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EXANTHEMA MEDICAMENTOSUM AS A SIDE EFFECT OF PROMAZINE

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SUMMARY

Dermatological side effects of psychopharmacological drugs are fortunately not so often. They are mostly presented in the group of mood stabilizers and antiepileptic drugs, particularly the carbamazepine and lamotrigine, and can be manifested through the Stevens Johnson syndrome, Toxic Epidermal Necrolysis (TEN)/Lyell's syndrome with about 30% lethality. According to the literature the group of phenothiazines is the category of drugs with rare appearances of skin reactions. Promazine, aliphatic phenothiazines antipsychotic, including less frequent side effects in the leaflet states increased skin sensitivity to sun, skin rash-associated with contact dermatitis, allergic reactions, cholestatic icterus. The only reported dermatological side effect of promazine is its metabolites deposition in the cornea. Analyzing the e-data basis we have not found references connecting the Exanthema medicamentosum as a side effect of promazine. A forty-two years old female patient was admitted to the Dermatological Clinic because of suspected exanthema, undoubtedly caused by promazine as a medication for Sy. Borderline.

Key words: *promazine - exanthema medicamentosum*

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INTRODUCTION

Dermatological side effects of psychopharmacological drugs were mostly presented in the group of mood stabilizers and antiepileptic drugs, particularly for the carbamazepine and lamotrigine and can be manifested through the Stevens Johnson syndrome, Toxic Epidermal Necrolysis (TEN)/Lyell's syndrome with about 30% lethality. The drug reactions occur within approximately 14 days. Generally, in the first two months of therapy, patients are mostly apt to develop this syndrome. Both genders are equally represented, the prevalence is higher among younger than 30 and older than 65 years. The higher risk of developing this syndrome exists with HIV infection, taking corticosteroids, hereditary tendency, allergy, immunization, SLE, and inflammatory bowel diseases. Promazine, aliphatic phenothiazines antipsychotic, including less frequent side effects in the leaflet states increased skin sensitivity to sun, skin rash-associated with contact dermatitis, allergic reactions, cholestatic icterus.

The group of phenothiazines is the category of drugs with rare appearances of skin reactions, according to literature. Dermatitis and photosensitivity are listed as dermatological side effects of chlorpromazine, levomepromazine and perazine, in both literature and databases. The only reported dermatological side effect of promazine is its metabolites deposition in the cornea.

CASE REPORT

A forty-two years old female patient was admitted to the Dermatological Clinic because of suspected exanthema. As stated in her medical history, she had been in the psychiatric treatment because of Personality disorder (F 60.3) and treated with venlafaxine and levomepromazine. She had been taking promazine drag a 25 mg 1,0,2 per os for two months. Three days before the hospital admission a macular, red-purple exanthema had suddenly occurred. The patient had listed extreme itching. On the day of admission a slight edema of face and hands was present. The lips and tongue were not swollen. A maculopapular exanthema of different sizes was present on the skin of her face, limbs and trunk. Rash occasionally coalesced, especially on the chest. During her stay in the hospital the exanthema coalesced, especially on the inner thigh with a blistering of approximately 1-2 cm, which could burst and form painful erosions. The patient received hospital treatment as following: injections of metilprednizolon (Medrol) in dose of 60 mg, with a gradual reduction of dose, kloropiramin (Synopen) injections in dose of 20 mg, cetirizin (Letizen) orally in dose of 10 mg, local betamethason+gentamicyn (Belogent) cream and hexitidin (Belosept) solution. The psychiatric treatment with promazine was discontinued. A psychiatrist was consulted and he introduced alprazolam tbl a 0.5 mg orally three times a day. The applied therapy led to improvement of clinical features.

DISCUSSION

Maculopapular exanthems (Figure 1.) are the most common adverse drug reactions, along with urticaria. A type IV delayed hypersensitivity reaction is suspected of causing most medicament exanthems.

The most common causes of exanthems include ampicilin, amoxicillin, other penicillins, phenylbutazone, sulfonamides, phenytoin, the group of mood stabilizers and antiepileptic drugs, carbamazepine (Table 1.). Less frequent offenders include some NSAIDs, cephalosporins, chlorpromazine, meprobamate.

