Case Report

Journal of Emergency Medicine Case Reports

Acute Lipodermatosclerosis-Like Eruption and Deep Vein Thrombosis due to Gemcitabine Use Concomittant Side Effects of Gemcitabine

Yasin Yıldız[1]
[1]Department of Emergency Medicine, Konya City Hospital, Konya, Türkiye

Abstract

Gemcitabine is a chemotherapy agent commonly used in the treatment of various solid tumors. Its cutaneous side effects are less well-documented, and its venous thromboembolic side effects are controversial. Here, we aim to present a case diagnosed with an acute lipodermatosclerosis-like eruption and deep vein thrombosis following gemcitabine treatment. A 66-year-old male patient presented with new-onset eruptions and swelling in the right lower extremity, four days after the first dose of gemcitabine treatment for metastatic lung cancer. On examination, there were purple-red plaques and petechiae on the right lower extremity and 2+ edema edema was detected. By superficial ultrasound (USG) diagnosis of DVT was made. The patient was discharged with recommendations for subcutaneous enoxaparin, leg elevation, and follow-up in the outpatient clinic on the fifth day with continued antibiotic therapy. Acute lipodermatosclerosis-like rash, a rare but potential cutaneous side effect in patients receiving gemcitabine treatment, should be well recognized and managed. This ensures the continuity or need for revision of treatment. Additionally, vigilance for possible venous thromboembolic events should be maintained in patients receiving gemcitabine treatment, and the possibility of concurrent occurrences with cutaneous side effects should not be overlooked.

Keywords: Acute lipodermatosclerosis-like eruption, deep vein thrombosis, emergency medicine, gemicitabine, side effect

Introduction

Gemcitabine is a chemotherapy agent commonly used in the treatment of various solid tumors such as sarcomas and hematological malignancies. While its side effects, such as bone marrow suppression, are well-defined, its cutaneous side effects are less well-documented, and its venous thromboembolic side effects are controversial (1).

Cutaneous reactions definitively associated with gemcitabine are described under the term pseudocellulitis and include lipodermatosclerosis-like and erysipeloid reactions, as well as radiation recall events (1,2). Additionally, these reactions are often confused with infectious cellulitis due to antibiotics, hospitalizations, and chemotherapy-related infections (3).

Gemcitabine has also been associated with increased arterial and venous thromboembolic events; however, this risk has not been clearly established. As the oncological indications for its use expand, the recognition and characterization of these complications become crucial (4).

In this case report, we aim to present a case diagnosed with an acute lipodermatosclerosis-like rash and deep vein thrombosis in the right lower extremity following gemcitabine treatment.

Case Report

A 66-year-old male patient presented to our emergency department with new-onset eruptions and swelling in the right lower extremity, four days after the first dose of gemcitabine treatment for metastatic lung cancer. The patient had a history of hypertension but no other comorbidities. On examination, there were purple-red, non-blanching, raised plaques and petechiae predominantly on the anterior and medial aspects of the right lower extremity (Figure-1). Additionally, 2+ edema edema was detected around the right ankle, particularly around the medial malleolus. The patient was afebrile, and a complete blood count revealed thrombocytopenia (platelet count of 149,000), but the white blood cell count was normal. The patient had been referred to dermatology by his oncologist for this rash and was started on antibiotics for suspected cellulitis. However, as his symptoms did not improve, he presented to our emergency department with the same complaints. A superficial ultrasound (USG) was requested due to possible deep vein thrombosis (DVT) and cellulitis. The USG showed intraluminal thrombosis in the distal segment of the right superficial femoral vein and the popliteal vein. There was no response to compression

Corresponding Author: Yasin Yıldız
e-mail: atuyasin02@gmail.com
Received: 09.06.2024 • **Revision:** 09.09.2024 • **Accepted:** 26.10.2024
DOI: 10.33706/jemcr.1498332

Cite this article as: Yıldız Y. Acute Lipodermatosclerosis-Like Eruption and Deep Vein Thrombosis due to Gemcitabine Use Concomittant Side Effects of Gemcitabine. Journal of Emergency Medicine Case Reports. 2024;15(4): 111-113

