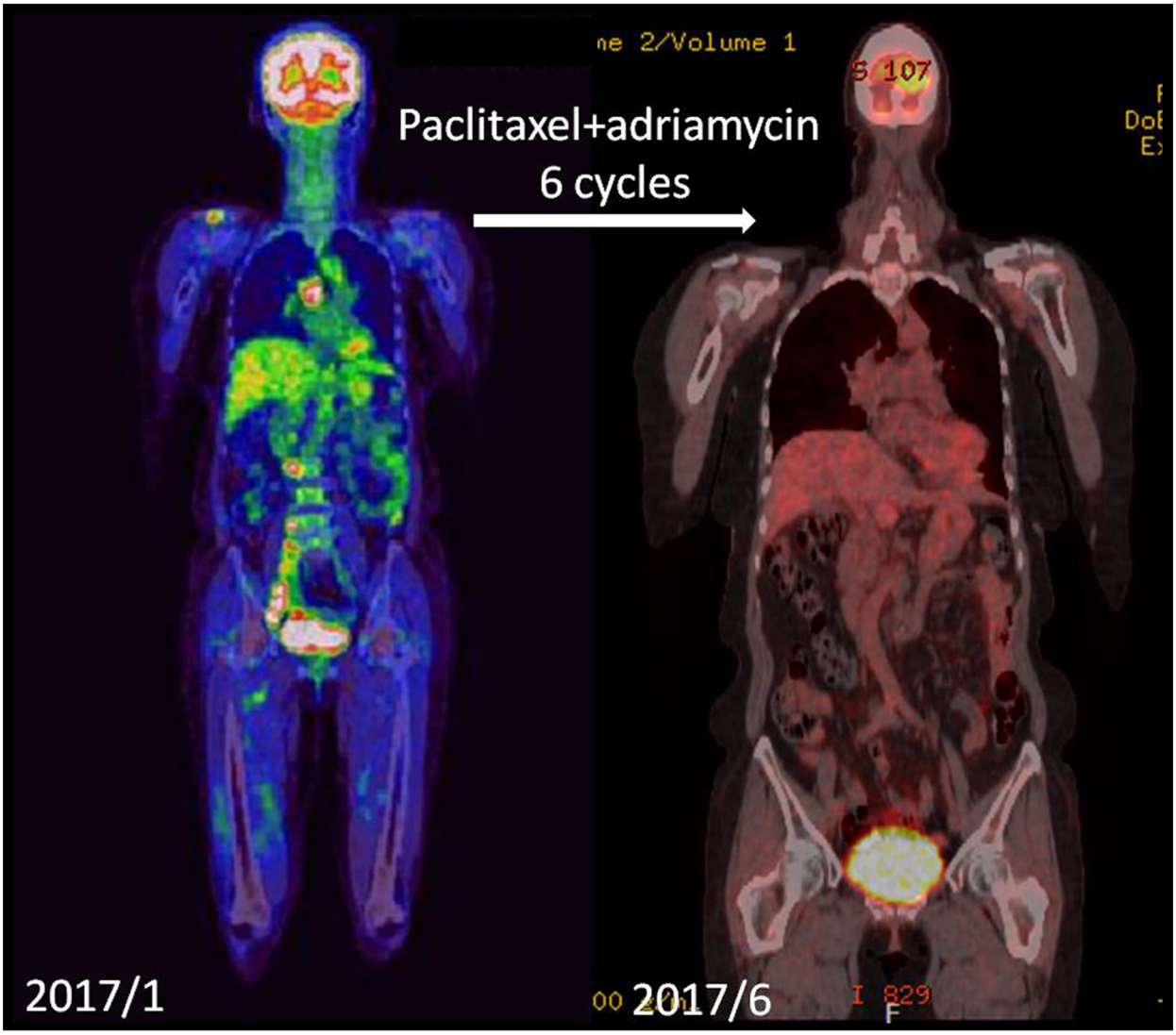

Figure 2. Positron emission tomography – computed tomography scan which followed after 6 cycles of Adriamycin and paclitaxel combination regimen showed disappearance of all metastatic lymph nodes in mediastinal and para-aortic regions.

