Case Report

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SJS/TEN Caused by Meloxicam: A Case Report

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1. Abstract

We reported a case of SJS/TEN in an elderly patient who took meloxicam tablets at home for the treatment of lumbar disc herniation and searched the literature to study the risk factors of SJS/TEN and the factors affecting the prognosis. The case was reported based on the patient's own situation and literature, hoping to provide reference for the clinical practice.

2. Keywords:
Meloxicam; SJS/TEN

3. Introduction

We reports a rare case of severe adverse reactions which was found for the first time in our hospital and successfully treated. We analyzed the risk factors of this adverse reaction and the corresponding treatment measures. It provides a reference for clinical use and the next use of this drug can be avoided according to related risk factors, We believe that this case can reduce or even avoid the occurrence of this serious adverse reaction.

4. Case Description

Ms. Lin, 71 suffers from pain and numbness of lower limbs due to lumbar disc herniation. She has been taking meloxicam once daily (7.5mg each time) at home since February 2, 2023. On February 12, 2023, she felt feverish and went to the local hospital for treatment with her maximum temperature testing to be 39 degrees, and scattered red rashes were seen in her abdomen with local fusion. After admission, the patient suffered from skin and mucous membrane ulceration and peeling all over the body, accompanied by blister formation, local bleeding and exudation, mainly in the trunk, limbs, face, neck, eye, mouth, nasal mucosa, anus and perineum. The local hospital diagnosis was "1. Pulmonary infection 2. Severe drug dermatitis (drug eruption)". The suspect drug meloxicam tablets were immediately stopped, and anti-infection cefoperazone sulbactam (3g+NS100ml, q8h, ivgtt) and Methyl-prednisolone sodium succinate (60mg, ivgtt, qd)was given, and at the same time symptomatic support treatment such as fluid replacement, phlegm reduction, calcium supplementation, and stomach protection were also given. After treatment, the patient's skin around the eyes, mouth, and lips peeled off, and the skin and mucous membranes of the whole body worsened. There was still persistent high fever symptom. For further diagnosis and treatment, she was transferred to our hospital on February 16, 2023. Admission examination: Acute painful facial features, pigmentation of the skin and mucous membranes throughout the body, weakened elasticity, thick respiratory sounds in both lungs, scattered wet rales in both lungs, numerous red rashes on the chest, back, and face, peripheral redness and swelling, skin ulceration, and a small amount of blisters. Previous history: hypertension for more than 3 years.

Auxiliary examination: anti Ro-52 antibody positive (+++), anti SSA antibody positive (+++). The glutamicpyruvic transaminase was 43U/L, the glutamic oxalacetic transaminase was 46U/L, the creatinine was 87μMol/L, CRCL:58.03ml/min, potassium 3.26mmol/L, hypersensitive C-reactive protein 116.13mg/L, red blood cell sedimentation rate 56.5mm/h; interleukin 6195.96pg/ml, procalcitonin 0.334ng/ml. After admission, symptomatic treatments such as anti-allergy and anti-infection treatments were given. After the consultation on February 17, 2023, considering the patient's skin and mucosa were significantly ulcerated and the oral mucosal white spots were more obvious than before, which meant it was necessary to be vigilant against Aspergillus infection, we added intravenous injection of human immunoglobulin (10mg, ivgtt, qd) and injection of voriconazole (0.2g, ivgtt, q12h, initial dose 300mg, ivgtt, q12h) for treatment.

On February 19, 2023, the patient's entire body was scattered with blisters accompanied by skin damage, with an increase in local skin lesions, aggravation of blister formation, and local skin ulceration. Sputum culture, urine culture, and wound secretion culture were all sterile. And

the intravenously human immunoglobulin was augmented (20mg, ivgtt, qd). On February 23, 2023, the patient's entire body was scattered with blisters. During dressing changes in anterior and back of the neck, chest and back, the patient felt pain because of the severe surface skin damaging and local exacerbation. The skin was severely ulcerated, with pus coating adhesion visible locally. There was no chest pain, chest tightness, fever, chills, dizziness, or other discomfort. Currently, the patient's skin lesion area was evaluated to be about 54% (3% in the head, 3% in the face, 3% in the neck, 18% in the limbs, and 27% in the trunk), and the condition was severe. After consultation, the patient was transferred to the ICU for further treatment. After entering the ICU, the treatment plans were immediately developed as following: 1. Basic treatment: single room ward, skin management (daily dressing changes, dressings), and various indicator tests; 2. Supporting treatment: Based on the patient's condition, personalized nutritional plans were developed to regulate various electrolyte levels. 3. Drug treatment: antibacterial drugs, hormones, and intravenous immunoglobulin therapy were given continually. Auxiliary examination: Lymphocytes: 0.18 × 109/L, lymphocyte percentage: 2.4%, albumin: 26.5g/L, white cell ratio: 0.66.