DOI: 10.33706/jemcr.1498332
Journal of emergency medicine case reports. 2024;15(4): 111-113

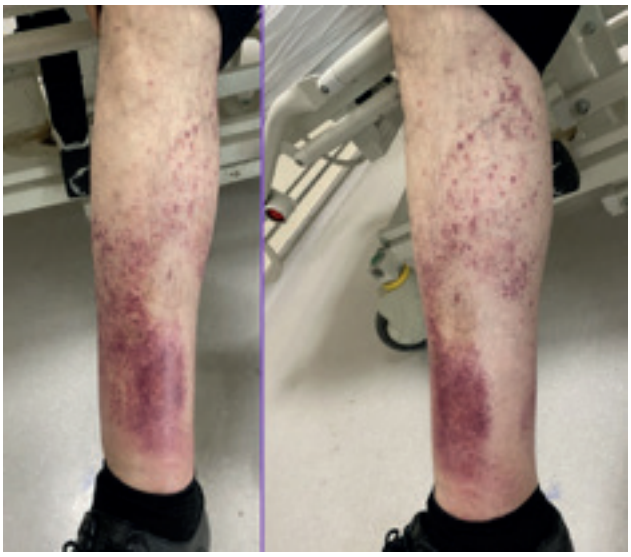

Figure 1. Tender, erythematous plaques on the bilateral lower extremities with overlying petechiae

and augmentation, and a diagnosis of DVT was made. The patient was consulted with Cardiovascular Surgery. He was discharged with recommendations for subcutaneous enoxaparin, leg elevation, and follow-up in the outpatient clinic on the fifth day with continued antibiotic therapy.

Discussion

Gemcitabine is a pyrimidine analog that blocks the cell cycle at the G1/S phase (5). It is used in various solid organ malignancies, including breast, ovarian, non-small cell lung, transitional cell bladder, pancreatic, and biliary tract cancers. Like other chemotherapeutic agents, it can be associated with alopecia, mucositis, and cutaneous hypersensitivity reactions. Additionally, it can be associated with rarer skin reactions (4).

Acute lipodermatosclerosis-like eruption associated with gemcitabine is a rare condition that is often treated as cellulitis. The differential diagnosis includes infectious cellulitis, drug hypersensitivity, toxic erythema secondary to chemotherapy, and other panniculitides such as erythema nodosum. It typically presents as sudden-onset erythematous and tender plaques, frequently on the lower extremities and often bilaterally. In our case, only the right lower extremity was affected. Additionally, patients often complain of lower extremity edema, as was observed with our patient's right ankle edema. Unlike cellulitis, these cases typically do not present with fever and leukocytosis; however, it should be noted that gemcitabine can cause drug-related fever and myelosuppression, complicating the diagnosis. The diagnosis of acute lipodermatosclerosis-like rash related to gemcitabine is primarily based on etiology and clinical findings. This side effect may necessitate the revision or discontinuation of treatment, as continuing therapy without dose reduction can lead to the persistence of the rash (4).

Classically, lipodermatosclerosis or sclerosing panniculitis develops on a background of venous insufficiency. The pathogenesis involves venous hypertension and increased vascular permeability leading to decreased fibrinolytic activity. In the acute phase, painful and erythematous plaques develop over the medial malleolus and other areas, followed by hyperpigmentation due to hemosiderin deposition. Diagnosis is primarily clinical and biopsy is not routinely performed (5,6).

In similar cases reported in the literature, bilateral involvement was observed in 85% of cases. In our case, involvement was unilateral, affecting only the right lower extremity. Additionally, edema was detected in 50% of cases in the literature, and our case also presented with edema. This edema is believed to be related to the accumulation of the drug's metabolites in the interstitial fluid and the pharmacokinetics of gemcitabine (5).

Cutaneous rashes typically occur 2 to 5 days after gemcitabine infusion. In the literature, these rashes were observed within the first 48 hours in 52% of cases (4). In our case, the rash appeared on the 4th day.