Table 1. Frequency of cutaneous reactions for various categories of drugs

Class	Examples	Frequency
Antibiotics	Penicillin (especially ampicillin and amoxicillin)	High
	Cephalosporins, tetracyclines	Moderate
	Erythromycin	Low
Sulfonamides	Cross-reaction with diuretics or oral hypoglycemic agents	Moderate
NSAIDs	Aspirin, indomethacin, phenylbutazone, oxicams	Moderate
Anti-seizure medications	Carbamazepine	High
	Phenytoin	Moderate
	Barbiturates Lamotrigine	Low
Psychotherapeutic agents	Phenothiazines	Low
	Benzodiazepines	Low
Others	Gold salts	High
	Allopurinol	High
	Isoniazid nevirapine	Moderate, low

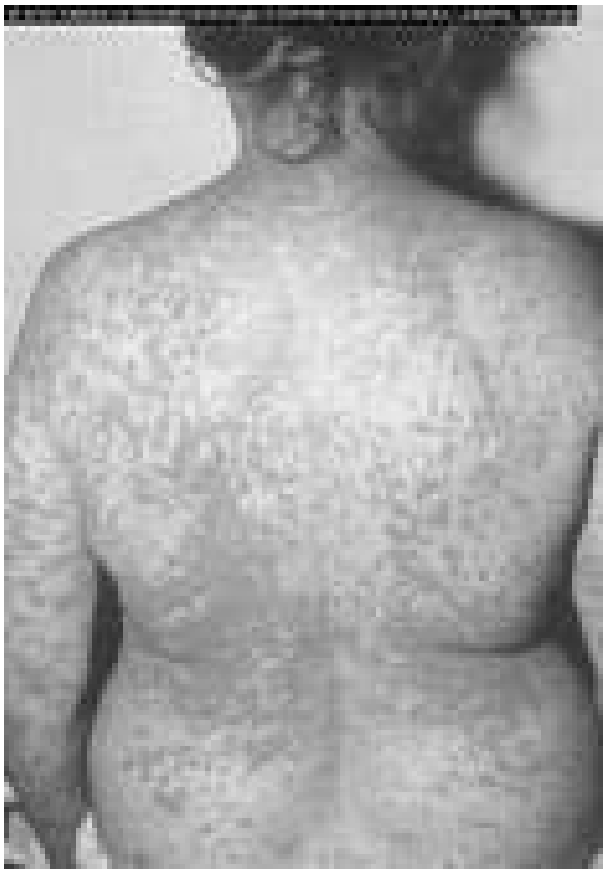

Figure 1. Exanthema medicamentosum

The clinical appearance of drug exanthems is highly variable, with the individual lesions varying greatly in size, shape, color and pattern of distribution. The most common scenario is initially edematous and thus papular lesions, some of which flatten out into macules. The exanthems are usually symmetric, favoring the trunc and extensor surfaces of the extremites and possibly sparing the face. Pruritus, fever and eosinophilia may accompany the exanthems. Macular exanthems may evolve to form vesicles, bullae or if they become extreme, large eroded areas of erythroderma. In any case, the extensive damage at the dermoepidermal junction produces epidermal instability and fragility. Maculopapular eruptions can also be associated with mucosal involvement and fever, as well as with systemic signs and symptoms.

The reaction is usually type IV so that in a sensitized patient, it occurs in 2-3 days, while in non-sensitized patient most reactions occur after 9-10 days. Most drug reactions involve medications that have been started within the preceding 8 weeks: carbamazepine, phenytoin and allopurinol typically cause exanthems after a few weeks but later on are a major case of severe skin reactions. The duration depends on both the severity of the exanthem and the length of time required to withdraw the causative agent, as well as on the metabolism of the drug.

The key to therapy is eliminating causative agent. In many instances, no systemic or topical therapy is required. If pruritus is a problem, topical antipruritic measures can be used, as well as systemic antihistamines. More inflammatory lesions may benefit from topical corticosteroids. If desquamation occurs, wet dressings or zinc lotion may be useful.

Systemic corticosteroids are commonly employed for more severe reactions, although it is unclear how much they actually help.

