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Case Report

A case of myofasciitis due to 1,200 IU vitamin D treatment in a patient with lung adenocarcinoma

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Abstract: Vitamin D and its analogs are broadly used for lung cancer treatment due to their anti-tumor action and low toxicity. Although vitamin D is relatively safe, there have been some adverse reactions reported clinically when it is used for tumor treatment. The present study describes a 49-year-old patient who presented with lung adenocarcinoma and developed gluteal myofasciitis due to post-surgical treatment with 1,200 IU of vitamin D only. This is the first time that it has been reported that gluteal myofasciitis is related to the administration of vitamin D in a patient with lung cancer. The aim of this case report was to remind clinical staff that attention should be paid to adverse reactions of fasciitis caused by vitamin D.

Keywords: Vitamin D, lung adenocarcinoma, myofasciitis

Introduction

Lung cancer ranks first in terms of prevalence and mortality among all cancer types [1] and its incidence rate is still increasing in both urban and rural populations [2]. Clinically, surgical resection and chemotherapy are the most common therapeutic regimen for early-stage lung cancer. However, this therapeutic regimen typically results in a high rate of recurrence. Therefore, finding methods to prevent recurrence represents a priority for clinicians. Vitamin D is broadly used for preventing the relapse of lung cancer due to its anti-tumor effects, low toxicity and cost-effectiveness [3]. It was previously reported that [4] the anti-tumor action of vitamin D is associated with its role in promoting cell apoptosis, and inhibiting cell proliferation and angiogenesis. Moreover, the underlying mechanism was reported to be via inhibition of the production of prostaglandins, proteases and proinflammatory cytokines [5]. In addition, the anti-tumor action of vitamin D was also reported to be associated with its function in immune regulation. It has been reported that vitamin D deficiency can impair human immune function, resulting in autoimmunity in genetically predisposed people, and an increased risk of infections [6]. Although it generally has a low toxicity and is relatively safe, vitamin D can exhibit side effects in lung cancer therapy. The most common adverse reaction of vitamin D [7] is hypercalcemia, which is associated with the physiological function of the vitamin D receptor (VDR). Rarely, vitamin D may also cause adverse reactions such as nausea, headache, neutropenia or elevated alanine aminotransferase. However, no research at present has reported that vitamin D contributes to myofasciitis, also known as myofascial pain symptom, which is a common chronic musculoskeletal condition caused by chronic muscle strain and aseptic inflammation [8]. To the best of our knowledge, cases of myofasciitis induced by vitamin D in patients with lung cancer are rare. In the present case study, an example of myofasciitis induced by vitamin D in a patient with lung cancer admitted to our hospital is reported.

Case presentation

The patient was a 49-year-old male who had no previous history of tuberculosis, typhoid fever, food or drug allergies, hypertension, hyperlipid-

