



CASE REPORT

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Introduction

- ★ ♂ 80y
- ★ Hypertension
- ★ Chronic kidney disease stage 3A
- ★ Duodenal ulcer 20 years ago
- ★ Hyperuricemia
- ★ Medication: Furosemide, allopurinol.



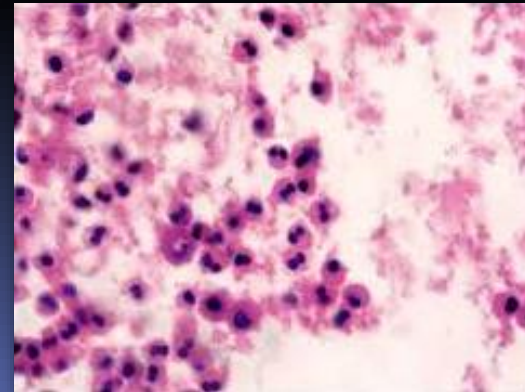
🏠 Admission to the hospital:

- ★ Asthenia, Anorexia, Abdominal pain.
- ★ Fever, Exfoliative dermatitis, Diarrhoea, Jaundice, Hepatomegaly.



☀ Complementary explorations:

- ★ Blood test: \uparrow WCC ($15.4 \times 10^9/L$) with 16% Eosinophilia, Creatinine $645 \mu\text{mol}/L$ (N: 53-106), ALT $328 \text{UI}/L$ (N < 41), Alkaline Phosphatase $6567 \text{UI}/L$ (N < 280), Bilirubin $535 \mu\text{mol}/L$ (N: 1,7 - 6,8), Prothrombin prolonged (24").
- ★ Abdominal sonography: Normal.
- ★ Abdominal CT scan: Normal.



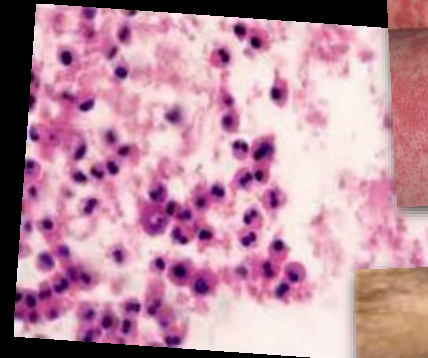
Now... what else???



- ✦ In the next days his clinical condition deteriorated with progressive liver failure, and hepatic encephalopathy that finally led to death.
- ✦ Autopsy: hepatic granulomas and cholestasis.

... Any ideas???

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DRESS SYNDROME

Drug Reaction with Eosinophilia
and Systemic Symptoms



... induced by allopurinol.

- ★ Is a rare drug-induced hypersensitivity reaction with a high mortality (up to 25%).
- ★ 2-8 weeks between drug exposure and disease onset.
- ★ Incidence unknown. No sex prediction.
- ★ Importance of : type of drug, immune status of the patient and herpesvirus reactivation.

- ★ Allopurinol: HLA-B*5801
 - Renal involvement
 - Absence lymphadenopathy
 - Overall mort 25% (liver, kidney, sepsis, GI bleeding)

RegiSCAR study group

More than 3 of the criteria are required for the diagnosis of DRESS

1. Hospitalization
2. Reaction suspected to be drug related
3. Acute rash
4. Fever above 38°C
5. Enlarged lymph nodes involving at least two sites
6. Involvement of at least one internal organ
7. Blood count abnormalities
 - Lymphocytes above or below laboratory limits
 - Eosinophils above laboratory limits (in percentage or absolute count)
 - Platelets below laboratory limits

Japanese consensus group

Typical DRESS (presence of all 7 criteria); atypical DIHS (all criteria present except lymphadenopathy and HHV-6 reactivation)

1. HHV-6 reactivation
2. Prolonged clinical symptoms 2 weeks after discontinuation of causative drug
3. Maculopapular rash developing >3 weeks after starting drug

4. Fe **Diagnostic criteria for allopurinol hypersensitivity syndrome¹**

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- A clear history of exposure to allopurinol
 - Lack of exposure to another drug which may have caused a similar clinical picture
 - A clinical picture including:
 - (1) At least two of the following major criteria:
 - Worsening renal function
 - Acute hepatocellular injury
 - A rash, including either toxic epidermal necrolysis, erythema multiforme, or a diffuse maculopapular or exfoliative dermatitis

Or:

- (2) One of the major criteria plus at least one of the following minor criteria:

- Fever
- Eosinophilia
- Leukocytosis

Recommended laboratory and imaging investigations in patients with suspected drug reaction with eosinophilia and systemic symptoms (DRESS)

| Confirmation of diagnosis | Exclusion of alternative diagnosis | Assessment of organ involvement |
|--|---|--|
| CBC with differential including research of atypical lymphocytes Inflammation markers Viral infection (PCR for HHV-6, HHV-7, CMV, EBV) | Blood cultures Antinuclear antibodies <i>Serology for viral hepatitis</i> <i>Lymph node biopsy</i> | Minimal screening Liver function test, creatinine, urinary protein and cells, pulse oximetry, creatine kinase, troponin, ECG |
| | | Additional investigations Prothrombin time/INR <i>CT scan</i> <i>Sonography</i> <i>Endoscopy</i> <i>Biopsy</i> |

In italics: secondary investigations based upon suspected organ involvement.

TREATMENT

- ★ Drug withdrawal and supportive measures
- ★ Corticoids: systemic if severe organ involvement.
- ★ Antivirals: generally not recommended.
- ★ IV immunoglobulins: generally not recommended.

PROGNOSIS

- ★ Average time to recovery: 6-9 weeks. Relapses.

PREVENTION

- ★ Avoidance of the offending drug as well as cross-reacting drugs. Avoidance also recommended to relatives.



Main errors

- ✦ Hypertension: Baseline treatment not recommended?
- ✦ Hyperuricemia: Dose? Indication?
- ✦ Timing at admission.
- ✦ Steroids? IV IG?
- ✦ ICU? Transplant?
- ✦ Palliative care?

Thanks!