At this time, palliative radiation therapy was performed to only the predominant metastasis. After that, capecitabine monotherapy was administered from October 2014 to February 2015. But the benefit of chemotherapy was marginal (Figure 1C, 1D). Because the patient wanted to stop medication due to hand foot syndrome, chemotherapy was interrupted. On January 2016, her disease again progressed. Palliative radiation therapy was performed to the newly developed lesions because they were apart from the internal major organs. Although capecitabine plus carboplatin was re-administered after radiation therapy, her disease did not respond this time. Moreover, the patient could no longer tolerate the side effects of capecitabine. In addition, the metastasis extended into the intra-abdominal lymph nodes and mediastinal lymph nodes.

Because there was no established regimen as salvage chemotherapy, we searched the PubMed literature, and after reviewing clinical reports, we decided to administer Adriamycin (60 mg/m^2) and paclitaxel (175 mg/m^2) as combination chemotherapy (every 3 weeks). After 6 cycles of chemotherapy (February 2017 to June 2017), all masses dramatically regressed as seen on positron emission tomography – computed tomography (PET-CT) (Figure 2). Unfortunately, her disease again progressed after a 3-month chemotherapy holiday. We recommended the patient participate in a clinical trial. Therein, she received anti-HGF antibody for 3 months. However, her disease did not show response. Although nivolumab was tried after disease progression, she complained of rapid growing subcutaneous nodules.

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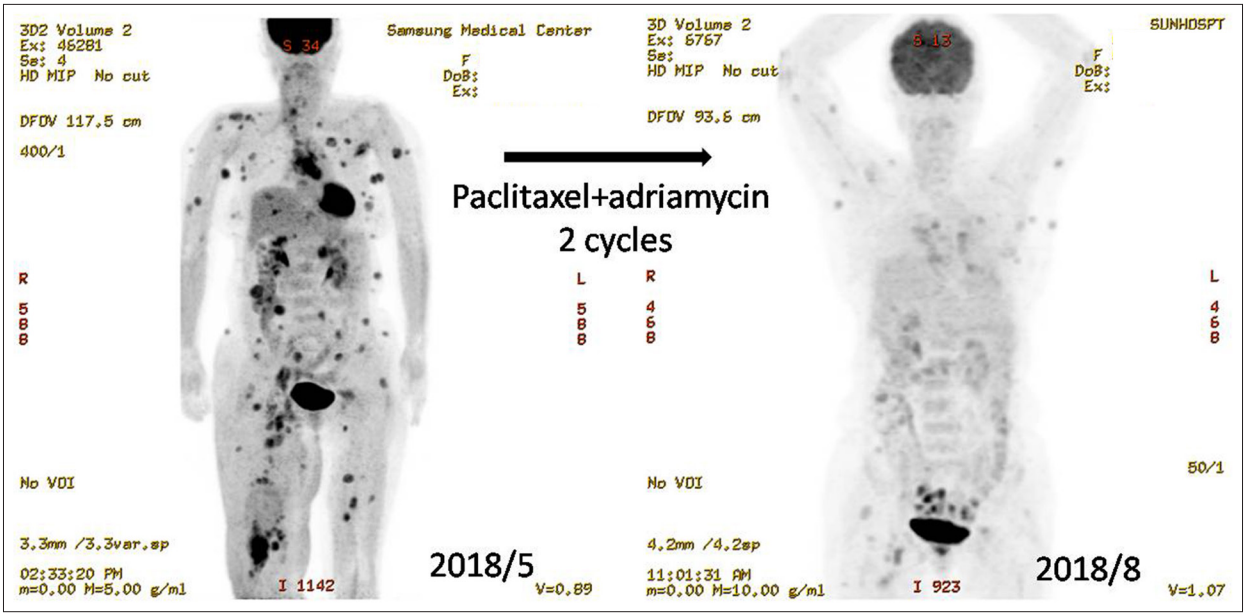

Figure 3. Positron emission tomography – computed tomography scan which followed after 2 cycles of Adriamycin and paclitaxel re-challenge showed marked regression of all metastatic nodules.

Finally, we decided to re-challenge with paclitaxel-Adriamycin because the cumulative dose of Adriamycin had not yet reach toxic range. After 1 cycle of chemotherapy, most subcutaneous nodules began to shrink. Follow-up PET-CT after 2 cycles of chemotherapy showed the size and FDG uptake intensity of metastatic nodules dramatically decreased (Figure 3). The patient is on her third cycle of the same regimen with good response.

