MANAGEMENT OF SUBACUTE LUPUS ERYTHEMATOSUS IN AN ONCOLOGIC PATIENT

ANDREEA CORINA ULICI*,**, CORINA TEODORA BUD*,**, MĂDĂLINA MARINA BARCUI**

Summary

Subacute lupus erythematosus is a distinct and rare clinical form of systemic lupus erythematosus. It is characterized by annular erythemato-squamous plaques with a polycyclic outline, scattered on photo-exposed areas. Biologically the presence of anti-Ro/SS-A antibodies is identified. A large number of drugs have been identified as being involved in the development of this condition, among which taxanes are the most commonly recommended chemo-therapeutics for cancer patients. [1]

We present the case of a 52-year-old male patient with a history of right laterocervical metastatic adenopathic block after a squamous cell carcinoma with an imprecisely demarcated starting point with localization in the ENT(ear-nose-throat) sphere, radio- and chemotherapy with taxane (Paclitaxel). The diagnosis of neoplasia was confirmed one year ago and after 25 sessions of radiotherapy and 6 of chemotherapy, the patient discontinued the onco-logical treatment and was admitted to the Dermato-Venerology clinic for the appearance of erythemato-squamous , psoriasiform, well-defined plaques with polycyclic outline, localized on photoexposed areas, which appeared 2 months after the cessation of treatment. From a biological point of view presents pancytopenia, hypocomplementemia and positive antinuclear antibodies, anti double catenary and anti RO2 antibodies.

Histopathologic examination reveals: the presence of an epidermis with isolated cellular dyskeratosis, covered by parakeratotic plaques, superficial vesicular structures with detritus and PMN(polymorphonuclear) debris, in the papillary dermis, a discrete perivascular chronic inflammatory infiltrate.

The recommended treatment includes avoiding exposure to UV rays, photoprotection, topical application of a stripping ointment (salicylate ointment 6%), medium potency dermatocorticoids (Advantan cream) and synthetic antimalarials (Plaquenil) 400 mg daily.

Key words: *subacute lupus erythematosus, oncologic patient, chemotherapy.*

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Introduction

Subacute lupus erythematosus is an autoimmune disorder, characterized by the appearance of erythemato-squamous plaques with annular shape, polycyclic outline, sometimes atrophic centre, scattered on photoexposed areas. Sun exposure and activation of adaptive immunity are involved in the pathogenesis of the disease. Laboratory tests identify the presence of anti-Ro/SS-A and ANA antibodies, but their presence is not absolute necessary for diagnosis. In the occurrence of this disease, a large number of drugs have been identified as triggers including taxanes. Some data in the literature, however, also show an association between malignancies and systemic lupus. We present a

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case of subacute lupus erythematosus in a patient with a squamous cell carcinoma in the ENT treated with Paclitaxel. Discussions are centered on the mechanisms of dermatosis onset in the context of neoplasia and taxane treatment. [1]

Case presentation

A 52-year-old male patient presents to DV consultation with a history of right laterocervical metastatic adenopathic block arising after a squamous cell carcinoma with an imprecisely demarcated starting point from the ENT sphere, radio- and chemotherapy with Paclitaxel. The diagnosis of neoplasia was confirmed one year ago, but after 25 courses of radiotherapy and 6 courses of chemotherapy, the patient discontinued oncologic treatment. He is admitted to the Dermato-Venerology ward for the appearance of erythemato-squamous, psoriasiform, well demarcated, elevated, plaques, with atrophic center, polycyclic outline, localized on photoexposed areas, appearing 2 months after stopping treatment.

The patient's associated comorbidities are: Child A ethanolic cirrhosis, epilepsy on toxic background, grade II essential hypertension kept under control with specific treatment with: carvedilol 12.5 mg/day, spironolactone/furosemide 50/20 mg/day, pantoprazole 20 mg/day, rifaximin 800 mg/day 7 days a month, ursodeoxycholic acid 750 mg/day.

In terms of lifestyle, it should be noted that the patient is a smoker and chronic drinker.

General clinical examination: patient in good general condition, overweight (BMI=27.78), excess abdominal adipose tissue, palpable liver 4 cm below the costal margin. The right latero-cervical shows a tumor mass, indurated, infiltrated, with hyperpigmented overlying hyperpigmented integument. Otherwise, no other changes were detected.

