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Case Report

Drug reaction with eosinophilia and systemic symptoms (DRESS) with severe and atypical lung involvement^{☆,☆☆}

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ABSTRACT

Drug reaction with eosinophilia and systemic symptoms is a rare and potentially fatal drug hypersensitivity reaction. Reactions include skin eruption, fever, hematologic abnormalities (eosinophilia or atypical lymphocytosis), enlarged lymph nodes, and/or organic involvement. The liver is the most commonly compromised organ.

We present a case of drug reaction with eosinophilia and systemic symptoms associated with Naproxen intake in a young female patient with severe lung involvement. The patient's chest tomography highlights the presence of adenomegalies, pericardial and pleural effusion, peribroncovascular consolidations, and centrilobular nodules.

After reviewing the literature few similar cases were found. The main radiological alterations in those cases included interstitial opacities attributed to pneumonitis. Therefore, this case study is considered an unusual case with atypical presentation of drug-induced eosinophilic lung disease.

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Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a condition, that requires the presence of the following symptoms for its diagnosis; skin eruption, fever, hematologic abnormalities (eosinophilia or atypical lympho-

cytosis), enlarged lymph nodes and/or organic involvement, with the liver being the most commonly compromised organ. It is considered an infrequent and severe reaction that is related to hypersensitivity disorders with eosinophilia [1–3].

DRESS has been associated with anticonvulsants, antibiotics, and non-steroidal anti-inflammatory agents (Table 1),

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Table 1 – Drugs most commonly associated with DRESS syndrome.

Drugs most commonly associated with DRESS syndrome
Non-steroidal anti-inflammatory drugs (NSAIDs).
Antibiotics (Nitrofurantoin, Minocycline, Sulfonamides, Ampicillin, Daptomycin).
Fenitoin.
L-tryptophan.

with a variable latency time between drug intake and clinical manifestations [3,4].

Currently, the scoring system proposed by the Registry of Severe Cutaneous Adverse Reactions offers diagnostic criteria for hospitalized patients with a drug associated rash. The system allows classification for suspected clinical cases as excluded, possible, probable or definite for DRESS (Table 2) [2,4–6].

The first step in DRESS management is to stop medication involved in the reaction, further interventions follow according the severity of organ involvement. Symptomatic treatment is acceptable in mild cases, while patients with interstitial pneumonitis or nephritis require systemic steroids, and those with acute liver failure require transplants [2,3,7].

Case report

A previously healthy 22-year-old female patient received Naproxen for mechanical dorsal pain, 5 days later she developed skin eruption and dyspnea.

An initial chest radiograph was performed showing multilobar consolidations and bilateral pleural effusion (Fig. 1). The main laboratory alterations included eosinophilia (1780 absolute count) and hypertransaminasemia, suggestive of acute liver failure.