Discussion

Sebaceous carcinoma is known as a potentially aggressive cutaneous malignancy because of frequent loco-regional spread and recurrence. Although many previous clinical studies demonstrated surgical excision with sufficient margins following radiation therapy can effectively control localized disease after curative resection, regional (including nodal) or distant metastasis occurs in 8% to 28% of patients at some point in the disease course [2]. Without a doubt, multimodal treatment is required for patients with recurrent or metastatic disease. However, the optimal chemotherapy of metastatic sebaceous carcinoma has not been studied and even the role of chemotherapy has not been determined. Furthermore, in the past, this rare cancer was considered to be not sensitive to chemotherapy. But recently, the role of chemotherapy has been evolving in the treatment of sebaceous carcinoma. In the beginning, a few case reports showed favorable outcome of palliative systemic chemotherapy in metastatic or recurrent sebaceous carcinoma. Encouraged by these result, some studies suggested the possible role of systemic chemotherapy as neoadjuvant or adjuvant chemotherapy and illustrated positive result based on a few case reports [3,4]. However, most previously published reports were confined to only a few chemotherapeutic agents, especially 5-FU and platinum agents because these agents have been preferred in non-melanoma skin cancer and head and neck cancers [3–9]. However, when this regimen confronts resistance, patients ultimately require other systemic treatment option in the late of disease course.

Although our case report describes just one case, it provides several important clinical tips regarding chemotherapy for sebaceous carcinoma.

First, we could confirm favorable response of capecitabine even after progression to 5-FU containing chemotherapy. To the best of our knowledge, only a few case reports have shown good responses to capecitabine or other fluorouracil agents (S-1) except 5-FU in sebaceous carcinoma [9–11]. Furthermore, in previous studies, capecitabine has been used in 5-FU naïve patients [10] and patients maintaining response to 5-FU [9]. Our case showed that capecitabine could be effective even after disease progression after 5-FU chemotherapy. Moreover, capecitabine is expected to be clinically more beneficial because it is usually more tolerable than 5-FU and its administration route and daily schedule provides more convenience and makes dose adjustment easy.

Second, combination regimen with platinum agent was more effective than monotherapy. Sebaceous carcinoma is frequently associated with germ-line defects in the DNA mismatch repair (MMR) mechanism which leads to increased predisposition to many cancers. This condition is called the Muir-Torre syndrome.

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As for therapeutic aspect, MMR deficiency has been known to be associated with resistance to some chemotherapeutic agents including platinum compounds and fluoropyrimidine [12]. Chemotherapeutic agents which rely on DNA damage to kill cancer cells are known to be less effective for tumor cells with poor MMR function [12,13]. But when reviewing clinical outcomes of previously published case reports, patients treated with platinum containing combination regimens achieved more favorable outcome than patients treated with monotherapy or platinum non-containing regimens, although this is not a direct comparison [5,14]. Our case report also demonstrated that adding platinum agent to capecitabine monotherapy was more effective than capecitabine monotherapy.

Last, several agents other than fluorouracil and platinum had favorable efficacy in our case. As third-line chemotherapy, we choose paclitaxel and Adriamycin as a combination regimen. Although Adriamycin and paclitaxel have been reported to be effective respectively in metastatic sebaceous carcinoma, there has been no report which showed the efficacy of a combination regimen containing Adriamycin and paclitaxel as systemic treatment of sebaceous carcinoma [5,15–17].

Recently, more drugs, including target agents, immunologic agents, and biologic agents, are being introduced and tried in the treatment of metastatic sebaceous carcinoma. Some reports have investigated the genetic profile of sebaceous carcinoma and suggested possible benefit of mammalian target of rapamycin (mTOR) inhibitor [18–20]. But there is no clinical evidence yet whether this approach can be applicable to real practice.

The authors suggest that our case report can be a good guide for clinicians who select chemotherapeutic agents in the treatment of sebaceous carcinoma.

Conclusions

Our case report demonstrated favorable clinical response of a capecitabine containing regimen and paclitaxel plus Adriamycin combination regimen in the treatment of metastatic sebaceous carcinoma. Although most of the reports in the literature, including our study, have been small sized case reports or case series, these reports suggest that sebaceous carcinoma is relatively sensitive to various anti-cancer regimens. More systemic studies or summaries are warranted to optimize systemic chemotherapy of metastatic sebaceous carcinoma.

Conflict of Interest

None.

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