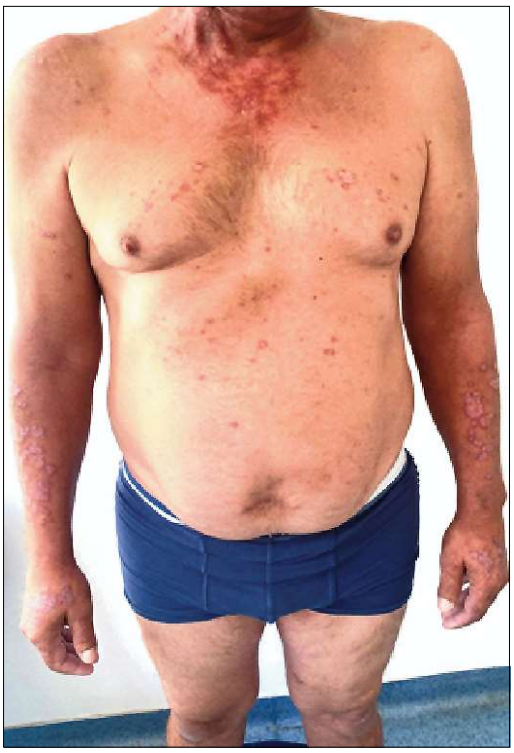

Figure 1. Well demarcated, erythemato-squamous, psoriasiform, plaques with polycyclic outline and hypopigmented macules localized on the neck, forearms, hands and posterior chest.

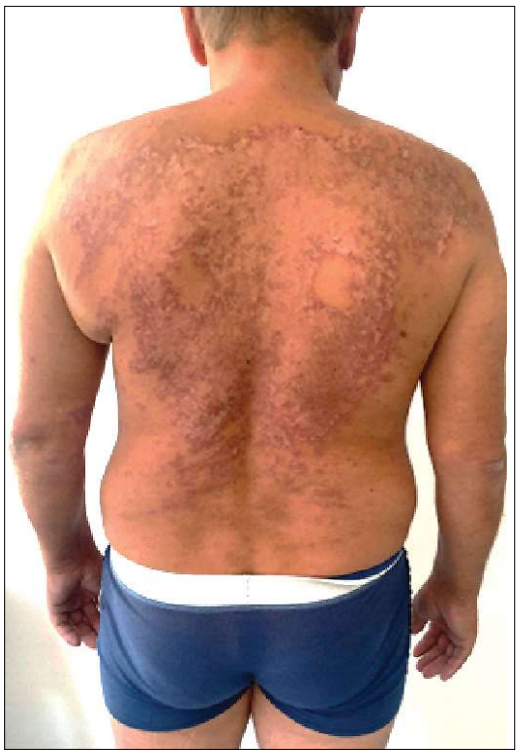

Figure 2. Well demarcated, erythemato-squamous, psoriasiform, plaques with polycyclic outline and hypopigmented macules localized on the neck, forearms, hands and posterior chest.

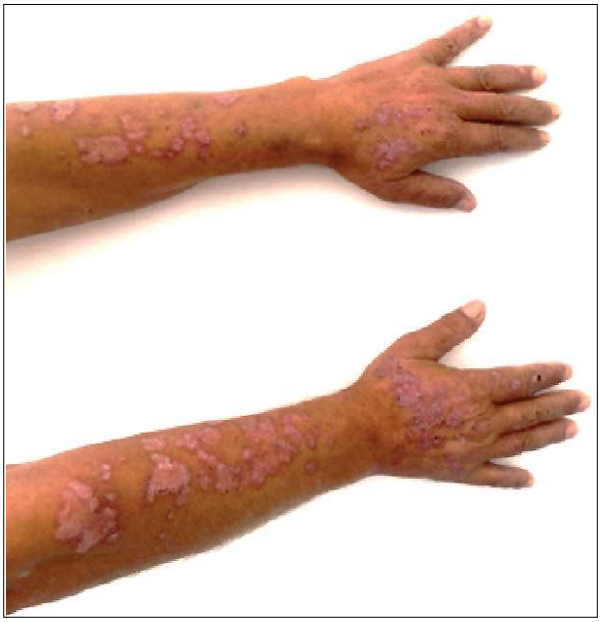

Figure 3. Well demarcated erythemato-squamous, psoriasiform, plaques with polycyclic outline and hypopigmented macules localized on the forearms.

