FIXED DRUG ERUPTION. A STUDY OF 11 CASES AND A REVIEW OF THE LITERATURE

ERITEMUL FIX MEDICAMENTOS. UN STUDIU DE 11 CAZURI ŞI UN REVIEW AL LITERATURII

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Abstract

Fixed drug eruption represents a drug-related cutaneous reaction which appears in the same place in case of repeated administration of a drug to which the patient shows intolerance. Skin lesions are characterized by erythematous patches or plaques that appear between 30 minutes and 8 hours after the therapy is introduced. The pathogenetic mechanism is represented by the awareness of CD 8 T lymphocytes from the skin, remaining in a sleeping state and reacting in case of a new administration. This type of after-treatment reaction is most frequently cited in connection with cotrimoxazole, betalactamine and nonsteroidal antiinfl amatory drugs (NSAIDs). We will present eleven clinical cases of fixed drug eruptions from the casuistry of the Dermatology Clinic from Târgu Mureş. The knowledge of this dermatosis by clinicians and pharmacists leads to full remission and it also helps avoid recurrence of the lesion.

Keywords: fixed drug eruptions, drug-related cutaneous reactions

Rezumat

Eritemul fix medicamentos reprezintă o reacţie cutanată postmedicamentoasă ce apare în acelaşi loc în cazul administrării repetate a unui medicament faţă de care pacientul prezintă intoleranţă. Leziunile cutanate se caracterizează prin pete sau plăci eritematoase ce apar între 30 de minute şi 8 ore de la introducerea terapiei. Mecanismul patogenetic este reprezentat de sensibilizarea limfocitelor T CD8 de la nivel cutanat care rămân în stare dormandă şi se reactivează la o nouă administrare. Acest tip de reacţie postmedicamentoasă este citată cel mai frecvent la cotrimoxazol, betalactamine şi antinfiamatoare nesteroidiene. Vom prezenta unsprezece cazuri clinice de eritem fix medicamentos din cazistica Clinicii de Dermatovenerologie din Târgu Mureş. Cunoaşterea acestei dermatozne de către clinicieni duce la o atitudine terapeutică corectă cu remisiunea completă, precum şi la prevenirea reapariţiei leziunii.
Introduction

Fixed drug eruption represents a drug-related cutaneous reaction which appears in the same place in case of repeated administration of a drug to which the patient shows intolerance (1). More rarely, it is possible to appear as a reaction to different drugs and in case of chronic administration, the number of the locations may also increase. Mixed sensitivity reactions may occur between tetracyclines and anticonvulsants (2, 3). Skin lesions are characterized by erythematous patches or plaques that appear between 30 minutes and 8 hours after introducing the therapy. In case of a favorable evolution preceded, of course, by ceasing the drug involved, the lesions evolve into crusting and scaling. These may be followed by residual pigmentation. We sometimes meet the central blister or nodular lesions or even lesions mimicking erythema multiforme. Limbs, especially the distal areas and the genital region, represent the localizations of choice. This type of after-treatment reaction is most frequently cited in connection with co-trimoxazole, betalactamine and nonsteroidal antiinflammatory drugs (NSAIDs). In this respect, acetylsalicylic acid is the drug most frequently involved in pediatric medicine. The pathogenetic mechanism is represented by the awareness of CD 8 T lymphocytes in the skin, remaining in a sleeping state and reactivating in case of a new administration.

Aim of the study

We aim to present eleven clinical cases of fixed drug eruption from the casuistry of the Dermatology Clinic of Târgu Mureş and a literature review on this drug-related skin reaction.

Results

All patients (7 females and 4 males) aged between 8 and 70 years were from urban areas. Skin lesions were asymptomatic and most frequently localized on the right flank (3 cases). The incriminated drugs were cotrimoxazole (3 cases), ibuprofen (2 cases), piroxicam (2 cases), silymarina (1 case), alprazolam (1 case), ciprofloxacin (1 case) and metamizol sodium (1 case) (Table 1, Figures 1-13). Based on the clinical appearance and personal medical history, we established the diagnosis of fixed drug eruption. Ceasing the responsible drug administration and locally applying corticosteroid creams led to remission of lesions with or without residual hyperpigmentation.

Discussions

A fixed drug eruption represents a relatively common cutaneous reaction. Its recognition by clinicians or pharmacists leads to full remission and avoidance. It is frequently connected to betalactam antibiotics or sulfonamides, rarely to fluconazole and levocetirizine (9, 10). According to the latest study conducted by Jung et al. in 2014, in Korea, on 134 patients, this after-treatment reaction was more common in males (four patients from this group required the reaction). The reaction was most probably connected to nonsteroidal antiinflammatory drugs (11). Among our patients, women were more affected than men, with flanks being the most common locations; the drugs mostly incriminated were co-trimoxazole and NSAIDs. Similarly, Heng et al. found the NSAIDs most frequently involved in a study on 126 patients in Singapore. Etoricoxib was the most widespread agent, being responsible for 62 out of 126 cases (12). In previous studies, the role of cotrimoxazole prevailed. Kanwar found it was involved in 45 cases out of 98 patients in which he had confirmed the eruption with challenge tests (13). At the same time, in a study on 31 patients, Lee proved the implication of cotrimoxazole in most cases (14). We have encountered this association with three patients.

