

DRUG INDUCED OF CUTANEOUS PSEUDO-LYMPHOMAS

S. Shtilionova¹, P. Drumeva¹, M. Balabanova², I. Krasnaliev³

1) Department of dermatology and venereology, Medical University - Varna

2) Department of dermatology and venereology, Medical University - Sofia

3) Department of pathology, Medical University - Varna

SUMMARY

Lymphoproliferative infiltrates could be seen in several skin diseases but they are very characteristic of cutaneous pseudolymphoma, which can mimic both clinically and histopathologically cutaneous malignant pseudolymphoma.

A big problem for the clinicians is the differential diagnosis between cutaneous pseudolymphoma and malignant cutaneous lymphomas, as well as possibility for transformation of cutaneous pseudolymphoma into malignant lymphomas.

Wide spectrum of medicaments could cause appearance of cutaneous pseudolymphoma. Some of them are: anticonvulsants, ACE inhibitors, neuroleptics and others. Many of them are responsible for a development of erythrodermia, simulating Sezary syndrome with peripheral blood changes.

Key words: Drug Inducement, Cutaneous Pseudolymphomas

Lymphoproliferative infiltrations are observed in a number of dermatoses but are particularly typical of the cutaneous pseudolymphomas which can stimulate malignant lymphomas both clinically and histologically (1).

The differential diagnosis between cutaneous pseudolymphomas and malignant cutaneous lymphomas may present a serious problem together with the possibility for the transformation of the cutaneous pseudolymphomas into cutaneous lymphomas (1, 3).

A number of authors seek a possible connection between the occurrence of cutaneous pseudolymphoma and preceding drug intake. A broad spectrum of medications are capable of inducing the occurrence of cutaneous pseudolymphomas (2, 3, 4).

The drug-induced pseudolymphomas can be divided into:

1. Induced by anticonvulsants
2. Induced by other drugs.

Drugs capable of inducing cutaneous pseudolymphomas.

Class	Drugs
Anticonvulsants	Phenytoin, carbamazepine, phenobarbital, mephenytoin, trimethadone, primidone, butobarbital, methsuximide, phensuximide
Antidepressants	Amitriptyline, fluoxetine, doxepin, desipramine, lithium
Neuroleptics	Chlorpromazine, thioridazine, promethazine
Tranquilizers (anxiolitics)	Бензодиазепини (clonazepam, lorazepam)
ACE-inhibitors	Сaptopril, enalapril, benazepril
β -blockers	Atenolol, labetolol
H ₂ - blockers	Cimetidine, ranitidine
Calcium antagonists	Verapamil, diltiazem
Antirheumatic drugs	Aspirin, phenacetin, D-penicillamin, allopurinol
Cytostatics	Cyclosporin, methotrexate
Antibiotics	Penicillin
Antihistamines	Diphenhydramine
Antiarrhythmic drugs	Procainamide
Diuretics	Hydrochlorothiazide, Moduretic
Antilipemic drugs	Lovastatin
Sexual steroids	Estrogen, progesterone
Local drugs	Menthol, etheric oils

Cutaneous pseudolymphoma induced by anticonvulsants (Phenytyion, etc.) develops during the first 2 to 8 months following the administration of the drug but can occur much earlier (5 days) or much later (up to 5 years) after the onset of the treatment (2).

Clinically, it presents with febrility, lymphadenopathy, hepatosplenomegaly, blood eosinophilia and erythemic eruption under the form of single papules, plaques and nodules, but occasionally, the lesions may be generalized. Erythrodermia has also been described, stimulating the Sezary's syndrome with the typical cells in the peripheral blood (Adams, Braddock et al., Harris et al., Wolf et al.). In Bulgaria, a case has been reported about a patient with erythrodermia, febrility, lymphadenopathy and blood eosinophilia, with a histological picture of Micosis Fungoides from the skin biopsy caused by treatment with Carbamazepine (Kavaklieva, Balabanova, Cankov).

The cutaneous pseudolymphomas may also be induced by other drugs (4, 5):

- Neuroleptics
- ACE-inhibitors
- β -blockers
- Antihistamines
- Cytostatics

These drug-induced cutaneous pseudolymphomas occur one month to one year following the administration of the therapy. Localized papules are observed together with

single or multiple nodules and plaques, generalized papulo-nodular lesions and exfoliating erythrodermia resembling the Sezary's syndrome (Ploysamgam et al.).

It is considered that in lymphatoid drug eruption, the immunological function is reduced and the immune control is impaired, leading to abnormal proliferation of lymphocytes, increased function of the T-suppressors and hypogamaglobulinemia. Relative increase in the absolute number of the peripheral T-lymphocytes by 85-95 % (5, 6).

DISCUSSION:

1. The differentiation of cutaneous pseudolymphoma from malignant cutaneous lymphoma presents a differential diagnostic problem for the clinical practice.

2. Drug-induced pseudolymphomas are due to reduced immune control leading to abnormal proliferation of lymphocytes and enhanced functioning of the T-suppressors.

3. The impaired immune control and the accompanying immunological processes can complicate the clinical manifestations toward the development of Micosis Fungoides.

4. When applying drug groups in chronic conditions, the possibility should be envisaged for the development of drug-induced pseudolymphoma.

5. In cases of developed pseudolymphoma as a result of drug administration, the latter must be discontinued or replaced for a more appropriate group with another chemical composition.

REFERENCES:

1. Adams JD. Localized cutaneous pseudolymphoma associated with phenytoin therapy: a case report. *Australas J Dermatol* 1981 Apr;22(1):28-29. <http://www.ncbi.nlm.nih.gov/pubmed/7259668>
2. Bernstein H, Shupack J, Ackerman B. Cutaneous pseudolymphoma resulting from antigen injections. *Arch Dermatol*. 1974 Nov;110(5):756-757. <http://www.ncbi.nlm.nih.gov/pubmed/4371290>
3. Brown MD, Ellis CN, Billings J, et al. Rapid occurrence of nodular cutaneous T-lymphocyte infiltrates with cyclosporine therapy. *Arch Dermatol* 1988 Jul;124(7):1097-1100. <http://www.ncbi.nlm.nih.gov/pubmed/3260470>
4. Burg G, Kerl H, Schmoekel C. Differentiation between malignant B-cell lymphomas and pseudolymphomas of the skin. *J Dermatol Surg Oncol*. 1984 Apr;10(4):271-275. <http://www.ncbi.nlm.nih.gov/pubmed/6608539>
5. Charlesworth EN. Phenytyion-induced pseudolymphoma syndrome: an immunologic study. *Arch Dermatol* 1977 Apr;113(4):477-480. <http://www.ncbi.nlm.nih.gov/pubmed/848977>
6. Crowson AN, Margo CM. Antidepressant therapy. A possible cause of atypical cutaneous lymphoid hyperplasia. *Arch Dermatol* 1995 Aug;131(8):925-929. <http://www.ncbi.nlm.nih.gov/pubmed/7632065>
7. Kavaklieva S, Pehlivanov G, Balabanova M, Cankov N. Erythrodermia, induced by carbamazepine histological resembling mycosis fungoides. *Dermatol* 2005; 44 (1): 42-43..