

Original Article

Psoriasis aggravation due to capecitabine in a colon cancer patient: a case report and literature review

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Abstract: Capecitabine, present significant clinical benefits in the treatment of colon cancer. However, capecitabine treatment also results in unwanted cutaneous toxic side effects, such as hand-foot syndrome (HFS). Psoriasis aggravation is rarely reported as a side effect; however, it causes cosmetic issues in patients, which may result in the early termination of capecitabine treatment. Therefore, although capecitabine-induced psoriasis aggravation is rare, it should be considered carefully by cancer physicians. Here, we review the case of a 50-year-old male colon cancer who suffered psoriasis aggravation after administration of capecitabine chemotherapy. To the best of our knowledge, this is the first reported case of capecitabine-induced psoriasis aggravation in a colon cancer patient.

Keywords: Psoriasis, capecitabine, fluorouracil, colon cancer

Introduction

Colorectal cancer (CRC) is the third most diagnosed cancer in the world and the fourth most common cause of cancer death. Since the 1960s, fluorouracil-based chemotherapy regimen has been the standard treatment for stage III CRC patients after surgery [1]. Commonly used first line chemotherapeutic agents in CRC are 5-fluorouracil (5-FU), oxaliplatin and irinotecan. The group of fluoropyrimid is widely used as an I.V. chemotherapy drug in clinical in recent 50 years, but the adverse reaction limited the use in some patients. The side effects include neutropenia, stomatitis, and other complication associated with chemotherapy by I.V. With the development of medical, a new drug, capecitabine attracts our attention. Capecitabine is an oral prodrug of 5-FU. In addition, together with oxaliplatin, capecitabine-based regimens have been found to be more effective and less costly than 5-FU-based regimens [1]. But the side effects still puzzle our clinical physicians. The main adverse reactions are hand-foot syndrome (HFS), nausea, diarrhea, leukopenia and so on. HFS is the common side effect with higher incidence [2], but few reports about the whole body skin toxicity. Capecitabine-associated psoriasis aggravation has been rarely reported and its incidence re-

mains unknown. In this study, a 50-year-old male patient with colon cancer that developed psoriasis aggravation following the administration of capecitabine is presented. To the best our knowledge, this is the first case of psoriasis aggravation associated with capecitabine treatment to be reported in the literature. As physicians administer capecitabine with increasing frequency, this untoward effect requires attention.

Case report

In January 2015, a 50-year-old male patient was referred to a local hospital due to sudden abdominal pain with defecation anal stop the exhaust for one day. Emergency abdominal stand flat piece showed low intestinal obstruction. Barium enema showed a colon mass with obstruction. The patient underwent a left hemicolectomy in our hospital on January 30, 2015. At surgery, lesions were located in colon splenic flexure with expansion of the proximal intestine. Pathology revealed a 6×5 cm moderately differentiated adenocarcinoma penetrating to the surface of the visceral peritoneum, with 4 out of 12 lymph nodes positive for carcinoma. He was classified as T4N2M0 according to the tumor size lymphadenopathy distant metastases (TNM) classification. After

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Figure 1. Psoriasis aggravation during the XELOX treatment.



Figure 2. Psoriasis symptoms regressed after stopping the XELOX treatment.

surgery, he began on XELOX (oxaliplatin, capecitabine) chemotherapy. After four cycles of chemotherapy, he appeared scattered plaque lesions in his limbs and trunk parts (**Figure 1**). Because of his past history of psoriasis, he was considered the recurrence of psoriasis. So we had to stop the treatment of XELOX. Taking into account of the good effect of XELOX in patients without disease progression, then we treated him with FOLFOX4 (oxaliplatin, fluorouracil, leucovorin) instead of XELOX. After changing the chemotherapy, his psoriasis symptoms regressed (**Figure 2**). Now, he remains under follow-up. We believe that capecitabine induced its psoriasis aggravation, which belong to the first report in the worldwide.

