Introduction: The diagnosis of erythroderma is frequently challenging due to subtle clinical and paraclinical clues necessary to differentiate between a variety of underlying dermatoses, infections, or systemic diseases. The management is also difficult, with severe systemic complications that impose an early medical intervention.

Objective: We aimed to analyze the epidemiological, clinical, and therapeutic profile of patients diagnosed with erythroderma in a tertiary dermatology referral center from Romania.

Materials and methods: We conducted a retrospective descriptive study of patients diagnosed with erythroderma in the Dermatology and Allergology Clinic, „Elias” Emergency University Hospital, Bucharest, Romania from January 2012 to August 2018. An in-depth analysis of the clinical, paraclinical, as well as therapeutic management was performed.

Results: The most frequent cause of erythroderma was represented by the exacerbation of psoriasis, followed by other chronic inflammatory dermatoses, as well as by hypersensitivity reactions to drugs. Less frequently, erythroderma was a paraneoplastic manifestation or a clinical presentation of rare genetic or autoimmune pathologies. The therapeutic management led to favorable results, with the remission or the amelioration of the disease. Few patients needed supportive care.

Conclusions: Although the prognosis of the majority of patients was favorable, it is important to take into consideration the possibility of an associated cancer diagnosis. The dermatologist plays an essential role within the multidisciplinary team involved in the diagnosis and management of erythroderma.

Keywords: erythroderma, exfoliative dermatitis, psoriasis, atopic dermatitis, paraneoplastic erythroderma.
The aim of this study was to analyze the epidemiological, clinical, and therapeutic profile of patients diagnosed with erythroderma in a tertiary dermatology referral center from Romania.

**Materials and methods**

We conducted a descriptive, retrospective clinical study of patients diagnosed with erythroderma in the Dermatology and Allergology Clinic, “Elias” Emergency University Hospital, Bucharest, Romania from January 2012 to August 2018. Other inclusion criteria were age over 18 years old or the consent of the legal representative in case of patients under the age of 18.

An informed consent was obtained from each patient or the legal representative. The study protocol was in accordance with the ethical prerogatives of the 1975 Declaration of Helsinki and respected Good Clinical Practice (GCP) standards.

The clinical and paraclinical data was collected from the archive of Dermatology and Allergology Clinic, „Elias” Emergency University Hospital, by analyzing the observation sheets. An in-depth analysis of the clinical, paraclinical, as well as therapeutic management was performed. The data obtained allowed a complex characterization of the patients according to age, sex, residence and occupational status. The following were also analyzed in detail: the medical history, the clinical manifestations, the comorbidities and aggravating factors. Increased attention was also given to the results of the laboratory and imagistic investigations, to the therapeutic means used in the management of erythroderma, as well as the evolution during the presentation and / or hospitalization periods.

**Results**

The average age of the patients at presentation was 61.7 years old. Sex repartition for the 27 cases was the following: 17 female cases (62.96%) and 10 male cases (37.03%) with a ratio of 1.7:1 (n = 17:10), a result in opposition with the male predominance described in prior studies.

**Patient distribution according to the etiology of erythroderma**

In conformity with anamnestic, clinical and paraclinical features, the etiologies of erythroderma were classified in seven major categories: exacerbation of preexistent inflammatory dermatosis (n=12), hypersensitivity drug reaction (n=5); eruptions in an oncological context (n=7), congenital ichthyosiform dermatosis (n=2); autoimmune conditions (n=1).

**Exacerbation of preexistent inflammatory dermatosis.** The most frequent cause of erythroderma was psoriasis (n=9). Other preexistent dermatosis (one case of atopic dermatitis and two cases of contact dermatitis) represented 11.11% from the total erythroderma cases.