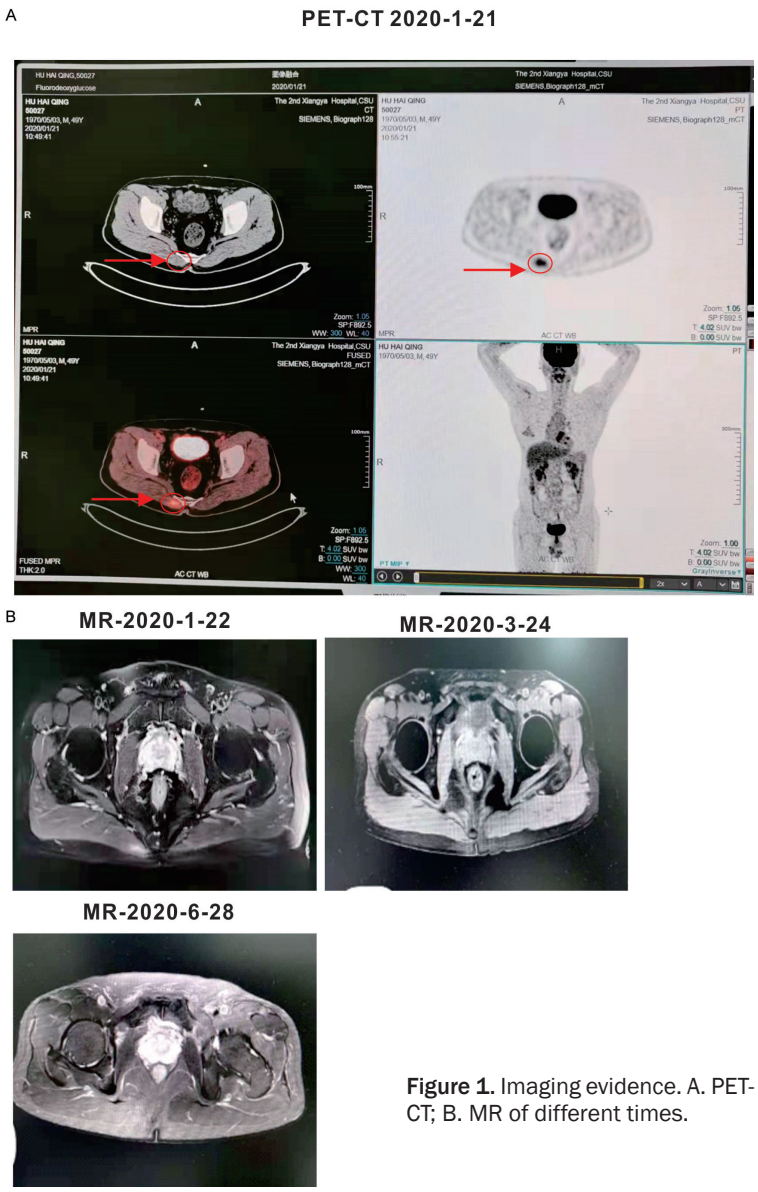

Figure 1. Imaging evidence. A. PET-CT; B. MR of different times.

emia or diabetes. The patient previously suffered from ureteral stones, but this was cured when he was 23 years old. On the 23rd October 2019, the patient underwent right lower lung resection and right upper lung wedge resection to remove tumor tissues with a size of 2 cm and 5 mm, respectively. The pathological examination results revealed that both tissues were stage IIa growing adherent lung adenocarcinoma samples. The patient recovered well and was discharged without incident on the 2nd of November 2019. After that, the patient was not treated further with chemotherapy or targeted drugs, but was administered vitamin D_3 (1,200 IU) daily, following the doctor's advice. On January 21st 2020, the patient was admitted to the hospital for examination after suffering from diffuse pain in the right gluteus. The bone PET-CT examination indicated that there was a low-density focus with a slight increase of flake sugar metabolism in the near midline of the right gluteus maximus, with a range of about 3.0×1.7 cm and a SUVmax value of 4.86. The other characteristics were normal (**Figure 1A**). On January 22nd 2020, an MR examination was performed on the patient and a patch-shaped region of long T2 signal was observed near the midline of the right gluteus maximus, with an unclear boundary and a smooth adjacent bone cortex (**Figure 1B**). This suggested that the patient may have been suffering from gluteal myofasciitis. Subsequently, the patient was given corresponding treatment and stopped taking vitamin D. On the 14th of March 2020, the patient was admitted to the hospital for re-examination and a further MR examination was performed. This revealed that the patch-shaped area of the long T2 signal was slightly smaller than before, and the signal was slightly decreased and exhibited enhancement on contrast-enhanced scanning. The edge of the signal was unclear and the adjacent bone cortex was smooth (**Figure 1B**). The remaining buttock soft tissue did not show any abnormal signal or abnormal enhancement focus. Considering that the patient has been taking vitamin D_3 since discharge, gluteal myofasciitis may represent a side effect of the drug. Thus, the patient stopped taking vitamin D_3 from May 25th 2020. On June 27th 2020, the patient visited the hospital for further consultation and MR results revealed that the patch-shaped long T2 signal was not found in the near midline of the right gluteus maximus muscle, the bone cortex was smooth, and the soft tissue of the remaining

Table 1. Studies regarding therapeutic effects of vitamin D in lung cancer

Citation	Compound	Evidence	Target	Summary
Wang W et al	Vitamin D; analogs [1,24(OH)2D3 and 1,25(OH)2D3]	Preclinical evidence	Cell lines (A549, H520 and NSCLC cell lines)	Suppression of proliferation
	Vitamin D	Preclinical evidence	Mice	Promotion of the survival rate and suppression of metastasis
	Vitamin D (1,200 IU/day)	Clinical evidence	Randomized, double-blind trial	Improved survival of NSCLC patients with early-stage lung adenocarcinoma in patients with lower levels of 25(OH)D
Nakagawa K et al	22-0xa-1a 25-dihydroxyvitamin D3	Preclinical evidence	Cell line (LLC); Female C57BL/6 mice	Inhibited metastasis and angiogenesis in lung cancer
Trump DL et al	1,25 dihydroxycholecalciferols	Clinical evidence	Human lung cancer model	Strong antiproliferative effects
Higashimoto Y et al	1 alpha, 25-dihydroxyvitamin D3	Preclinical evidence	EBC-1 squamous cell carcinoma	Inhibited the growth of the lung cancer cell line, EBC-1
M Güzey et al	1 alpha, 25-dihydroxyvitamin D3	Preclinical evidence	Human small cell lung carcinoma cell lines, NCI-H82 and NCI-H209	Inhibited the proliferation of lung cancer cell line and induced their apoptosis
Saito T et al	1,25-dihydroxyvitamin D (3)	Preclinical evidence	H520 cell	Antiproliferative activities against cancer cells
Yoshiaki Omura et al	Vitamin D3	Clinical evidence	Human lung cancer tissue	Optimal dose of vitamin D3 was 400 IU. This had safe and effective anticancer effects, while commonly used doses of 2,000-5,000 IU vitamin D3 often resulted in a 2-3-fold increase in cancer markers

buttock was without any abnormal signals (**Figure 1B**). This indicated that inflammation had been absorbed and that the gluteal myofasciitis was no longer present. On October 25th 2020, the patient visited the hospital for the third re-examination. The doctor advised the patient to continue taking vitamin D_3, but adjusted the dose to 800 IU. No further discomfort was reported by the patient.

