Enliven Archive
Intensifying Thoughts

Case Report www.enlivenarchive.org Enliven: Pharmacovigilance and Drug Safety

A Case of Steven's Johnson Syndrome Probably Related to Antibiotic- Indomethacin/Caffeine/Prochlorperazine Coadministration

Ferraro Maria[1],Rende Pierandrea[2], Squillace Aida[2], Palleria Caterina[2], Gratteri Santo[3], De Sarro Giovambattista[2], and Gallelli Luca[2]

[1]*Internal Medicine Operative Unit, Spoke Acri/Castrovillari- ASP Cosenza, Italy*

[2]*Chair of Pharmacology, Department of Health Science, University of Catanzaro, ClinicalPharmacology and Pharmacovigilance Unit, AO Policlinico MaterDomini Catanzaro, Italy*

[3]*Chair of Forensic Medicine, University of Catanzaro, Italy*

***Corresponding author**: Luca Gallelli, Chair of Pharmacology, Department of Health Science, University of Catanzaro, Clinical Pharmacology and Pharmacovigilance Unit, AO Policlinico MaterDomini Catanzaro, Italy, Tel: +390961712322; Fax: +390961774174; E-mail: gallelli@unicz.it

Received Date: 22nd August 2014

Accepted Date: 18th September 2014

Published Date: 19th September 2014

Citation: Ferraro M, Rende P, Squillace A, Palleria C, Gratteri S, et al.(2014) A Case of Steven's Johnson Syndrome Probably Related to Antibiotic- Indomethacin/Caffeine/Prochlorperazine Coadministration. Enliven:Pharmacovigil Drug Saf1(1):001.

Abstract

Steven Johnson syndrome (SJS) is a skin reaction commonly related to drug treatment. In this case we report a woman who developed a Steven Johnson syndrome during antibiotic treatment, probably related to concomitant administration of indomethacin/caffeine/prochlorperazine.

Keywords

Steven Johnson Syndrome; Woman; Antibiotics; Indomethacin/Caffeine/Prochlorperazine

Steven Johnson syndrome (SJS) is a mucocutaneous cell-mediated hypersensitivity reactions, characterized by fever, malaise, facial puffiness, mucous membrane eruptions, skin lesions, vomiting, and skin eruptions [1,2]. In this paper we report a case of SJS during a drug co-administration.

Case Report

A 49-year-old woman with a medical history of Gilbert's disease, blood hypertension and headache treated with zofenopril (30mg) and caffeine 75mg+ indomethacin 25mg+ prochlorperazine 2mg (Difmetre®), presented to our observation for the onset of diarrhoea, fever, vomiting and asthenia in the last 10 days. At the admission (December 19, 2013), clinical evaluation revealed the presence of fever (38.9°C), and vomiting (6 episodes), while blood pressure was in normal range (125/82 mmHg). Blood chemical evaluation revealed higher levels of C-reactive protein, eritro-sedimentation rate, total and direct bilirubin and procalcitonin (Table 1). Radiological evaluation of thorax, abdomen and brain were negative, as well as the echography of liver, kidney and thyroid. Gastroenteritis was diagnosed and a treatment with ciprofloxacin (Ciproxin®; 500 mg/12 h), piperacilline + tazobactam (Tazocin®; 2gr/12h), rifaximin (Normix®; 2 tablets/day), probiotic (Saccharomyces boulardii 1 tablet/8h), esomeprazole 20mg/day, and a glucosate solution 5% was started. About 7 days later, the patient developed a skin erythematous rash with itch and livid macules having a tendency to rapid coalescence on both hands (Figure 1), followed by ulcers in his mouth. An infectious disease specialist excluded the presence of systemic or local infections, while blood microbiological test excluded the presence of infections related to atypical bacteria or virus. Patient denied history of allergy or autoimmune diseases. The improvement of gastroenteritis, induced the dismission of antibiotics, probiotic and glucosate solution, without the improvement of skin and oral manifestations. 2 days later, dermatologist consultant diagnosed a probable SJS confirmed by skin biopsy excluded the presence of other skin disease (e.g. fixed drug eruptions and erythema multiforme) andrevealed the presence of subepidermal bullae with epidermal cell necrosis and perivascular areas infiltrated with lymphocytes and neutrophils, red blood cell extravasation, pigment incontinence, and parakeratosis.