**Eruptions in an oncological context** were divided in the categories of cutaneous T-cell lymphoma and paraneoplastic eruptions from solid malignancy. Five patients (18.52%) presented erythroderma as a clinical manifestation of T-cell lymphoma, from which four were diagnosed with mycosis fungoides and one patient was diagnosed with Sezary syndrome. Two patients (7.40%) presented paraneoplastic erythroderma in the context of solid cancers (breast cancer and ovarian carcinoma), diagnosed after the detailed etiological investigation of the patients.

The category of erythroderma secondary to **hypersensitivity drug reactions** included five patients, 18.52% from the total number, on the third place after the neoplasic etiology. In the present study there are incriminated the following drugs: antihypertensives (n=1), anticonvulsants (n=1), acetylcholinesterase inhibitors (n = 1), nonsteroidal anti-inflammatory drugs (n = 1) and anti-gout agents or inhibitors of uric acid synthesis (n = 1). In other specialized studies, the drugs most frequently associated with the development of erythroderma were antiepileptics and antihypertensives [4].

**Congenital ichthyosiform dermatosis.** Two cases of erythroderma (7.40%), one male and one female came in, during the study, for clinical and biological reevaluation with the purpose of monitoring the ichthyosiform erythroderma developed from the neonatal period.
B and C serology were performed, with negative results. The screening for malignancy was performed: from all tumor markers that were dosed, carcinoembryonic antigen (CEA) and CA125 recorded positive values in patients with paraneoplastic erythroderma associated with solid malignancy. Also imaging investigations were performed (chest x-ray, abdominal-pelvic ultrasound, thoracic-abdominal-pelvic computed tomography) leading to the diagnosis of an ovarian tumor in one patient. Skin biopsy was performed in 4 of 27 patients and the histopathological examination revealed the following diagnoses: paraneoplastic dermatomyositis, chronic spongiocytic dermatitis, pityriasis lichenoides et varioliformis acuta, mycosis fungoides. Peripheral blood smear revealed a relevant increase in the number of Sezary cells in the patient with Sezary Syndrome.

**Clinical manifestations detected at the time of presentation following anamnesis and physical examination.**

The clinical manifestations that appeared most frequently in patients diagnosed with erythroderma were represented by erythema, scales, and pruritus. Other manifestations can be observed in Figure 1. However, fever (3.70%), hepatomegaly (3.70%) and lymphadenopathy (14.81%) were more rarely objectified in the present study compared with other studies. In both the current study as well as in other specialized studies, nail changes were a predictive clinical sign for the diagnosis of psoriasis.

**Laboratory investigations** were non-specific. The most frequent modifications of the laboratory tests were represented by leukocytosis (44.44%), increased inflammation markers- the erythrocyte sedimentation rate (44.44%) and C reactive protein (33.33%), hyperuricemia (29.63%), hypercholesterolemia (29.63%), hypertriglyceridemia (25.93%), and anemia (25.93%). In order to exclude infectious causes, human immunodeficiency virus (HIV), hepatitis viruses

One patient suffered from an **autoimmune disorder**, pemphigus foliaceus (n=1, 3.70%).

**Distribution of patients according to the treatment performed during the hospitalization and their evolution**

**Systemic therapy.** The classes of drugs with systemic administration used during the hospitalization are shown in figure 2. For the treatment of erythroderma and its comorbidities, 24 patients (92.31%) received systemic cortico-
steroids, 13 (50.00%) received antibiotic therapy, and 14 (53.85%) received antihistamines to fight pruritus generated by exfoliative dermatitis. Other systemic therapeutic agents used were retinoids (n=7, 26.92%), chemotherapy in the ovarian cancer patient (n=1, 3.84%), immunosuppressive therapy (n = 2, 7.69%), gastric or hepatic protectors to neutralize or prevent the adverse effects of electron therapy (n = 8, 30.77%). Only one patient (3.85%) known with psoriatic arthropathy, continued the biological therapy with adalimumab, an anti-tumor necrosis factor-alpha (TNF-α) agent. The supportive treatment (n = 7, 26.92%) was aimed to rebalance hydro-electrolytic, metabolic, and acidobasic alterations, to ensure prophylaxis of deep vein thrombosis by anticoagulation, to combating fever, pain and general discomfort, healing the outbreaks of infection.

