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# Eosinophilic Pneumonitis Complicated by ARDS Following DRESS Syndrome: Case Report

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**Abstract** **Case Report**

***Introduction*:** Drug reaction syndrome with eosinophilia and systemic symptoms (DRESS) is a rare and potentially fatal hypersensitivity reaction, The reaction usually manifests as a febrile skin rash accompanied by lymphadenopathy and malaise between two and eight weeks after drug exposure. The pulmonary manifestations of DRESS are variable and may include interstitial pneumonia, pleural effusion, pneumonia, pulmonary nodules and (in the most severe cases) acute respiratory distress syndrome (ARDS). We report the observation of an acute eosinophilic pneumonitis which is unique in that it is part of a DRESS syndrome following the use of non-steroidal anti-inflammatory drugs and Ciprofloxacin. ***Observation*:** This was a 63-year-old patient admitted to the outpatient department of the Mohamed VI University Hospital in Marrakech for acute respiratory distress. Her history included a chronic depressive syndrome for 7 years under Taraxet and Deroxat; a megaloblastic anemia under Tardyferon; a non-dialyzed renal failure; a Gout having been under Zyloric for 7 months; a DRESS syndrome following the intake of non-steroidal anti-inflammatory drugs and Ciprofloxacin (Cystitis) having been hospitalized in the dermatology department 15 days before. The diagnosis of community-acquired pneumonia had been evoked and treated with Amoxicillin-clavulanic acid + Azithromycin (Suspicion of covid infection and appearance of Crazy Paving on thoracic Angioscanner), The evolution had been marked the following day by severe respiratory distress with hypoxia at 68% with MHC at 15, the respiratory frequency was at 51 cycles per minute with generalized cyanosis, signs of respiratory struggle. The blood gases on admission:Ph 7. 43 PaCo2 40.3 pAo2 45 HCo3- 25.8, PaO2/FiO2 at 98; The picture of hypoxaemia on a severe and very hypoxaemic pneumopathy required orotracheal intubation. Refractory hypoxemia (PaO2/FIO2 = 69 in the control gasometry despite a PEEP = 14 cmH2O, deep sedation completed with curarisation, and the occurrence of a state of shock justifying vascular filling and the introduction of noradrenaline. The installation of a state of shock and the impossibility of ensuring sufficient hematosis led to the indication of respiratory assistance by ECMO on D1, but this was impossible to achieve in our context. The patient remained very hypoxic with an SpO2 of 45% or less for a FIO2 of 100%. This was an eosinophilic lung disease complicated by severe ARDS on DRESS Syndrome. ***Discussion*:** The retained diagnosis is eosinophilic pneumonitis fits into a DRESS syndrome induced by ciprofloxacin. Hypereosinophilia, eosinophilic lung disease with adenopathy, and skin involvement are supportive. The diagnostic criteria for DRESS syndrome include a drug-related skin rash, haematological abnormalities with eosinophilia greater than 1500G/L and/or the presence of atypical lymphocytes, and at least one systemic involvement including diffuse adenopathy greater than 2 cm, hepatitis (transaminases greater than twice normal), interstitial lung disease, and renal disease. Hepatic involvement is predominant among the visceral disorders. Pulmonary involvement may determine the prognosis. Adult acute respiratory distress syndrome (ARDS) is one of the most frequent complications leading to admission to the ICU [4]. ***Conclusion*:** This is a case report of eosinophilic lung disease in the setting of DRESS syndrome, associated with ciprofloxacin use complicated by acute respiratory distress syndrome with fatal outcome.

**Keywords:** DRESS, acute respiratory distress syndrome (ARDS), interstitial lung disease, adenopathy.



## INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms syndrome (DRESS) is a rare and potentially fatal hypersensitivity reaction.

The reaction usually manifests as a febrile rash with lymphadenopathy and malaise between two and eight weeks after drug exposure. Internal organ involvement occurs in up to 90% of patients, and

multiple organs may be affected in about half of patients (most commonly the liver, kidneys and lungs).

The pulmonary manifestations of DRESS are variable and may include interstitial pneumonia, pleural effusion, pneumonia, pulmonary nodules and (in the most severe cases) acute respiratory distress syndrome (ARDS).

We report the observation of an acute eosinophilic pneumonitis which is unique in being part of a DRESS syndrome following the use of non-steroidal anti-inflammatory drugs and Ciprofloxacin.

## OBSERVATION

This was a 63 year old female patient admitted to the outpatient department of the Mohamed VI University Hospital in Marrakech for acute respiratory distress. Her history included a chronic depressive syndrome for 7 years under Taraxet and Deroxat; megaloblastic anaemia under Tardyferon; non-dialysed renal insufficiency; Gout having been under Zyloric for 7 months; a DRESS syndrome following NSAID and Ciprofloxacin (Cystitis) having been hospitalized in the dermatology department 15 days earlier.

