

## Gemcitabine Induced Drug Rash with Eosinophilia and Systemic Symptoms: Dress Syndrome: A Case Report

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**Abstract:** Drug Rash with Eosinophilia and Systemic Symptoms, currently considered as a systemic reaction with a life-threatening and drug-induced visceral manifestation, has never been described with a chemotherapy drugs. A 52 years-old women with metastatic uterine leiomyosarcoma under chemotherapy second line gemcitabine, presents an extensive erythema with a 38 c° fever, two weeks after chemotherapy. The laboratory studies revealed a mild increase of inflammatory markers, mild anemia, and hyper-leukocytosis and hepatic cytolysis. The histology of skin's biopsy finds an important lymphocytic infiltrate. The diagnosis is Drug Rash with Eosinophilia and Systemic Symptoms: DRESS syndrome. The patient was treated with corticosteroid therapy, with favorable evolution, the gemcitabine was permanently discontinued. The exact cause is unknown, most likely polyfactorial, It is described as a genetic predisposition. The definitive discontinuation of the drug product in question and systematic emergency corticosteroid therapy is compulsory.

**Keywords:** Gemcitabine, DRESS syndrome, corticosteroid.

### INTRODUCTION

Gemcitabine is an antimetabolite drug, analogue of deoxycytidine, one of the four nitrogen bases of DNA, considered to be safe and a tolerated cytostatic drug with little known side effects. The reported toxic effects of gemcitabine include fever, myelosuppression and flu-like syndrome. Skin reactions are rarely reported, with an incidence being 7%-30% [1].

Drug hypersensitivity syndrome or drug rash with eosinophilia and systemic symptoms (DRESS) is a serious form of toxidermia that associates cutaneous manifestations and systemic attack [2].

We report one patient with Metastatic uterine leiomyosarcoma who developed gemcitabine-induced Drug Rash with Eosinophilia and Systemic Symptoms. Gemcitabine is one of the drugs that showed a benefit in uterine leiomyosarcoma with metastatic situation with 18% response and especially prolonged control of the disease [3]. The skin toxicity described with gemcitabine was alopecia and transient macular lesion[4].

### CASE REPORT

A 52 years-old women with lung metastases of a uterine leiomyosarcoma under chemotherapy second line gemcitabine, admitted to our department for extensive macular-papular rash with a 38 c° fever (figure1). The patient benefited from a chemotherapy

cure two weeks ago, she was benefited from an intravenous infusion of gemcitabine 1000 mg/m<sup>2</sup>, and the premedication was by an intravenous dexamethasone.

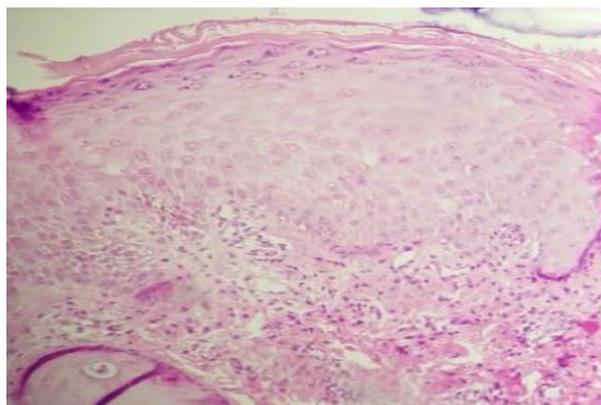
The laboratory studies revealed a mild increase of inflammatory markers, mild anemia and Hyper-leukocytosis (C-reactive protein 25 mg/dl, hemoglobin 10g/dl, leukocytosis 19.3x10<sup>3</sup> µl), Hepatic cytolysis (ALAT: 580 UI/l, ASAT: 427 UI/l).

The skin's biopsy specimen was taken from the erythematous; the histology finds a perivascular inflammatory infiltrate rich in lymphocytes and polynuclear eosinophils (figure 2).