Topical therapy. All 27 patients received local therapy in order to reduce inflammation, itching and skin dryness. Thus, for this purpose there were used dermatocorticoids (n = 27, 100%), emollients (n = 27, 100%), and keratolytics (n = 4, 17.39%). Moreover, there were applied creams, lotions or compresses with anti-inflammatory (n = 1, 4.35%), antiseptic (n = 5, 21.74%), antibiotic (n = 2, 8.70%), and antifungal (n = 1, 4.35%) effects. Phototherapy was recommended to eight patients (34.78%), from the group with exacerbation of pre-existing dermatoses as well as for those with cutaneous T-cell lymphoma.

Discussions

Given the rarity of this diagnosis the study included a significant number of patients- 27 patients selected over six years, with an incidence of 4.5 cases per year. The incidence of erythroderma has a large geographical variability from 0.9 cases per 100,000 inhabitants per year registered in Netherlands [5], to an annual hospital incidence of 6.5 cases in Tunisia [6,7]. Erythroderma appears generally in the sixth decade of life and predominantly in males [7]. A possible explanation for the increased number of cases of erythroderma in men may be related to the increased consumption of alcoholic drinks and the increased exposure to specific professional factors associated with the exacerbation of psoriasis or eczema [8]. The results of the present study are close to those of the literature regarding the average age of erythroderma (56 years), but the ratio of sex was different, in our study women being more affected by erythroderma than men.

The most common cause of erythroderma suggested by the current study was the exacerbation of pre-existing dermatoses (44.74% of the total causes) and in particular psoriasis.
The differences in incidence of the main etiologies of erythroderma can be partially attributed to genetic, geographical and socio-economic discrepancies existing worldwide [6]. Erythema, scales and pruritus were the most commonly objectified or reported clinical signs and symptoms, a result similar to that of many other specialty studies [9]. However, fever (3.70%), hepatomegaly (3.70%), and lymphadenopathy (14.81%) were much less objectified in the current study compared to data reported by other studies [8]. In both the current study and other specialized studies, nail changes represented a predictive clinical element for the diagnosis of psoriasis [6].

The most frequent alterations in laboratory tests were leukocytosis, increased inflammatory markers, hyperuricemia, dyslipidemia, and anemia. Recent studies have shown that eosinophilia is associated with cutaneous lymphoma, psoriasis and eczema [10], but also with drug rashes [7]. This is also true in the case of the present study, where eosinophilia was associated with post-drug erythroderma, with cutaneous lymphoma and eczema.

The most used classes of drugs and therapeutic procedures were corticosteroids, antihistamines, antibiotics, retinoids, along with emollients and topical corticosteroids and phototherapy.

The evolution of the disease varies according to the etiology. If the cause is medication, the evolution is short, in case of exacerbation of pre-existing dermatosis the evolution is prolonged, and in the context of neoplasia the evolution is unpredictable.

**Conclusions**

In the study all patients presented a favorable evolution during hospitalization. The prognosis of erythroderma is variable, depending on etiology. Although the most common cause of erythroderma was the exacerbation of preexisting dermatosis, the study highlighted the large proportion of patients who developed the disease in an oncological context.

Paraneoplastic erythroderma is associated with a numerous solid cancers, therefore screening for certain malignancies is essential for those with uncertain initial etiology. Patients with paraneoplastic erythroderma manifested previously to the diagnosis of cancer might have a more favorable prognosis. The skin condition accelerates the oncological diagnosis, and, implicitly, its early management.

The dermatologist plays an essential role within the multidisciplinary team in the diagnosis and management of erythroderma.

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**Bibliography**

Conflict of interest
NONE DECLARED

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