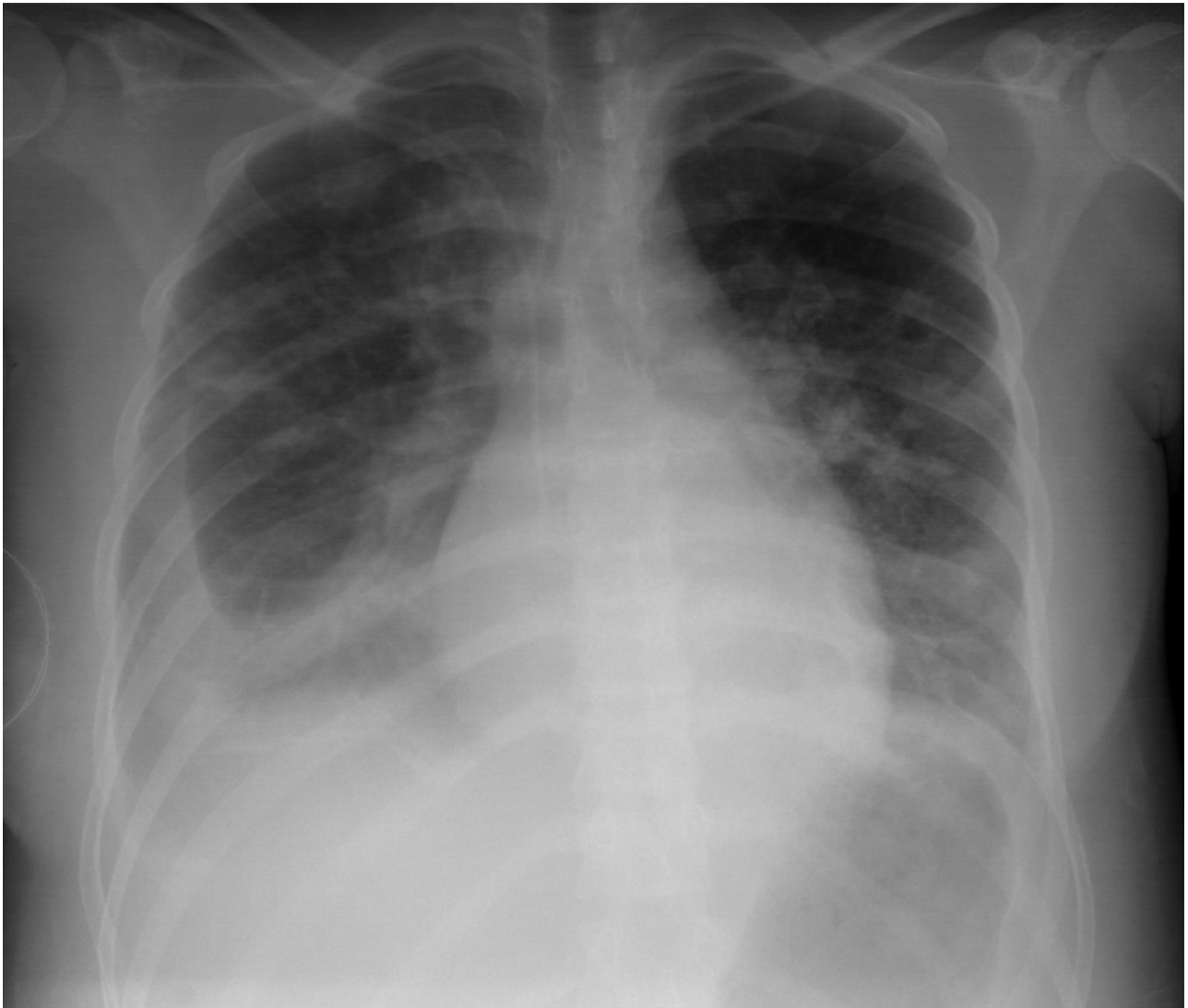
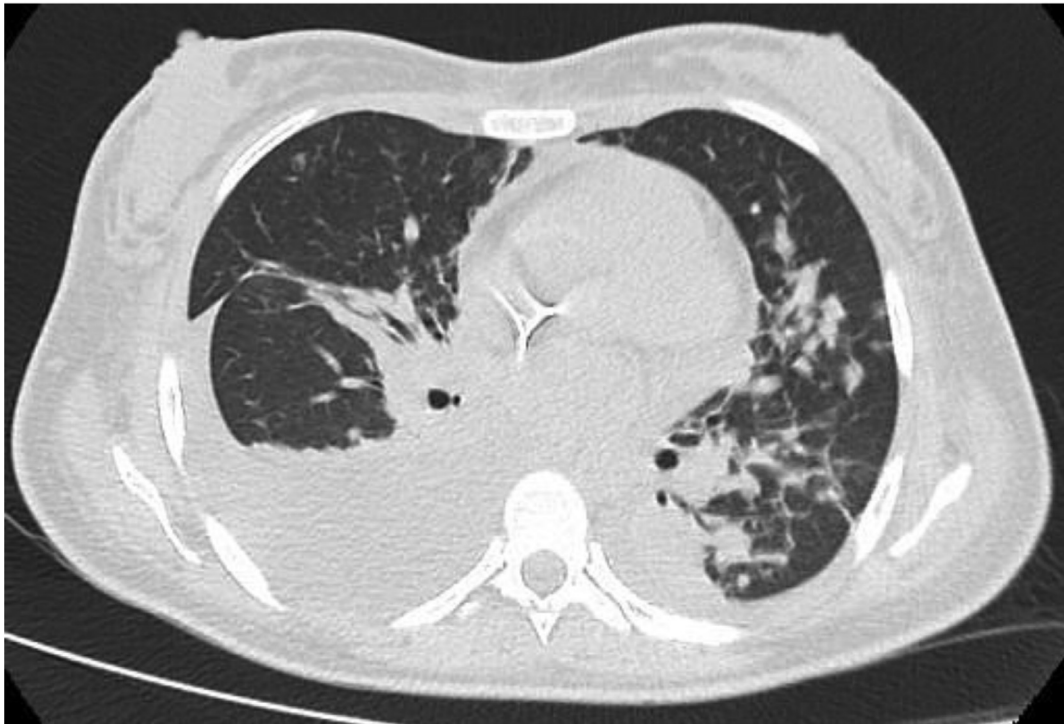