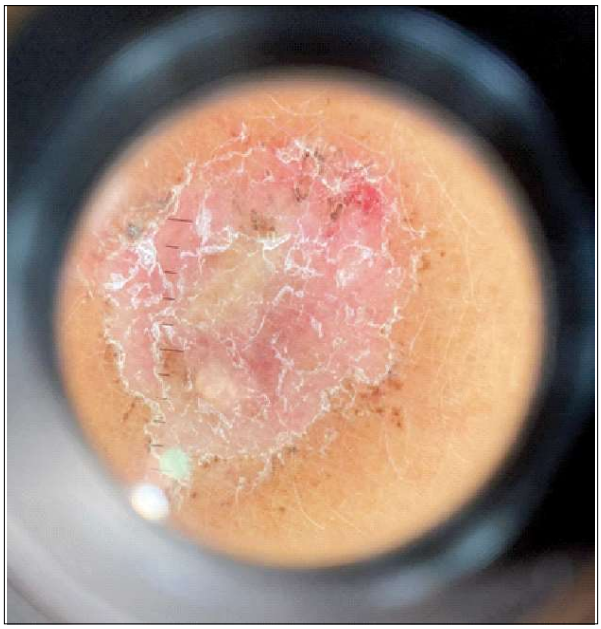

Figure 4. Dermoscopic evaluation of a lesion on the forearm shows an erythematous background, without structure, with white scaling, peripheral hyperpigmentation and punctate vessels.

The history of the disease shows that the patient was diagnosed with squamous cell carcinoma with an imprecisely demarcated starting point localized in the ENT sphere one year ago; he underwent 6 courses of chemotherapy and 25 courses of radiotherapy, after which he discontinued oncologic treatment. Two months after the cessation of her oncologic treatment, he was hospitalized in the Dermato-Venerology ward for the onset of the clinical manifestations mentioned above.

Dermoscopically, an erythematous background without structure, white scaling, peripheral hyperpigmentation and punctate vessels are observed in a lesion on the forearm.

From the biological point of view, the patient presents: pancytopenia (leukocytes 2740U/L, erythrocytes 3600000 U/L, platelets 46100 U/L), fibrinogen 189 mg/dL, CRP 1.6 mg/L, TGO 34 U/L, TGP 24 U/L, GGT 68 U/L, ANA 6.5, Anti RO2/SSA 200 U/mL, Anti ds DNA-positive, complement C3 72 mg/dL, C4 9.1 mg/dL, the other usual tests were within normal limits. We note that the PET-CT performed 1 year ago did not detect the primary tumor.

An incisional biopsy of a lesion of the forearm was taken to establish a definite diagnosis. Histopathologic examination revealed an epidermis with isolated cellular dyskeratosis, covered by parakeratotic plaques, vesicular structures with detritus and PMN debris in the superficial layers; in the papillary dermis pigmentary incontinence around ectatic vessels and a discrete perivascular chronic inflammatory infiltrate. Immunofluorescence could not be performed for financial reasons.

Treatment was recommended: avoid exposure to UV rays, photoprotection, synthetic antimalarials (Plaquenil) 400 mg per day per os, local application of a stripping ointment (salicylate ointment 6%), a dermatocorticoid with medium potency (Advantan cream).

The evolution at 8 months was favorable, with only the persistence of some erythematous plaques and some postlesional hyperpigmented macules, and kept under control with specific therapy.

The short term prognosis in this patient, we consider to be good from a dermatologic point of view, but in the long term possibly unfavorable,

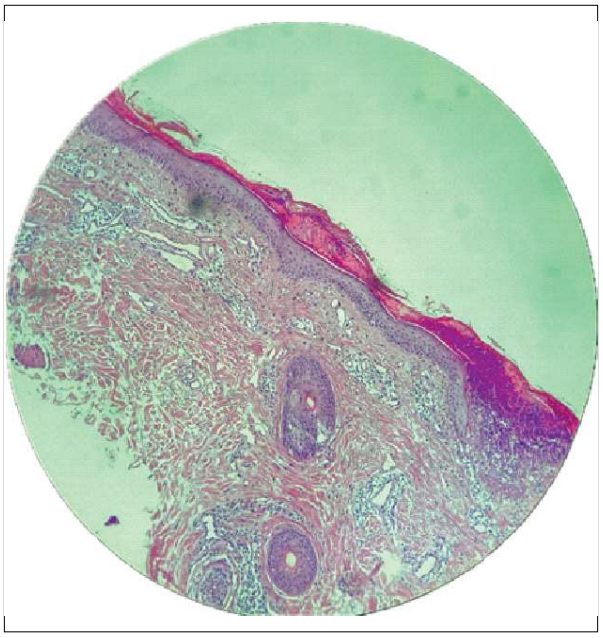

Figure 5. Histopathological examination, hematoxylin-eosin staining, x10 objective-epidermis with isolated cellular dyskeratosis, covered by parakeratotic plaques, vesicular structures with detritus and PMN debris in superficial layers; in the papillary dermis pigmentary incontinence around ectatic vessels and discrete chronic perivascular inflammatory infiltrate.