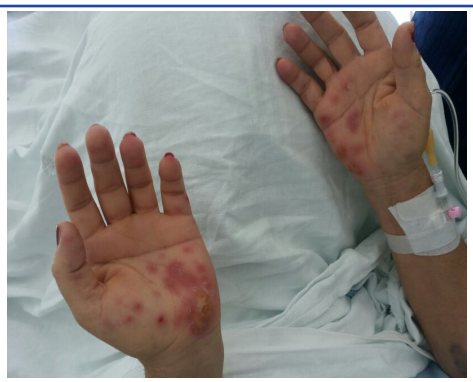

Figure 1 Representation ofskin rash on both hands after the treatment with antibiotics and the fixed association caffeine+indomethacin +prochlorperazine.

Using, the World Health Organization-Uppsala Monitoring Centre causality assessment scale and the Naranjo probability scale (score 6), [3,4] we postulated a probable association between antibiotics, indomethacin/ caffeine/prochlorperazine and SJS.

The absence of headache induced the dismission of Difmetre® with an initial improvement of symptoms in 7 days, with both complete improvement of symptoms and normalization in chemical blood test in about 4 weeks (Table 1).

Parameter (Normal value)	19 December, 2013	21 December, 2013	26 December, 2013	29 December, 2013	03 February 2014
C-reactive protein (CRP; 0.5 -10 mg/L)	300			96	7
Eritrosedimentation rate (<5 mm/h),	55	72	88	107	3
Total bilirubin (0.1-1.3 mg/dL)	3.05	2.6	2.31	1.64	1.2
Direct bilirubin (0.1-0.3 mg/dL)	3.82			1.75	1.1
Indirect bilirubin (0.1-1.2 mg/dL)	0.16				0.14
Procalcitonin (<0.5 ng/mL)	5.76			0.06	0.02
White blood cells (4,500-11,000 per µL)	10,800	10,100	10,900	12,200	8,500
Red cells (3.9 e 5.2 Mil/µl)	3.85		3.74	3.74	4.1
Haemoglobin (12-16 gr/L)	10.5	10.8	9.8	9.6	12.5
Platelets (150.000 e 450.000 per µL)	770,000	772,000	897,000	1,018,000	220,000
Anti double stranded deoxyribonucleic acid (<35 IU/mL)				27.3	
Creatinine (0.5-1.2 mg/dL)	0.9	0.9	1	1	1
Alanine transaminase (0-41IU/L)	34	34	34		32
Aspartate transaminase (0-38 IU/L)	29	30	30		30
gamma glutamyltranspeptidase (5-36 IU/L)	21	21	22		21
Thyroid-Stimulating Hormone (0.3-5 mIU/L)	1.7		1.9		1.7
Triiodothyronine T3 (80-180 mg/dL)	115		118		116
Thyroxine T4 (4.5-13 mg/dL)	9		9.2		9.1

Table 1 Time-table of blood chemical findings

Discussion

In the present case we report the development of SJS, confirmed by skin biopsy, in a 49-year old woman without a previous history of allergy or autoimmune disease. Clinical evaluation and laboratory test excluded the presence of bacterial or viral diseases, and/or other systemic diseases. Since the patient was treated with antibiotics inducing skin reactions [5-9], their discontinuation did not improve symptoms.

