Cases of drug reaction with eosinophilia and systemic symptom syndrome due to anti-inflammatory drugs

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Objective

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare but severe adverse drug reaction characterized by fever, cutaneous eruption, and involvement of one or more internal organs, usually appears 2 to 8 weeks after the start of the suspected drug. DRESS is still inconsistent due to its variable clinical manifestations and inconsistent level of eosinophil, thus making the diagnosis challenging and an effective approach for objective causality assessment is necessary to make consistent and accurate identification of this adverse drug reaction (ADRs). **The objectives of this study is to evaluate the incidence and the clinical characteristics of DRESS syndrome associated with anti-inflammatory drugs and the causality assessment for estimating the strength of relationship between drug(s) exposure and occurrence of adverse reaction.**

Study design

- ✓ The **database 'Vigibase'** of the national pharmacovigilance center (NPC) of Morocco was used from January 2008 to January 2016, using **Vigiflow Software**.
- ✓ The WHO causality assessment method was sused as a tool for clinical assessment of ADRs (Table 1).
- ✓ Search criteria was: Dress- anti-inflammatory drug-Morocco.

Table 1: WHO Causality assessment criteria

Causality term	Assessment criteria*
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon) • Rechallenge satisfactory, if necessary
Probable/ Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanations
Conditional/ Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable/ Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory • Data cannot be supplemented or verified

Results

-Of the **72** reports of Dress syndrome recorded in **Vigibase** during 8 years, we reviewed **16 (22.2%)** reports coded DRESS associated **with anti-inflammatory drugs. The outcome was serious in 14 (51,85%) cases.**

Demographic characteristics:

- ✓ Sex ration: 1,03;
- ✓ Median age: 27 [19-60].

Clinical characteristics:

Fever	100 %
Skin rash	100%
Eosinophilia	82%
Lymphadenopathy	22%
Cheilitis	12,5%
Altered state of consciousness	12,5%
Median days from onset of symptom	18 days
Hospitalization	100% of patients

The most common causative agents were **prednisolone** (31.2%), **Ibuprofen** (12.5%), **Ibuprofen** (12.5%) and **Ketoprofen** (12,5%).

Causality assessment :

Score	Pourcentage %
Possible	57.7
Probable	42.1

Discussion and Conclusion

- ✓ Dress syndrome is a ADRs that causes morbidity and can be life-threatening.
- ✓ In this retrospective study, Prednisolone was the main agent causing DRESS syndrome in Morocco.
- ✓ The altered state of consciousness and cheilitis were associated with Indometacin.
- ✓ All patients recovered after corrective treatment.
- ✓ However, a consensus on criteria is essential to facilitate diagnosis.

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