The diagnosis is Drug Rash with Eosinophilia and Systemic Symptoms: DRESS syndrome; the patient is treated with corticosteroid therapy 1mg/kg, with favorable evolution, the gemcitabine is permanently discontinued.



**Fig-1: Macular-papular rash**



**Fig-2: Skin coating with acanthotic epidermis on spongiosis with basal layer vacuolation. The underlying dermis is oedematous site of a perivascular inflammatory infiltrate rich in lymphocytes and polynuclear eosinophils. (Histological section colored with HE X 100)**

**Table-1: Major criteria of RegiSCAR**

RegiSCAR inclusion criteria for DRESS syndrome.
Acute Rash*
Fever > 38 °C*
Lymphadenopathy in at least two sites*
Involvement of at least one internal organ*
Blood count abnormalities (lymphopenia or lymphocytosis*, eosinophilia*, thrombocytopenia*)
Hospitalization
Reaction suspected to be drug-related

## DISCUSSION

Drug Rash with Eosinophilia and Systemic Symptoms: DRESS syndrome, also called Drug-induced Hypersensitivity Syndrome: DIHS, is a systematic response condition that can be triggered by an Immunological effects on certain drugs [5 6].

The pathogenesis of DRESS syndrome is still very controversial. A hypersensitivity reaction mediated by lymphocytes T (LT) with cytokine secretions is partly responsible for the clinical picture [7]. In the early phase of DRESS syndrome; elevated levels of plasma interleukin-5 secreted by LTs could be highlighted and may explain the observed eosinophilia [8].

There is an inflammatory reaction often eosinophilic at different organs. Given that the

Symptoms (fever, exanthema, swelling of the Lymph nodes, hepatitis) are suggestive of diseases or autoimmune serious diseases, they often occur only after several weeks of the treatment that was initially well tolerated. DRESS syndrome is triggered by only a relatively small number of drugs, including anticonvulsants (phenytoin, Carbamazepine, lamotrigine), sulfonamides such as dapson, sulfasalazine (due to its sulfapyridine component) and sulfamethoxazole, as well as allopurinol, minocycline, abacavir and nevirapine[9].

Patch and skin tests may be useful in determining the offending drug, but they can trigger a systemic reaction [7]; for this reason, they are not performed if the drug suspected can be avoided. There is no Golden Standard for diagnosis, RegiSCAR

proposed criteria for diagnosis: Three Major criteria are required for diagnosis [10] (table: 1)

DRESS syndrome is associated with a mortality of about 10%. Early detection of the syndrome, immediate cessation of the drugs and Systemic corticosteroid therapy is recommended and vitally important. Gemcitabine is an antimetabolite nucleoside, one of the drugs that showed a benefit in uterine leiomyosarcoma in metastatic situation with 18% response and especially prolonged control of the disease, the skin toxicity described in relation to gemcitabine was alopecia and transient macular lesion [4].

The absence of convincing argument in favor of autoimmune disease or the use of incriminated treatments led us to retain the diagnosis of DRESS syndrome related to Gemcitabine, this case has never reported in the literature before.

Currently, there are no recommendations based on prospective randomized studies for the management of DRESS syndrome. The proposed treatments are based on the expert's advices and the goal is to control the deleterious immune response. The first step of the care consists in stopping the offending drug. In the acute phase of the disease, all treatments, which are not necessary, should be discontinued [7].

The therapeutic management depends on the severity of the systemic involvement. Therefore, it is necessary to assess the damages of organ cibles [11]. Systemic or topical corticosteroid therapy may be introduced depending on the severity of the systemic involvement [9]. The clinic evolution is slow (several weeks to months) and requires a close monitoring.

## CONCLUSION

Anti-cancer drugs, like all drugs can be the cause of toxidermia, severe immuno-allergic disorders such as, DRESS syndrome. The diagnosis is often complicated by the presence of several associated therapeutic classes, potentially inducing such reactions.

The cessation of suspect drugs is essential, fast, specialized and symptomatic and the reintroduction of the molecule is formally contraindicated.

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