History revealed that in the last month, she assumed Difmetre® every day and this could represent the trigger of SJS. Erythema multiforme (EM), SJS and Fixed drug eruptions are acute bullous disorders that may be accurately differentiated. Erythema multiforme, is a self-limiting disease without important residual symptoms, usually initiated by infection with herpes simplex virus [10], while fixed drug eruptions is a drug-related skin disorder characterized by a limited number of round erythematous patches resolving in a few days but recurring on the same sites a few hours after the drug rechallenge [11].

In the present report, skin manifestation and history excluded these skin diseases. In fact, it has been reported that NSAIDs are involved in skin reactions [12-14], therefore we can't exclude that indomethacin administered in low dosage (25 mg) for a long time (30 days) might have had a role in both development and maintenance of SJS. To date no other reports documented an association between antibiotic, indomethacin/caffeine/prochlorperazine and SJS. However, since other clinical data are necessary in order to validate this observation, we suggest evaluating carefully the drugs during a co-administration.

Conflict of Interest

We have no conflict of interest.

Reference

1 Castana O, Rempelos G, Anagiotos G, Apostolopoulou C, Dimitrouli A, et al. (2009) Stevens-johnson syndrome: a case report. Ann Burns Fire Disasters 22: 147-151.

2 Gau SS, Chao PF, Lin YJ, Chang CJ, Gau CS (2008) The association between carbamazepine and valproate and adverse cutaneous drug reactions in patients with bipolar disorder: a nested matched case-control study. J Clin Psychopharmacol 28: 509-517.

3 Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, et al. (1981) A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 30: 239-245.

4 http://www.WHO-UMC.org/graphics/4409.pdf

5 Cholongitas E, Georgousaki C, Spyrou S, Katsogridakis K, Dasenaki M (2009) Stevens-Johnson syndrome related to ciprofloxacin, possibly enhanced by overadministration of levothyroxine. Dermatol Online J 15:16.

6 Okan G, Yaylaci S, Peker O, Kaymakoglu S, Saruc M (2008) Vanishing bile duct and Stevens-Johnson syndrome associated with ciprofloxacin treated with tacrolimus. WJG 14: 4697-4700.

7 Gallelli L, Ferreri G, Colosimo M, Pirritano D, Guadagnino L, et al. (2002) Adverse drug reactions to antibiotics observed in two pulmonology divisions of catanzaro, Italy: a six-year retrospective study. Pharmacol Res 46: 395-400.

8 Patel AS, Supan EM, Ali SN (2013) Toxic epidermal necrolysis associated with rifaximin. Am J Health Syst Pharm 70: 874-876.

9 Prabhu VA, Doddapaneni S, Thunga G, Thiyagu R, Prabhu MM, et al. (2013) Phenytoin induced Stevens-Johnson syndrome exacerbated by cefepime. J Pharmacol Pharmacother 4: 291-293.

10 Tomasini C, Derlino F, Quaglino P, Caproni M, Borroni G (2014) From erythema multiforme to toxic epidermal necrolysis. Same spectrum or different diseases? G Ital Dermatol Venereol 149: 243-261.

11 Kauppinen K, Stubb S. (1985) Fixed eruptions: causative drugs and challenge tests. Br J Dermatol 112: 575-578.

12 Giofre C, Scicchitano F, Palleria C, Mazzitello C, Ciriaco M, et al. (2013) Pharmacovigilance and drug safety in Calabria (Italy): 2012 adverse events analysis. J Pharmacol Pharmacother 4: 55-60.

13 Gallelli L, Colosimo M, Pirritano D, Ferraro M, De Fazio S, et al. (2007) Retrospective evaluation of adverse drug reactions induced by nonsteroidal anti-inflammatory drugs. Clin Drug Investig 27: 115-122.

14 Weinand C, Xu W, Perbix W, Lefering R, Maegele M, et al. (2013) 27 years of a single burn centre experience with Stevens-Johnson syndrome and toxic epidermal necrolysis: analysis of mortality risk for causative agents. Burns 39: 1449-1455.