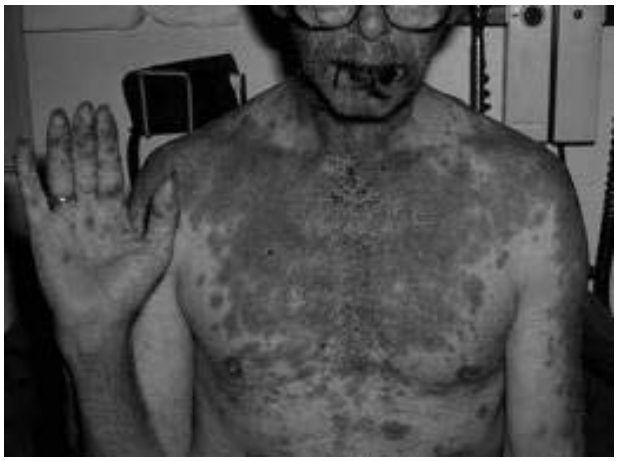

Figure 2. Stevens-Johnsov syndrom

There are a variety of drug reactions that can be severe and life-threatening. Among these are Stevens-Johnson sy. (SJS) - (Figure 2.) and Toxic Epidermal Necrolysis (TEN) - (Figure 3.). Both are characterized by erythematous, blisters and mucosal involvement that together lead to a clinical picture resembling that of severe burn. Together with erythema multiforme, SJS and TEN comprise a spectrum of severe blistering skin reactions. Severe blistering skin reactions are acute, often life-threating, drug-induced disorders characterized by a widespread loss of epidermis. They prove fatal in about 20% of patients.

SJS/TEN overlap and TEN are almost exclusively caused by drugs. SJS has extensive mucosal involment accompanied by truncal lesions. A macular exanthem starts on the trunk, face and extremities, spreads rapidly and becomes confluent. Vesicles and large unstable blisters may form. In SJS/TEN overlap and TEN widespread areas of epidermis become denuded. The Nikolsky sign is positive, as modest lateral pressure separates the epidermis from dermis. The skin lesions heal without scarring althought hypo and hyperpigmentation may persist for months or years. Since it is impossible to distinguish sharply between SJS and TEN the term SJS/TEN overlap is used to describe patients with blisters and erosions covering 10-30% of the body surface. TEN with macules describes patients who start with a diffuse macular exanthem that coalesces with a loss of >30% of the epithelium. The mortality for SJS is 6%, SJS/TEN overlap has a significantly higher mortality of 25%, while more then 45% of patients with TEN. The most frequent Dermatological side effects of psychiatric drugs are listed in the table 2.

Figure 3. Toxic epidermal necrolysis (TEN)

Table 2. Dermatological side effects of psychiatric drugs

Carbamazepine	urticaria and rush with icthing, macular rash. Stevens-Johnson sy., dermatitis exfoliativa, erithema multiforme, photosensitivity and SLE
Valproate	alopecia, pruritus
Lithium	acne, ulcus pretibialis and worsening of psoriasis, alopecia
Maprotiline	rash (4-5%)
Clomipramine	rash, erythema, photosensitivity
Amitriptyline	rash, erythema, photosensitivity, petechials
Fluoxetin	Stevens-Johnson sy.
Chlorpromazine	dermatitis allergica, photosensitivity, blue-gray spots, urticaria, makulopauilar, petechial and oedematous eflorescence
Diazepam – Oxazepam	urticaria
Klonazepam	alopecia, changes in pigmentation, face edema
Biperiden	rash and contact dermatitis
Barbiturate	Stevens-Johnson sy.
Metadone	urticaria, icthing

CONCLUSION

Each psychopharmac, regardless of its administration safety and the positive clinical experiences, can pose a potential risk of side effects. Dermatological side effects of psychopharmacological drugs are most commonly associated with carbamazepine.

Aliphatic phenothiazines antipsychotic promazine is in use for over 50 years and searching literature and electronic databases we did not find references associating the promazine with Exanthema. Clinical features and dermatological evaluation of our patient confirmed the correlation between the appearances of Exanthema Medicamentosum with the promazine medication.

Dermatological side effects are fortunately very rare but they should be constantly kept in mind.

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