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Case Report

Drug Eruptions with Cases: Fixed Drug Eruption and Dress Syndrome

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ABSTRACT

Cutaneous drug reactions usually occur with mild and self-limiting lesions, but severe forms can be life-threatening. Non-steroidal anti-inflammatory drugs, antibiotics, and anticonvulsants often cause drug reactions. Herein, we presented two cases of immunological drug reaction, one with mild and localized fixed drug eruption and the other with more severe and diffuse DRESS syndrome.

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Introduction

Adverse drug reactions are undesirable side effects of routinely used or newly started drugs and are most common in the skin. Cutaneous drug reactions (CDR) are common and usually occur with mild and self-limiting lesions, and some of its severe forms can be life-threatening.[1,2] CDR may occur due to non-immunological (90-95%) and immunological (5-10%) mechanisms. Examples of non-immunological drug reactions are pharmacological side effects, drug-drug interactions, and drug toxicity. Immunological drug reactions are mainly divided into four types: Type 1 (IgE-mediated), Type 2 (cytotoxic), Type 3 (immune complex-mediated), and Type 4 (delayed-type/cell-mediated reactions).[3] However, some unclassifiable, immunological skin reactions include maculopapular skin rashes with specific T cell reactivation, fixed drug eruption, and specific drug-associated hypersensitivity syndromes.[4,5] Risk factors for non-immune drug reactions are female gender, renal impairment, liver disease, severe comorbidity, polypharmacy, HIV infection, herpes infection, systemic lupus erythematosus and alcoholism. Risk factors for immunological skin reactions are female gender, being an adult, HIV infection, history of drug hypersensitivity, asthma, beta-blocker use, concurrent viral infection, systemic lupus erythematosus.[6]

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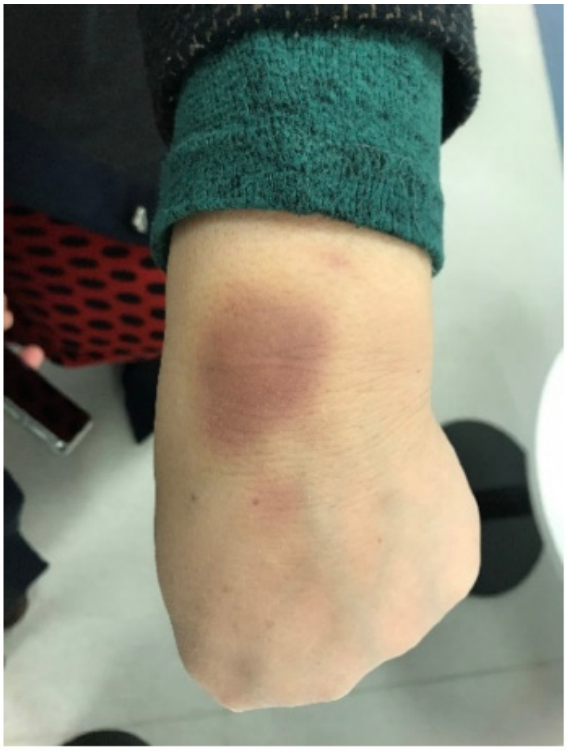
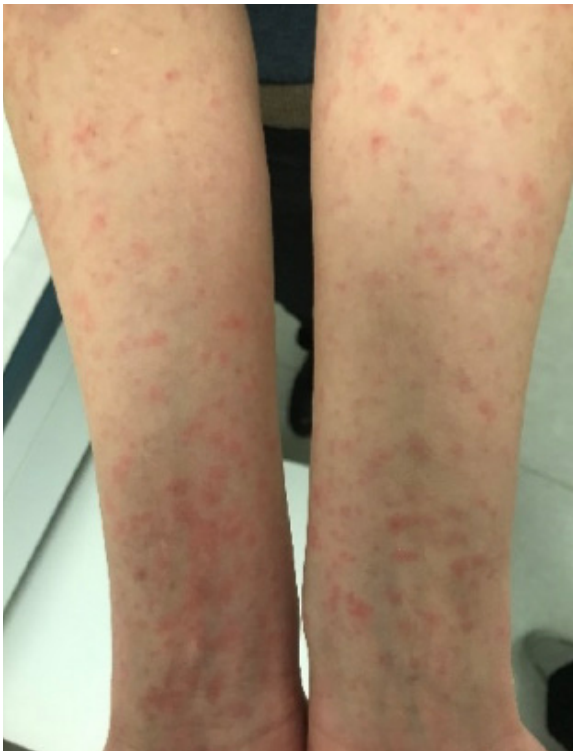
Physicians of all branches should be familiar with cutaneous drug reactions for early diagnosis and treatment since they may encounter it frequently in their daily practice.[5] There are nearly 30 skin-drug reactions, and the most common forms are exanthematous drug eruptions and urticarial.[6,7] Fatal skin reactions with skin detachment or necrosis on large areas of the body include Steven-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and drug rash with eosinophilia and systemic symptoms syndrome (DRESS).[6] The drug groups to often cause drug reactions for the skin are non-steroidal anti-inflammatory drugs, antibiotics and anticonvulsants.[8] Herein, we presented two cases of immunological drug reaction, one with mild and localized fixed drug eruption and the other with more severe and diffuse DRESS syndrome.