Fig. 1 – Portable Chest X-Ray, unique AP projection: Normal heart size. Multilobar and bilateral consolidations. Bilateral pleural effusion, most marked in the right side. Also note the presence of a central venous catheter (right subclavian) with the tip located in the right auricle.

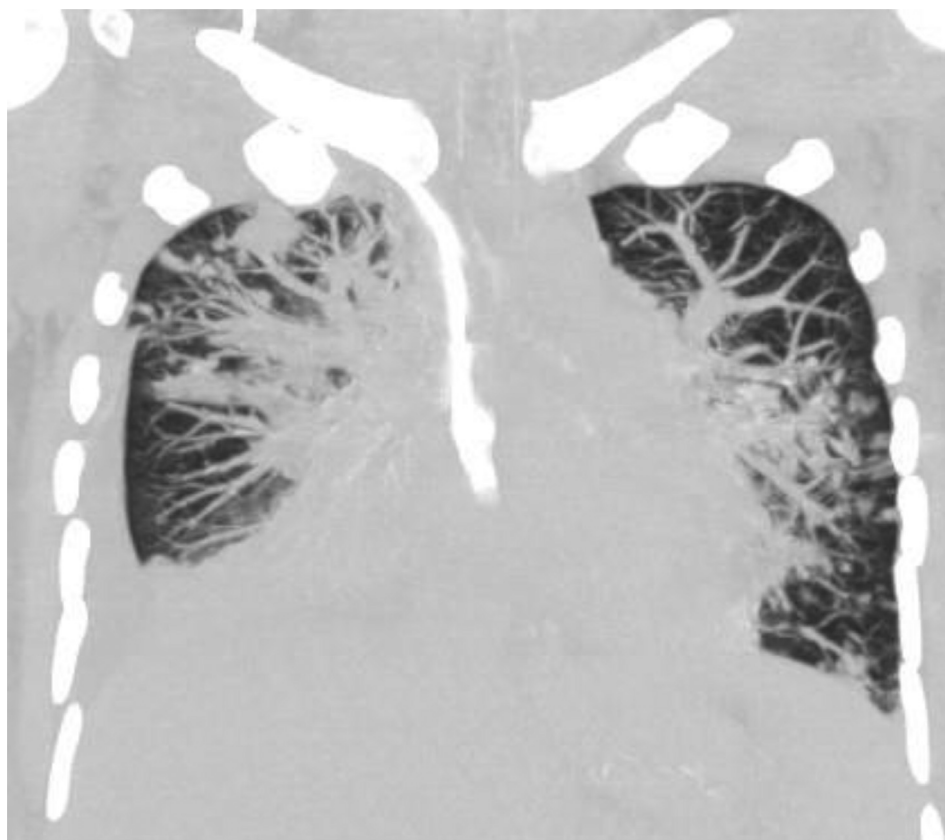


a.



b.

Fig. 2 – Computed Tomography (CT) of chest: Mediastinal and lung windows: (A-C). Axial mediastinal window (A) with axilar adenomegalies, prominent mediastinal lymph nodes, mild pericardial effusion (not showed), and bilateral pleural effusion most marked in the right side. Axial lung window (B) and Coronal maximum intensity projection -MIP- (C) in lung window with peribronchovascular consolidations in both lungs, diffuse centrilobular nodules and atelectasis in both inferior lobes.