due to the oncologic disease. It should be noted that the disease may evolve over time to systemic lupus, therefore the patient should be kept under regular control.

Discussions

Lupus erythematosus is the most common autoimmune disorder encountered in dermatology, clinical immunology and rheumatology. Some literature data present the association between malignancies and subacute lupus. However, few cases of subacute lupus are reported, indicating the possibility that the condition may represent a paraneoplastic disease and is a rare form of systemic involvement. The association between subacute lupus and internal cancers has been recognized since 1980. The subacute form has a very characteristic clinical appearance by the appearance of multiple annular erythemato-squamous erythematous plaques with raised margins, spontaneously involuted center and hypopigmented, non-scarring, postlesionaly hypopigmented macules that persist naturally for months or years. The disease occurs after even moderate but repeated artificial sun or UV exposure. [7,11]

It is considered that the trigger for auto-reactivity is a tumor antigen homologous to Ro antigen (SS-A). [9]

According to McLean criteria for a dermatologic condition to be considered paraneoplastic, the following criteria must be met: the dermatosis must occur after the development of the malignant tumor, but may or may not precede the diagnosis of the tumor; both the dermatosis and the malignant tumor must follow a parallel course. The latency period is defined as the time period between the onset of dermatosis and the diagnosis of the associated malignancy. One article reports that, in 9 of 11 reported cases, the cutaneous lesions appeared before the underlying neoplasm was detected, with a latency of between 3 and 36 months. [9,12]

However, the disease can also be induced post-medication. The association between lupus and certain drugs has been well documented in the literature, although there are no standard diagnostic criteria for iatrogenically induced lupus erythematosus. The condition has been defined as a possible lupus-like syndrome associated with continued drug exposure and remitting on discontinuation of therapy. The main drugs implicated are: thiazide diuretics, calcium channel blockers, angiotensin converting enzyme inhibitors, terbinafine, proton pump inhibitors, statins, NSAIDs, TNF-α antagonists (infliximab, adalimumab) and chemotherapeutic agents (taxanes). [10]

Taxane chemotherapy can both predispose to and cause subacute lupus erythematosus. The disease may manifest de novo, weeks or months after the initiation of cancer therapy, or it may develop in the presence of another pre-existing autoimmune disorder. [2]

The pathogenetic mechanisms by which taxanes induce autoimmunity are not fully elucidated but the clinical and histopathologic manifestations in hematoxylin-eosin staining are sufficiently relevant for diagnosis. The association with autoantibody formation (anti Ro2-SSA) is noted. [3]

Other articles suggest that taxanes contribute to disease induction in immunogenetically predisposed oncologic patients. Anti-Ro/SS-A (Ro52) antibodies recognize a specific antigen found in cell microtubules. The action of taxanes to inhibit cellular mitosis by stabilizing microtubules leads to impaired expression of the Ro/SS-A (Ro52) antigen, resulting in skin lesions. [1]

With regard to McLean's second criterion, in 7 out of 11 cases presented in one study, the skin lesions improved after oncologic treatment. Thus the occurrence of metastases in a patient with neoplasia leads to exacerbation of dermatosis. [9,12]

The simple coexistence of the two diseases and their simultaneity in terms of evolution can not be excluded and thus lupus to be a de novo occurrence unrelated to the tumor.

Another article considers that sun exposure and activation of adaptive and humoral immunity leading to cytokine production are involved in the pathogenesis of subacute lupus erythematosus. [4]

The Ro antigen is a complex of plasma ribonucleoproteins that translocate surface keratinocytes under UV radiation. The possibility that in paraneoplastic lupus, the tumor antigen homologous to Ro(SS-A) may be the trigger for photosensitization. [12]

Our case was challenging in terms of the underlying mechanism, given the association of lupus with taxanes and oncologic disease, respectively. Either of these two triggers could have triggered lupus and thus the disease had a dual trigger mechanism. In our patient's case, however, the dermatosis appeared after the completion of chemotherapy which can be considered late for its onset. The presence of Ro(SS-A) antigen in the tumor could not be demonstrated, which also raises the possibility of de novo onset of dermatosis. We consider that the disease was nonetheless triggered by malignancy because when oncologic therapy was stopped, the dermatosis did not completely remit. The nonresolution of the oncologic disease is an argument for the persistence of cutaneous lesions.