Her biological work-up showed: hypereosinophilia at 1854, thrombocytopenia at 119,000, a biological inflammatory syndrome with white blood cells at 11170, predominantly neutrophilic at 6624, worsening of the alteration of her renal function with urea at 1.16 and creatinemia at 61.5, GFR at 7, disturbed hepatic function with ASAT at 2x the normal value and ALAT at 3x the normal value, troponin at 45.5, with negative kinetics, and CRP at 82.9.

The probability of a ciprofloxacin-induced DRESS syndrome was considered "definite", with 5 scores assessed by RegiSCAR.

| Items | Score | | | Comments |
|---|---|---|---|---|
| | −1 | 0 | 1 | |
| Fever ≧ 38.5 °C | N/U | Y | | |
| Enlarged lymph nodes | | N/U | Y | >1 cm and ≧ 2 different areas |
| Eosinophilia ≧ 0.7 × $10^9$/L or ≧ 10% if WBC < 4.0 × $10^9$/L | | N/U | Y | Score 2, when ≧ 1.5 × $10^9$/L or ≧ 20% if WBC < 4.0 × $10^9$/L |
| Atypical lymphocytosis | | N/U | Y | |
| Skin rash | | | | Rash suggesting DRESS: ≧ 2 symptoms: purpuric lesions (other than legs), infiltration, facial edema, psoriasiform desquamation |
| Extent > 50% of BSA | | N/U | Y | |
| Rash suggesting DRESS | N | U | Y | |
| Skin biopsy suggesting DRESS | N | Y/U | | |
| Organ involvement | | N | Y | Score 1 for each organ involvement, maximal score: 2 |
| Rash resolution ≧ 15 days | N/U | Y | | |
| Excluding other causes | | N/U | Y | Score 1 if 3 tests of the following tests were performed and all were negative: HAV, HBV, HCV, Mycoplasma, Chlamydia, ANA, blood culture |

ANA: anti-nuclear antibody; BSA: body surface area; HAV: hepatitis A virus; HBV: hepatitis B virus; HCV: hepatitis C virus; N: no; U: unknown; WBC: white blood cell; Y: yes.

She had been treated with corticosteroid therapy (stopped at discharge) and a magistral preparation for 8 days. After regression of the symptoms and improvement of her biological check-up, the patient was discharged from the Dermatology Department and returned home.

At 5 days post hospitalization she presented a respiratory distress in the aftermath of an influenza syndrome which required a readmission to the emergency room of the University Hospital of Marrakech, she was conscious BP 12/7 FC 97 FR 30 Spo2 86% under AA febrile at 38°c with bilateral basithoracic crackles, no signs of IC.

Her work-up was a biological inflammatory syndrome with Gb at 15730, eosinophilia at 1432, neutrophilia at 14786, lymphopenia at 708, CRP 82.3, natraemia at 139, kalaemia at 4.8, chloraemia at 103, alkaline reserve at 26, creatinine at 16, urea at 0.73, and D-dimer levels at 2. 20 and Abdominal ultrasound showed a simple looking right renal cyst, trans thoracic ultrasound showed an LV of preserved size and function, LVEF 63%, LV filling pressures not elevated, right cavities normal, no significant valvulopathy, no http, non-dilated vena cava complicating with a dry pericardium, non-dilated ascending aorta.

The diagnosis of community-acquired pneumonia was evoked and treated with Amoxicillin-clavulanic acid + Azithromycin (Suspicion of covid

infection and appearance of Crazy Paving on thoracic Angioscanner), The evolution was marked the next day by severe respiratory distress with hypoxia at 68% with MHC at 15, the respiratory rate was 51 cycles per minute with generalized cyanosis, signs of respiratory struggle.

Blood gases on admission: Ph 7.43 PaCo2 40.3 pAo2 45 HCo3- 25.8, PaO2/FiO2 98:

The picture of hypoxaemia on severe very hypoxaemic lung disease required orotracheal intubation. Refractory hypoxemia (PaO2/FIO2 = 69 in the control gasometry despite a PEEP = 14 cmH2O, deep sedation completed with curarisation, and the occurrence of a state of shock justifying vascular filling and the introduction of noradrenaline. The installation of a state of shock and the impossibility of ensuring a sufficient hematosis made it possible to indicate respiratory assistance by ECMO at D1 but impossible to carry out in our context. The patient remained very hypoxic with an SpO2 of 45% or less for a FIO2 of 100%.

It was an eosinophilic pneumopathy complicated by severe ARDS on DRESS Syndrome.

The evolution was marked on the first day of hospitalization in the outpatient department by a respiratory arrest for which conventional cardiopulmonary resuscitation measures did not allow spontaneous cardiac activity to be recovered.