C.

Fig. 2 – Continued

Table 2 – Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) in DRESS syndrome.

Item	Present	Absent	Patient
Fever $\geq 38.5^{\circ}\text{C}$	0	-1	0
Enlarged lymph nodes (>1 cm size, at least 2 sites)	1	0	1
Eosinophilia: ≥ 700 o $\geq 10\%$ (leucopenia) / ≥ 1500 o $\geq 20\%$.	1 / 2	0	2
Atypical lymphocytes	1	0	0
Rash ≥ 50 percent of body surface area	1	0	1
Rash suggestive (≥ 2 of facial edema, purpura, infiltration, and desquamation)	1	0	1
Skin biopsy suggesting alternative diagnosis	-1	0	0
Organ involvement: 1 / 2 or more	1 / 2	0	2
Disease duration >15 days	0	-2	0
Investigation for alternative cause (blood cultures, ANA, serology for Hepatitis viruses, mycoplasma, and Chlamydia) ≥ 3 done and negative	1	0	0
Total score in the patient			7

Total score <2 : excluded; 2-3: possible; 4-5: probable; ≥ 6 : definite.

A high-resolution chest computed tomography was performed due to progressive dyspnea (Fig. 2). Axillary and mediastinal adenomegalies, pericardial and pleural effusion, peribronchovascular consolidations, and diffuse centrilobular nodules were visible.

Given the described tomographic findings, peripheral eosinophilia, and the clinical context, a diagnosis of

eosinophilic pneumonia was performed. Other etiologies such as bacterial or viral infection were excluded and the Registry of Severe Cutaneous Adverse Reactions score reached 7 points, confirming a definitive diagnosis of DRESS. The patient showed an optimal response to systemic steroids, resolving the lung and liver alterations, with no requirement of liver transplant.

Table 3 – Respiratory symptoms and tomographic findings associated to DRESS syndrome with lung involvement.

Symptoms
<ul style="list-style-type: none"> • Dyspnea. • Cough. • Pleuritic chest pain.
Chest tomographic findings
<ul style="list-style-type: none"> • Interstitial opacities. • ARDS pattern. • Lobar consolidation. • Centrilobular nodules. • Adenomegalies.

Discussion

DRESS is a rare and potentially fatal drug hypersensitivity reaction with organ involvement in up to 90 percent of patients. The most affected organs are the liver, kidneys, and lungs. Severe lung involvement in DRESS is considered infrequent, as it is present in about 5%-25% of cases and is associated with worst prognosis [8–11].

A systematic review published in 2019 by Taweeseedt et al., included 22 patients with lung involvement due to DRESS syndrome finding dyspnea, cough, and pleuritic chest pain as predominant clinical manifestations. The main imaging findings included the presence of interstitial opacities related to pneumonitis in 50% of patients, compatible findings characteristic of acute respiratory distress syndrome in 31% of cases, and less frequently pleural effusion (22.7%), lobar consolidations (14%), and centrilobular nodules (14%), (Table 3) [11].

Enlarged lymph nodes are a common finding in DRESS syndrome; therefore, adenomegalies are part of the possible chest tomographic alterations.

On the other hand, a case series study published by Lee et al. [12] included 5 patients with DRESS and lung involvement finding consolidations in 60%, and pleural effusion in 40% of the cases.

There are few case reports in the literature of lung involvement in DRESS syndrome however, it is recognized as an unusual finding the small airway's compromise exhibited as centrilobular nodules and there is no report, to our knowledge, of pericardial effusion, as it is described in the present case report.

Conclusion

DRESS syndrome is an infrequent but severe entity, with the worst prognosis occurring when lung involvement is present.

It is manifested with a broad spectrum of imaging findings such as multilobar consolidations, pleural effusion, and adenomegalies.

Diagnosis of DRESS syndrome should be considered in patients with compatible clinical history, previous related drug exposition, and eosinophilia.

Our case represents an unusual manifestation of DRESS syndrome as it showed centrilobular nodules and pericardial effusion associated to the classic findings previously described.

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