Discussion

Complications, such as dyspnea, pulmonary emboli, pneumothorax, pleural effusions, and/or pericardial effusions, are very common in lung cancer. Among them, dyspnea represents the most common complication, with an incidence of approximately one-third to one-half of patients with lung cancer. Hemoptysis is another common symptom and is present in nearly one-quarter of patients with lung cancer [9]. Other signs of intrathoracic diffusion include superior vena cava syndrome, dysphagia and pain in the arm or shoulder, all of which are due to the mass effect of various structures. In addition, besides certain non-specific signs (such as weight loss, anorexia and fatigue), patients with lung cancer may also develop symptoms of metastases outside the chest [10]. Recently, vitamin D or its analogs were broadly used for lung cancer treatment, due to their anti-tumor effect that was extensively supported by preclinical or clinical evidence (**Table 1**). It was previously reported that vitamin D can suppress the proliferation of lung cancer cells originating from the epithelial cells expressing VDR [11, 12]. In addition, analogs of vitamin D have been demonstrated to inhibit the proliferation of lung cancer cells [12, 13]. However, a randomized, double-blind trial that was conducted to compare 1,200 IU/day vitamin D supplements with a placebo for 1 year after operation in patients with non-small cell lung cancer, revealed no significant difference in relapse-free survival and overall survival between the intervention and placebo groups [3]. However, when patients were stratified into subgroups according to early-stage adenocarcinoma with low 25(OH)D levels, it was found that the vitamin D group had a significantly improved 5-year relapse-free survival and overall survival compared with the placebo group [3]. Based on these previous studies, a daily dosage of 1,200 IU vitamin D_3 was administered to the patient in the present study in order to prevent lung cancer relapse after he underwent right lower lung resection and right upper lung wedge resection. However, other studies have found that 400 IU vitamin D_3 is safe and effective as an anti-cancer therapy

and have even reported this as the optimal dose [14].

It is well demonstrated that vitamin D has become a routine treatment for patients with lung cancer due to its low toxicity. However, there are also adverse reactions of vitamin D clinically, mainly hypercalcemia and phosphatemia, which have certain effects on the urinary, digestive, respiratory, cardiovascular and skeletal systems. In addition, previous studies have demonstrated that vitamin D also has roles in immune system regulation [15]. When vitamin D content in the blood is very high, it can promote the production of IL-4 and TGFβ-1. As both IL-4 and TGFβ-1 are factors that can inhibit the activity of inflammatory T cells, vitamin D may serve a role in impairing the immune function of the body. In a previous study, it was demonstrated that dysregulation of the immune system can also induce necrotizing fasciitis in mice [16]. This indicates that high-dose vitamin D may induce the occurrence of gluteal myofasciitis in patients with lung cancer. In the present case report, the patient began to take 1,200 IU vitamin D_3 every day from November 2nd 2019 and, during this process, he did not take other chemotherapeutic or targeted drugs. However, the patient reported buttock discomfort in January 2020 and this was diagnosed as gluteal myofasciitis on January 21st 2020. This indicated that myofasciitis may have been an adverse reaction of vitamin D_3. Subsequently, the patient stopped taking vitamin D_3 and found that the inflammation disappeared. This confirmed that high dose of 1,200 IU vitamin D may induce gluteal myofasciitis. Thus, the patient adjusted the dosage and began to take 800 IU vitamin D_3 daily from October 25th 2020. Notably, the patient had not reported any discomfort following this change in dosage. Basing on these above data, we have drawn the conclusion that patients with lung cancer taking 1,200 IU vitamin D_3 may be at risk of developing gluteal fasciitis. Therefore, clinicians should pay attention to the rationality of drug use when guiding patients to use vitamin D. They must take the patient's physical condition into consideration, as well as the type, dosage form, dosage and drug collocation of vitamin D.

Clinically, the etiology of fasciitis remains unclear. It may be related to accumulated strain, or it may be caused by cold, trauma and poor immune function. Vitamin D can regulate the immune function of the body, which may be one of the causes of fasciitis. However, to our best knowledge, there is no clinical report of fasciitis induced by vitamin D in patients with lung cancer. In the present case, the patient presented with gluteal myofasciitis, which was related to the administration of high dose vitamin D (1,200 IU). The purpose of this case analysis was to remind clinical workers to pay attention to the adverse reaction of fasciitis in patients with lung cancer caused by taking vitamin D, and to make timely adjustment to avoid subsequent adverse reactions.

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Disclosure of conflict of interest

None.

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