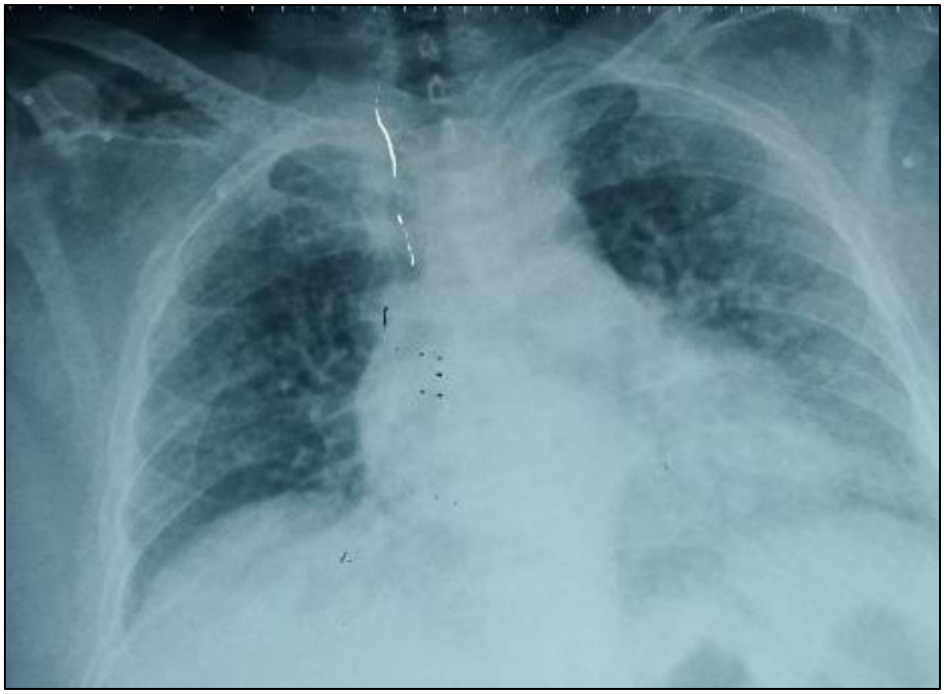

**Figure 1: Frontal X-ray of the lung diffuse interstitial syndrome, blunted cds, CMG**

## DISCUSSION

The retained diagnosis is eosinophilic pneumonitis fits into a ciprofloxacin-induced DRESS syndrome. Hypereosinophilia, eosinophilic lung disease with adenopathy, and skin involvement are supportive. In our case, the onset of symptoms, the chronology within a compatible timeframe after the drug was taken, and the resolution of the symptoms upon discontinuation of the drug, without corticosteroid treatment, make it probable that ciprofloxacin was responsible. The term "DRESS syndrome" was first used in 1996 by Bocquet *et al*., The drugs most often incriminated are anticonvulsants (carbamazepine, diphenylhydantoine, valproic acid), allopurinol, antibiotics (sulphonamides, minocycline) and antiretrovirals (Efavirenz) [2]. The syndrome usually occurs within six weeks of the introduction of the causative drug [3]. The diagnostic criteria for DRESS syndrome include a drug-related rash, haematological abnormalities with eosinophilia greater than 1500G/L and/or the presence of atypical lymphocytes, and at least one systemic involvement including diffuse adenopathy greater than 2 cm, hepatitis (transaminases greater than twice normal), interstitial lung disease, and nephropathy. Hepatic involvement is predominant among the visceral disorders. Pulmonary involvement may determine the prognosis. It can affect up to 33% of patients depending on the series and takes the form of eosinophilic pneumonitis, hence the importance of drug investigation in the context of eosinophilic pneumonitis. The pathophysiological mechanisms of DRESS syndrome are not well understood. Viral reactivation has been demonstrated in a number of patients. These are most often viruses of the herpesviridae family (HHV6, EBV and CMV) [6, 7]. In this hypothesis, the clinical symptoms of DRESS would be linked to an

oligoclonal proliferation of CD8+ T lymphocytes. The incriminating drugs would induce reactivation and antigenic presentation of EBV or other viruses of the Herpes family such as HHV-6. The imputability of ciprofloxacin to the origin of a DRESS syndrome has been reported few times in the literature, with a predominant cutaneous involvement and evidence of a serological reactivation towards the HHV-6 virus.Adult acute respiratory distress syndrome (ARDS) is one of the most common complications leading to admission to the ICU [4]. Unfortunately, many patients escape optimal management and die from complications of hypoxia.

## CONCLUSION

This is a case report of eosinophilic pneumonitis in the setting of DRESS syndrome, related to ciprofloxacin use complicated by acute respiratory distress syndrome with fatal outcome.The basic treatment for the main unusual causes of ARDS is systemic corticosteroids, the dose and duration of which are poorly codified. The earlier the corticosteroid therapy is initiated, the more effective it is.This observation underlines the importance of evoking the possibility of a DRESS syndrome before any infiltrating pulmonary pathology with hypereosinophilia, in the aftermath of the initial cutaneous attack, which it may follow by several days.

**Declaration of Interest:** The authors declare that they have no conflicts of interest in relation to this article.

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