Discussion

Psoriasis is a common chronic recurring inflammatory skin disease [3, 4]. The common skin is

covered with layers of silver-white scaly erythema, papules, the lesion boundary is clear, the scales can be higher than normal skin, sometimes can be accompanied by a pruritus. This disease is most common in young adults, especially in the scalp, the joints and anterior sides of extremities, and can be affected to the whole body, the systemic damage is very rare in psoriasis vulgaris. Drug intake is a major cause trigger psoriasis or aggravate the pre-existing psoriasis, especially new drugs. Drug induced psoriasis is characterized as follows: plaque psoriasis, palm foot pustular sore and erythroderma, involving the nails and scalp. Some drugs administered for nondermatological diseases may affect the course of psoriasis in the following ways: exacerbation of preexisting psoriasis, induction of psoriatic lesions on apparently normal skin in patients with psoriasis, and precipitation of psoriasis in persons with or without family history of psoriasis. Analysis of the clinical and histological data on drug-exacerbated or drug-induced psoriasis, involving the latent period between the start of therapy and the occurrence of cutaneous eruptions, as well as the drug metabolism and its biochemical and immunological actions, may provide a clue to the etiology and pathogenesis of this disease [5].

Many classes of drugs were reported to trigger psoriasis, including β -Blockers [6, 7], lithium [8], tetracyclines [9], and synthetic antimalarial drugs [10]. Drug in affecting psoriasis in the following ways [11]: 1) exacerbation of pre-existing psoriasis; 2) induction of psoriatic lesions on their normal skin in patients with psoriasis; 3) precipitation of psoriasis in persons no matter if he has a family history of the condition. But due to the puzzle of the causes of psoriasis, the mechanism of drug in triggering and aggravating psoriasis is still unknown. Some scholars believe it involves both immunological and nonimmunological pathways [12].

The exact cause of psoriasis is not yet fully understood in the worldwide, but it had been proved that has a very close relationship with immune factors and genetic factors, an inducing factor can be complex. The therapy for psoriasis is just for symptomatic treatment, only by means of comprehensive treatment can make the skin lesion recover quickly, reduce the recurrence rate and prolong the interval of treatment. At present time, systemic therapy

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and physical therapy, and biological agents therapy has been growing rapidly in recent year.

Capecitabine is a widely used oral fluoropyrimidine prodrug that is both effective and well-tolerated in the treatment of a number of cancers, including breast cancer [13], gastrointestinal cancer [14], CRC [15] and other malignant tumors [16]. With high efficacy and good tolerability, capecitabine has certainly similar clinical efficacy to I.V. 5-FU [17-19]. Capecitabine can replace 5-FU/LV as the standard adjuvant and palliative treatment for patients with CRC. Capecitabine was designed to generate 5-FU preferentially in tumor tissue compared with healthy tissue [20]. Capecitabine is metabolized to 5-FU via a three-step enzymatic process. In the first step, capecitabine is hydrolysed by carboxylesterase in the liver to the intermediate 5'-deoxy-5-fluorouracil. In the second step, 5'-deoxy-5-fluorouracil is converted to 5-FU by thymidine phosphorylase (TP), which is present in tumor tissue, resulting in the release of 5-FU preferentially in tumor tissue. Compared with bolus 5-FU/LV, capecitabine is associated with more HFS but less stomatitis, alopecia, diarrhea, nausea and neutropenia [21-23]. The pathogenesis of capecitabine-related HFS is not fully understood, but may be due to COX inflammatory-type reaction, or related to enzymes involved in the metabolism of capecitabine, namely, TP and dihydropyrimidine dehydrogenase [24]. TP is markedly expressed in the skin. This result strongly suggests that elevated TP expression in the HFS target tissue may favour cell cytotoxicity through elevated local production of 5-FU during capecitabine treatment. Therefore, we hypothesized that elevated production of capecitabine expression in the skin, stimulate epidermal cell proliferation, and may lead to aggravation of psoriasis lesions.

There is no report about capecitabine-induced psoriasis aggravation in the world. But one case reported that a 50-year-old female patient consulted with subacute cutaneous lupus erythematosus (SCLE), occurring 4 months after the initiation of capecitabine for advanced colon cancer, but disappeared after discontinuation of capecitabine. Our patient also appeared psoriasis aggravation when recei-

ving the forth cycle of capecitabine chemotherapy, which illustrated that capecitabine-induced skin lesions aggravation was associated with the continued use of the drug.

Conclusion

In conclusion, we reported the first case of psoriasis aggravation associated with capecitabine treatment. We propose that psoriasis should be taken into account in patients being treated with capecitabine.

Disclosure of conflict of interest

None.

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