Case Report

The first case was a 56-year-old female patient diagnosed with ankylosing spondylitis and was receiving 40 mg of adalimumab every two weeks for three years. She stated that she was using diclofenac sodium 50 mg oral tablets and sometimes intramuscular injections of diclofenac sodium and thiocolchicoside due to the joint pain she experienced from time to time over the past year. Neither she uses other drugs, nor does she smoke. The patient applied to the dermatology outpatient clinic with a sharply defined, hyperpigmented macular-looking lesion on the dorsal aspect of the left hand (*Picture 1*). The patient stated that similar lesions had appeared in the same area from time to time in the last year. When it first appeared, it was a more vivid purple colour. The colour of the lesions became brownish over time and was accompanied by complaints such as itching and burning. The blood tests of the patient were no pathological findings. We diagnosed the patient with fixed drug eruption due to a history of diclofenac sodium drug use and lesion characteristics. We discontinued the suspected diclofenac sodium drug and gave topical corticosteroid treatment.



Picture 1. Hyperpigmented macular lesion of the dorsal left hand of the patient developing a fixed drug eruption.



Picture 2. Erythematous maculopapular lesions are seen on the inner sides of the bilateral forearms and throughout the body of the patient with DRESS Syndrome.

The second case, a 35-year-old female patient, started treatment of carbamazepine 400 mg/day with the diagnosis of epilepsy one month ago, and the patient did not have an additional disease or a history of any other drug use. The patient applied to the hospital with the complaint of a widespread erythematous maculopapular rash on the body (*Picture 2*) and itching, which started three days ago and is becoming increasingly severe. The patient had a fever reaching 38 °C from time to time, and in her dermatological examination, there were no findings in the oral and genital mucosa. She had bilateral cervical lymphadenopathy in lymph node examination. The laboratory evaluation revealed a more than ten-fold increase in liver function tests (AST: 313 U/L, ALT: 624 U/L, ALP: 291 U/L, GGT: 261 U/L). We diagnosed the patient with DRESS syndrome with clinical and laboratory findings, discontinued the carbamazepine drug, and replaced it with 1,000 mg/day levetiracetam. She was hospitalized for systemic steroid treatment and further examination in the dermatology service.

Discussion

Fixed drug eruptions are common cutaneous drug reactions with recurrent characteristic lesions on the same areas of the skin or mucosa after repeated administration of the causative drug. Among the drug groups, antibiotics (trimethoprim-sulfamethoxazole, tetracycline, penicillin, erythromycin) are first, and non-steroidal anti-inflammatory drugs (diclofenac sodium, aspirin, naproxen, ibuprofen) are in the second place of cause.[9,10] Acute lesions can be seen usually 30 minutes to 8 hours after ingestion of the causative drug. However, this period can last up to 2 weeks.[11,12] In the first case, diclofenac sodium was the causative drug for fixed drug eruption. Fixed drug eruptions can usually be seen characteristically in the same region after drug intake. They may also observe in different body parts with repeated drug doses. Lesions are often sharply delimited by round or oval, itchy, erythematous plaques that may sometimes turn dark purple and sometimes become vesiculobullous.[9] The most common site of involvement for men is the genital area, and for women, it is the extremities.[11] In this case, the location of the observed itchy lesion, which has a more vivid purple colour at first and becomes a paler plaque over time, was the dorsal aspect of the hand.

DRESS syndrome is a drug-associated hypersensitivity reaction that may be accompanied by haematological abnormalities such as generalized mucocutaneous rash, fever, lymphadenopathy, hepatitis, eosinophilia, leukocytosis or atypical lymphocyte, and sometimes with eosinophilic infiltration, especially kidney, heart, lung and pancreas organ involvement.[13] The aetiology role played by the drugs used between 3 weeks and three months is a picture that differs from other cutaneous drug reactions with multiorgan involvement.[13] The drug groups that most often cause DRESS syndrome include anticonvulsants (carbamazepine, phenytoin, lamotrigine, phenobarbital), allopurinol and antibacterials.[14] Scoring criteria established by the RegiSCAR (registry of severe cutaneous adverse reactions) group are often used to confirm or exclude a diagnosis of DRESS syndrome.[15,16] The patient also used carbamazepine as a suspected agent. 6 out of 7 potential DRESS cases determined by the RegiSCAR group were seen for the case. When evaluated with advanced diagnostic criteria, it was considered a possible DRESS case with a rate of 3/9. Haematological abnormalities such as eosinophilia are not always seen in DRESS cases at diagnosis but may develop over time.[14,16] Hematological abnormalities were not observed at the diagnosis for that case.

As a result, physicians of all branches should be familiar with cutaneous drug reactions that they may frequently encounter in their daily practice for early diagnosis and treatment. When cutaneous drug reactions are suspected, it is necessary to approach the patient holistically and systematically. First of all, the characteristic of the primary lesion should be identified, and its distribution determined. All prescription/nonprescription drugs used by the patient in the last three months should be questioned. The patient should be evaluated regarding mucosal involvement, fever, lymphadenopathy, and internal organ involvement. In all CDRs, it is essential to discontinue the known/suspected agent at the first stage. In the presence of a severe cutaneous

drug reaction, immediate referral to an advanced centre or consultation with the relevant branch is required.

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Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors' Contribution

Study Conception: SHA, YG; Study Design: SHA, YG; Supervision: SHA, YG; Materials: SHA, YG; Data Collection and/or Processing: SHA; Statistical Analysis and/or Data Interpretation: SEY; Literature Review: SHA, YG; Manuscript Preparation: SHA, YG; Critical Review: YG.

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