Treatment is conservative and includes high-potency topical steroids, compression therapy, leg elevation, and anti-inflammatory therapy (4).

Venous and arterial thromboembolic events are major causes of mortality and morbidity in cancer patients (7-9). Approximately 20% of cancer patients develop these events, and those who do are reported to be at increased risk of poor prognosis and increased mortality. Gemcitabine-based chemotherapy regimens have been reported to carry a significantly increased risk of thromboembolic complications (4). However, this relationship is mostly based on case reports.

In a prospective study involving 108 patients treated with gemcitabine and cisplatin for non-small cell lung cancer, thromboembolic events were reported in 17.6% of cases (10).

In a meta-analysis by Qi et al., arterial and venous thromboembolic events were investigated in patients receiving gemcitabine treatment. As a result, they found that gemcitabine use did not increase the frequency of these thromboembolic events compared to other chemotherapeutic treatments (4).

The pathogenesis of gemcitabine-associated thrombogenicity is not fully understood. It is believed that gemcitabine-associated thrombocytopenia and thrombocytosis may directly increase the risk of thromboembolic events. Additionally, due to the effects of gemcitabine on the coagulation cascade and potential endothelial damage, the frequency of these events may also increase (4).

Current guidelines do not recommend routine VTE prophylaxis for patients receiving outpatient chemotherapy. However, some new data suggest low molecular weight

heparin therapy to reduce the risk of VTE in patients with certain types of cancer (4).

Conclusion

Acute lipodermatosclerosis-like rash, a rare but potential cutaneous side effect in patients receiving gemcitabine treatment, should be well recognized and managed. This ensures the continuity or need for revision of treatment. Additionally, vigilance for possible venous thromboembolic events should be maintained in patients receiving gemcitabine treatment, and the possibility of concurrent occurrences with cutaneous side effects should not be overlooked.

References

1. Tan DH, Bunce PE, Liles WC, Gold WL. Gemcitabine-related "pseudocellulitis": report of 2 cases and review of the literature. Clin Infect Dis. 2007;45:e72-e76.
2. Brandes A, Reichmann U, Plasswilm L, Bamberg M. Time- and dose-limiting erysipeloid rash confined to areas of lymphedema following treatment with gemcitabineea report of three cases. Anticancer Drugs. 2000;11:15-17.
3. Mittal, A., & Leventhal, J. S. (2017). Gemcitabine-associated acute lipodermatosclerosis like eruption: an under recognized phenomenon. JAAD Case Reports, 3(3), 190-195.
4. Qi, W. X., Lin, F., Sun, Y. J., Tang, L. N., Shen, Z., & Yao, Y. (2013). Risk of venous and arterial thromboembolic events in cancer patients treated with gemcitabine: a systematic review and meta analysis. British Journal of Clinical Pharmacology, 76(3), 338-347.
5. Dasanu CA. Gemcitabine: vascular toxicity and prothrombotic potential. Expert Opin Drug Saf. 2008;7:703-716.
6. Chu CY, Yang CH, Chiu HC. Gemcitabine-induced acute lipodermatosclerosis-like reaction. Acta Derm Venereol. 2001; 81:426-428.
7. Khorana AA, Francis CW, Culakova E, Kuderer NM, Lyman GH. Thromboembolism is a leading cause of death in cancer patients receiving outpatient chemotherapy. J Thromb Haemost 2007; 5: 632–4.
8. Lyman GH et al. American Society of Clinical Oncology guideline: recommendations for venous thromboembolism prophylaxis and treatment in patients with cancer. J Clin Oncol 2007; 25: 5490–505.
9. Lyman GH, Khorana AA. Cancer, clots and consensus: new understanding of an old problem. J Clin Oncol 2009; 27: 4821–6.
10. Numico G et al. Prospective evaluation of major vascular events in patients with nonsmall cell lung carcinoma treated with cisplatin and gemcitabine. Cancer 2005; 103: 994–9.