On March 2, 2023, the skin lesions of the patient's limbs were improved and the hemogram was also improved. The temperature was controlled well, and there was no evidence of positive bacteria infection. Cefoperazone sodium, sulbactam sodium and vancomycin were substituted with cefuroxime (1.5g, ivgtt, q8h) and methylprednisolone (40mg, ivgtt, qd). Other treatments included symptomatic support treatments such as fluid replacement, maintaining internal environment stability, etc. On March 6, 2023, the patient's general condition improved significantly. Her vital signs were stable and the skin and mucosa throughout the body were red and swell. The scabs on the skin of the chest and abdomen have receded, while some scabs on the skin of the waist and back can still be seen. She was transferred from the ICU to the routine treatment. On March 13, 2023, the patient's overall rash had become epithelialized, and no new rash, fever, cough, and normal bowel movements were observed. The treatment was considered effective, and she was allowed to be discharged. The skin changes were detailed in Figures 1, 2, 3, and 4.

5. Discussion

Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) were rare severe skin and mucosal decomposition diseases [3-7]. According to the degree of skin detachment, SJS/TEN can be divided into SJS, TEN, and SJS TEN overlap. It can affect the skin, oral mucosa, eyes, esophagus, mouth, pharynx, throat, skin, and genitalia. In some studies, before the onset of SJS/TEN disease, the prodromal symptoms persisted for 1 to 7 days, including the discomfort, difficult swallowing, and eye itching, and followed by high fever, respiratory symptoms, and rash accompanied by blisters or lesions, causing mucosal inflammation. Skin lesions usually developed a few days later after inflammation and dryness in the oral and genital areas. The oral, eye, and genital mucosa were gradually affected by erythema, erosion, and pseudomembranes [8,9]. The mortality rate which reported by Liqin Wang et al. ranged from 4.8% to 14.8% [4], while the rate reported by Abhigan Babu Shrestha et al. ranged from 10% to 34% [5], and Erika Yue Lee et al. reported the highest of over 50%[10].The mortality Mainly caused by the drugs, infections, immunosuppression, and radiation therapy [5,6]. In terms of drugs, the most reported drugs were antibiotics, anticonvulsants, analgesics/anesthetics, and anti-tumor drugs [4,6,9,11-14], the death generally appeared 4 to 28 days after using the drugs [5], and then decreased within 8 weeks or longer [14]. Among NSAIDS drugs, Oxycam derivatives have the largest correlation with SJS and TEN, while the correlation between COX-2 and meloxicam is still unclear [12]. The risk of developing SJS or TEN after drug exposure appeared to be the highest in elderly women during the first few weeks of treatment [5,8,12]. The development of SS-like symptoms and positive anti SS-A antibodies in SJS/TEN are closely related with the high incidence rate. Yuko Watanabe et al. reported that comparing with negative results, patients with positive SS-A antibodies at the onset of SJS/TEN exhibited more severe SJS/TEN symptoms and more severe eye symptoms, such as mucus involvement. Therefore, antibody positive patients exhibited a higher rate of adverse prognostic outcomes [13]. Qian Wang et al. believed that lymphocyte ratio (NLR) and albumin ratio (CAR) could partially reflect the severity and inflammatory status of SJS/TEN patients and the Lymphocyte ratio (NLR) was also a predictor of death [15].

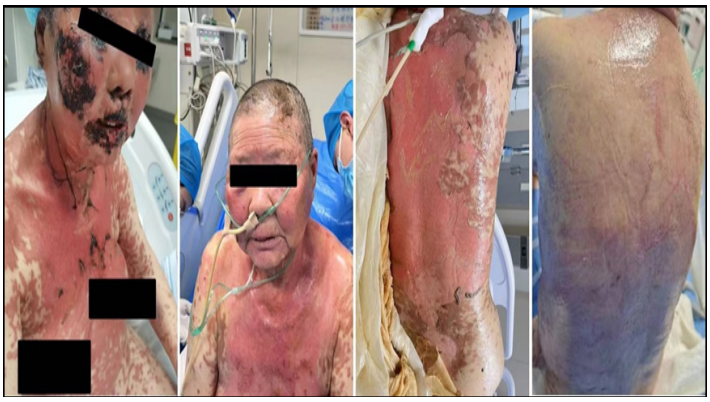

Figure 1: Details of the patient's skin changes

The elderly woman developed a skin rash within 10 days after using the suspected drug. Although the suspected drug was stopped in time, the patient's skin continued to deteriorate and there was a continuous progression of more than 30% of the affected skin area, which ultimately leading to severe TEN. SJS/TEN was a specific drug hypersensitivity reaction, whose pathogenesis was not fully understood, but was considered immune mediated [14]. When the patient was admitted, both anti Ro-52 and anti SSA antibodies were positive, and the ratio of lymphocytes to white blood cells was very low. The Lymphocytes was 0.18×109/L and the white cell ratio was 0.66. The patient's eyes, mouth, perineum, mucus, etc. were also affected ultimately. The patient had many factors that led to poor prognosis, and was later transferred to the ICU for diagnosis and treatment due to severe conditions. Through collaboration among various disciplines, scientific treatment and meticulous care in

the ICU, the patient's skin condition gradually improved and other basic conditions were acceptable. Finally, the patient was successful treated and discharged.

6. Conclusion

When the doctor used drugs in clinical practice, high attention should be paid to the suspicious skin rashes. Then the relevant causes should be promptly investigated, the relevant suspicious drugs should be stopped as soon as possible, and symptomatic treatment should be given to avoid more serious skin damage diseases. After the occurrence of SJS/TEN, the treatment methods required multidisciplinary collaboration and the potentially pathogenic drugs should be immediately stopped. Besides, it was crucial that the patients were referraled to a suitable medical center timely for specific supportive treatment.

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