Reviewer’s report

Title: Phenytoin-induced DRESS syndrome: a case report

Version: 1 Date: 7 September 2012

Reviewer: Mona BEN M’RAD

Which of the following following best describes what type of case report this is?: Other

If other, please specify:

The authors report a phenytoin induced-DRESS syndrome which is a known classical adverse event but unfortunately underrecognized and underdiagnosed. It might be still interesting to publish DRESS case-reports if they give some new insights on the disease, or in order to increase the number of reports on the topic and allow other authors to perform some relevant reviews of the literature or meta-analysis.

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

In the abstract, authors say that DRESS occurs after initiation of antiepileptic medications. It is true, of course, since Chaiken’s first description in 1950 of a an anticonvulsant-induced DRESS (reference below). But practionners should be aware that DRESS may occur with any drug, not only with aromatic
anticonvulsants, but also with homeopathy or phytotherapy or a drug used intermittently, or withdrawn in the last 2 months. Main drug families triggering DRESS have been commented elsewhere (see below). Drug hypersensitivity should always be considered as a differential diagnosis when a reaction is not understood. It is also of a major importance to describe DRESS induced by drugs which have not been reported yet as offenders.

In table 1, it would be more useful to present drugs families rather than isolated drugs, (such as aromatic anticonvulsants, sulfonamides, #lactams etc) since biologically reactive products derived from drug metabolism, (arene oxides for aromatic antiepileptics, hydroxylamines for sulfamethoxazole etc.) are believed to play an important role in triggering DRESS. If a patient experiences hypersensitivity syndrome with a medication, all drugs having the same chemical structure should be avoided. For example, a severe DRESS has been reported triggered by bosentan in a patient having a past medical history of allergy to sulfonamides. Bosentan actually contains a –SO2NH2 moiety and belongs to the sulfonamide nonantibiotic drugs. After a careful search, practitioners in charge of the patient have understood that because of this common sulfonamide functional group, bosentan might have contributed to this adverse event.

In the introduction,

1. The usual terminology in literature is drug-induced hypersensitivity syndrome (DIHS) rather than drug-induced hypersensitivity reaction (DIHR).
2. The description of the rash is interesting since it is always useful to provide tools to practitioners in order to recognize skin lesions induced by DRESS. Nevertheless, rash may be lacking, that’s why R for Rash in diagnostic criteria defined by Bocquet in 1996 became later R for Reaction (Bégon in 2004 and Roujeau in 2005).
3. “the defining characteristic of DRESS syndrome is organ dysfunction, typically of the liver, kidneys, or lungs”. I would add heart dysfunction also, since hypersensitivity myocarditis is believed to be an important feature of DRESS, unfortunately underrecognized, although life-threatening (Bourgeois, Ben m’rad, Sabatine).
4. “Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome …. is rare”; “DRESS syndrome is estimated to occur in approximately 1 out of 1500 new users of phenytoin or carbamzepine”. Unfortunately epidemiologic estimations are provided by a rather old literature, essentially in pediatric patients exposed to antiepileptics. Thus, Carroll gave the incidence of 1/1000–1/10000 DRESS in 2001, for children treated with anticonvulsants. Precise epidemiologic data are scarce: the real incidence of DRESS is unknown probably because this condition is underdiagnosed and because data are retrieved mainly from retrospective series and literature review of case-reports.
5. “DRESS syndrome often includes hepatitis, pericarditis, interstitial nephritis or interstitial pneumonitis”. Hepatitis is probably the most common feature during the course of DRESS: Cacoub and colleagues extracted 172 cases of DRESS in literature through a Pubmed search over a 12 years-period and found that liver
Involvement occurred in 94% of cases, eosinophilia in 66%, lymphadenopathy in 56%, myocarditis in 2%, kidney in 8%, lung in 5%, central nervous system in 2%. In a cohort of 24 consecutive patients over a four year-period, clinical involvement was as follows: liver 54%, kidney 17%, heart 21%, lung 17%, brain 17%. Other authors suggest that hypersensitivity myocarditis might be largely underecognized (Bourgeois).

6. “First described as a distinct syndrome by Bocquet et al”. Chaiken has first described drug-induced hypersensitivity syndrome in 1950 as a triad of fever, rash and multiorgan failure occurring 1–8 weeks after an aromatic anticonvulsant drug had been started. Bocquet et al have later designated the acronym DRESS. “… fulminant liver failure, occurring in as many as 10% of cases and accounting for the principle cause of mortality in patients affected by DRESS syndrome.” As far as we know, mortality rate during the course of DRESS is also ignored. Several authors advanced a mortality rate of 10%, although Bourgeois reported a mortality of 50% in a series of 22 cases of DRESS-associated myocarditis retrieved from literature. Cacoub retained 5% of mortality from liver origin. In our series published in Medicine in 2009, there was no death for 24 DRESS cases.

Case presentation: questions to the authors

1. Since increase of liver enzymes may also be due to myocarditis, did the authors searched for heart involvement by eventually using biologic tools such as N-terminal-probrain natriuretic peptide (NT-proBNP), Creatin PhosphoKinase (CPK), troponin, electrocardiogram, echocardiography?

2. How long has been the patient followed-up? Do the authors know if patient experienced later any flare on glucorticoids tapering or withdrawal? Is there any hepatic sequela?

3. Will it be possible to precise if other causes of transaminitis have been eliminated, such as viral infection with the following viruses: hepatitis A, B, C, Human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), cytomegalovirus (CMV)? Will it be also possible to precise if the following data are available: antinuclear antibodies?

Discussion

1. As mentionned above, “rare” could be changed for underdiagnosed or underecognized or for another adjective or sentence explaining that its real incidence is unknown

2. “in response to antiepileptic medications”. It would be better to say that DRESS might occur with any drug although the majority of DRESS are due to a small list of drug families such as aromatic anticonvulsants, sulfonamides, fluindione, etc. (Cacoub, Ben m’rad)

3. “recently” is usually used for a period <2 years.

4. Apart Shiohara, Kardaun et al. have also designed a very pertinent scoring system for classifying DRESS cases as definite, probable, possible or no case. This tool has been used for the european registry of severe cutaneous adverse reactions (SCAR) including Stevens-Johnson Syndrome, Toxic epidermal
necrolysis, Acute generalized exanthematous pustulosis and DRESS.

References


Quality of written English: Acceptable

Declaration of competing interests:

I declare that I have no competing interests.