Interestingly, the occurrence of this type of reaction was described after administrating antihistamine H1 such as pheniramine, loratadine, cetirizine and levocetirizine (15, 16). There were two cited cases located on penis and fingers, due to anesthesia with propofol (17).

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Sex</th>
<th>Localization</th>
<th>Relaps</th>
<th>Drug</th>
<th>Figure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>M</td>
<td>right flank</td>
<td>no</td>
<td>cotrimoxazole</td>
<td>Fig. 1</td>
</tr>
<tr>
<td>2.</td>
<td>M</td>
<td>right flank</td>
<td>yes</td>
<td>cotrimoxazole</td>
<td>Fig. 2</td>
</tr>
<tr>
<td>3.</td>
<td>M</td>
<td>penis</td>
<td>no</td>
<td>cotrimoxazole</td>
<td>Fig. 3</td>
</tr>
<tr>
<td>4.</td>
<td>M</td>
<td>left leg</td>
<td>no</td>
<td>alprazolam</td>
<td>Fig. 4</td>
</tr>
<tr>
<td>5.</td>
<td>F</td>
<td>abdominal</td>
<td>no</td>
<td>ciprofloxacin</td>
<td>Fig. 5</td>
</tr>
<tr>
<td>6.</td>
<td>F</td>
<td>right forearm</td>
<td>yes</td>
<td>ibuprofen</td>
<td>Fig. 6</td>
</tr>
<tr>
<td>7.</td>
<td>F</td>
<td>right flank</td>
<td>no</td>
<td>silymarin</td>
<td>Fig. 7</td>
</tr>
<tr>
<td>8.</td>
<td>F</td>
<td>left hypochondrium</td>
<td>no</td>
<td>piroxicam</td>
<td>Fig. 8</td>
</tr>
<tr>
<td>9.</td>
<td>F</td>
<td>neck</td>
<td>no</td>
<td>piroxicam</td>
<td>Fig. 9</td>
</tr>
<tr>
<td>10.</td>
<td>F</td>
<td>right gluteal region</td>
<td>no</td>
<td>metamizol sodium</td>
<td>Fig. 10</td>
</tr>
<tr>
<td>11.</td>
<td>F</td>
<td>right foot, fingers II-V</td>
<td>no</td>
<td>ibuprofen</td>
<td>Fig. 11</td>
</tr>
</tbody>
</table>
In 2014, a case of mixed reaction was reported regarding quinolones. Kameswari et al. described a case of fixed drug eruption after administering ciprofloxacin. The lesion relapsed after administering ofloxacin (18). The 68 year old female patient hospitalized in our clinic for venous ulcers on her right shin presented an erythematous plaque on her abdomen, which debuted 7 hours after administering 500 mg of ciprofloxacin. The antibiotic therapy was continued with Amoxicillin/clavulanic acid, and the lesion remitted in 20 days, leaving a post inflammatory hyperpigmentation.

This reaction is rarely cited for clarithromycin. Malkarnekar reported a case of fixed drug reaction localized on fingers, lower lip and left thigh (19). Lithium was described as an inducer of fixed drug eruption by Metha et al in 2014, on a patient with bipolar psychiatric disorder. This drug is known as...
Clinical study

Gruber in 1997, describing the occurrence of the lesion on a male known with this type of reactions to cotrimoxazole. The lesion debuted after sexual intercourse with a woman using the drug (21). Our case presenting an erythematous lesion on the penis is a result of personal ingestion of cotrimoxazole approximately three hours before.

If normally lesions are unique or relatively few in number, sometimes dermatitis with extensive tegument involvement can occur. Nitya et al. described a severe case after doxycycline in a 37 year old patient. She developed extensive erythematous plaques covered with blisters, leaving extensive erosions which predisposed to dehydration and a high risk of sepsis with cutaneous starting point (22). Cotrimoxazole is frequently cited for these generalized reactions (23). Among our patients, edematous plaques covered with blisters were seen only in the woman with silymarin ingestion (single medication) (Figure 7). Similar lesions are also cited regarding the antituberculous therapy, tranexamic acid, ursodeoxycholic acid, flurbiprofen, azithromycin, and metformin (24-29).

Conclusions

Fixed drug eruption is a cutaneous reaction most frequently caused by cotrimoxazole and nonsteroidal antiinflammatory drugs. The recognition of this dermatosis by clinicians and pharmacists is important for the remission and prevention of new appearances.

Bibliography

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