Conclusions

The association between subacute lupus and malignancies is rare, suggesting a possible paraneoplastic form of the disease. In oncologic patients who respond poorly to conventional therapy, paraneoplastic subacute lupus should be considered. Various drugs, such as taxanes, can induce subacute lupus erythematosus, although the mechanisms are not completely understood. Autoantibody formation is frequently observed. Aggravation of dermatosis may represent the development of metastases and thus the patient should be regularly monitored. [1,2,3,4,7,9,10,11].

Bibliography

1. Marchetti MA, Noland MM, Dillon PM, Greer KE. Taxane associated subacute cutaneous lupus erythematosus. Dermatol Online J. 2013 Aug 15;19(8):19259. PMID: 24021438.
2. Sibaud V, Lebœuf NR, Roche H, Belum VR, Gladieff L, Deslandres M, Montastruc M, Eche A, Vigarios E, Dalenc F, Lacouture ME. Dermatological adverse events with taxane chemotherapy. Eur J Dermatol. 2016 Oct 1;26(5):427-443. doi: 10.1684/ejd.2016.2833. PMID: 27550571; PMCID: PMC5526115.
3. Lamond NW, Younis T, Purdy K, Dorreen MS. Drug-induced subacute cutaneous lupus erythematosus associated with nab-paclitaxel therapy. Curr Oncol. 2013 Oct;20(5):e484-7. doi: 10.3747/co.20.1546. PMID: 24155645; PMCID: PMC3805417.
4. Rusia K, Madke B, Kashikar Y, Meghe S. Paclitaxel-Induced Cutaneous Lupus Erythematosus and Raynaud's Phenomenon. Cureus. 2023 Dec 22;15(12):e50974. doi: 10.7759/cureus.50974. PMID: 38259408; PMCID: PMC10801347.
5. Lowe G, Henderson CL, Grau RH, et al. A systematic review of drug-induced subacute cutaneous lupus erythematosus. Br J Dermatol. 2011; 164:465–72. [PubMed: 21039412]
6. Grönhagen CM, Fored CM, Linder M, Granath F, Nyberg F. Subacute cutaneous lupus erythematosus and its association with drugs: a population-based matched case-control study of 234 patients in Sweden. Br J Dermatol. 2012 Aug;167(2):296-305. doi: 10.1111/j.1365-2133.2012.10969.x. Epub 2012 Jul 5. PMID: 22458771.

7. Evans KG, Heymann WR. Paraneoplastic subacute cutaneous lupus erythematosus: an underrecognized entity. Cutis. 2013 Jan;91(1):25-9. PMID: 23461055.
8. Amaral M, Michels A, Jamiolkowski D, Mühleisen B, König D, Maul LV. Paraneoplastischer subakut kutaner Lupus erythematodes [Paraneoplastic subacute cutaneous lupus erythematosus]. Dermatologie (Heidelb). 2024 Jul;75(7):568-571. German. doi: 10.1007/s00105-024-05319-6. Epub 2024 Mar 5. PMID: 38441569.
9. Chaudhry SI, Murphy LA, White IR. Subacute cutaneous lupus erythematosus: a paraneoplastic dermatosis? Clin Exp Dermatol. 2005 Nov;30(6):655-8. doi: 10.1111/j.1365-2230.2005.01900.x. PMID: 16197381.
10. Laurinaviciene R, Sandholdt LH, Bygum A. Drug-induced cutaneous lupus erythematosus: 88 new cases. Eur J Dermatol. 2017 Feb 1;27(1):28-33. doi: 10.1684/ejd.2016.2912. PMID: 27799135.
11. Alexandru D. Tătaru - LUPUS ERITEMATOS – AFECȚIUNE CU ASPECTE CLINICE POLIMORFE, DermatoVenerol. (Buc.), 64(1): 57-64
12. McLean DJ. Cutaneous paraneoplastic syndromes. Arch Dermatol 1986; 122: 765–7.

Conflict of interest
NONE DECLARED

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