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Exfoliative dermatitis as a complication of drug eruption associated with COVID-19

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Abstract

We report a clinical case of exfoliative dermatitis associated with a novel coronavirus disease. A patient with moderate COVID-19 and decompensation of insulin-dependent diabetes mellitus, hypertension and obesity developed a generalized drug eruption. Treatment of coronavirus infection included drugs associated with the frequent development of skin allergic reactions: third-generation cephalosporin and hydroxychloroquine. In this clinical case, the patient had a generalized form of exfoliative dermatitis with moderate COVID-19. Thus, the generalization of drug eruption occurred with a decrease in the viral pneumonia foci area and was accompanied by repeated deterioration of general condition of the patient. Skin rashes resolved in the correction of concomitant pathology. Erythroderma has a benign course in hemostatic disorders and the use of systemic glucocorticosteroids, hyperglycemia therapy. For managing such patients, it is important to use an integrated approach, providing both the treatment of the underlying disease and the correction of comorbidity and complications. This is relevant for both dermatologist-venereologist and specialists involved in the treatment of COVID-19.

Keywords: exfoliative dermatitis, drug eruption, COVID-19.

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Background. Exfoliative dermatitis refers to the generalized damage of the skin cover in the form of bright erythema with pronounced infiltration and peeling. The patient may show symptoms of general intoxication, chills, fever, and increased appearance of lymph nodes. The disease is etiologically heterogeneous and often occurs against the background of a preexisting skin pathology (e.g., psoriasis, atopic dermatitis, drug toxidermia, lymphoproliferative diseases, Devergie's disease). However, the condition may not have a clear etiology in up to 20% of all cases [1].

Exfoliative dermatitis occurs against the background of medicinal hypersensitivity in 15% of all patients. The literature mentions β-lactam antibiotics, nonsteroidal anti-inflammatory agents, and hydroxyquinolone as drugs commonly associated with the development of skin sensitization.

Immune-mediated inflammation plays an important role in the pathogenesis of exfoliative dermatitis. The interactions of pro-inflammatory cytokines and cell adhesion molecules could lead to epidermal proliferation, acceleration of cell dynamics, and redundant loss of keratinocytes. A distinctive clinical feature of exfoliative dermatitis associated with drug allergies is the rapid occurrence of the skin process over an average of 2–6 weeks [2].

Given the wide distribution of new coronavirus infections worldwide, the data on dermatological manifestations associated with COVID-19 have begun to increase. These manifestations may be classified into seven groups, namely, skin angiitis, papulo-squamous lesions and pityriasis rosea, measles-like rash and infectious erythema, papulo-vesiculate rash, toxidermia, urticaria, and artificial trophic lesions [3, 4].

Toxidermia during COVID-19 may occur due to patient sensitization to a specific drug used as therapy for the underlying disease. The preparations of various pharmacological groups, such as β-lactam antibiotics, fluoroquinolones, hydroxyquinolone, and antiviral agents, may cause drug allergies, one of the more severe manifestations of which is exfoliative dermatitis.

The aim of the present work is to describe a clinical case of exfoliative dermatitis that developed as a complication of toxidermia associated with the treatment of COVID19 infection.

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Table 1. Routine blood test results of patient G.I.F. (age, 39 years)

Parameters	Date					
	12.10	22.10	05.11	18.11	24.11	30.11
Hemoglobin, g/l	135	127	117	92	85	95
Erythrocytes, $\times 10^{12}$/l	4.4	4.4	4.07	3.3	3.03	3.38
Platelets, $\times 10^{9}$/l	226	322	207	388	402	338
Leukocytes, $\times 10^{9}$/l	7.5	10.2	10.8	8.8	12.7	9.4
Banded neutrophils, %	2	—	11	17	18	4.1
Segmented, %	89	—	62	59	50.9	64.5
Lymphocytes,%	4	—	21	23	27.3	26.8
Monocytes,%	5	—	2	1	3.8	4.5
Eosinophils,%	0	—	2	0	0	0.1
ESR, mm/h	52	52	52	48	39	28

Note: ESR – erythrocyte sedimentation rate.

Table 2. Biochemical blood assay of patient G.I.F. (age, 39 years)

Parameters	Date					
	12.10	30.10	10.11	18.11	24.11	30.11
Total Bilirubin, μmol/l	8.4	7.0	10.4	12	7.2	6.4
Aspartate aminotransferase, units/l	63	16.1	38.8	17	11	14
Alanine aminotransferase, units/l	52.9	32	13.4	12	13	24
Total Protein, g/l	69	69.5	62	53	48	57.9
Glucose, mmol/l	31.7	20.9	9.6	29.4	27.2	11.6
Urea, mmol/l	10.5	8.7	4.4	3.7	6.3	5.5
Creatinine, μmol/l	130.8	98	58	67	52	50
CRP, mg/l	144	117	43	36	161.7	17.1

Note: CRP – C-reactive protein.

Patient G.I.F. (date of birth, 08.02.1981) was admitted on 10.02.2020 to Naberezhnye Chelny Infectious Hospital No. 32 with complaints of increased body temperature of up to 38.5 °C, weakness, cough, and shortness of breath during physical activity. The general condition of the patient was moderate on account of first-degree respiratory failure (blood oxygen saturation, 94%), and their skin and visible mucous membranes were clean. The patient's body mass index was 46.87 kg/m^2.

Chest computed tomography (CT) revealed bilateral viral pneumonia and a high probability of COVID-19 infection (CT 2, 50%).

The results of polymerase chain reaction for SARS-COV2 ribonucleic acid (RNA) via nasal and pharyngeal swabs revealed the following diagnosis: "U07.1. Coronavirus infection COVID-19, the virus is identified, moderate form. Community-acquired bilateral viral pneumonia of moderate severity. Respiratory failure (RF) of the 1st degree. Obesity of the 3rd degree."

The patient's complete blood count at admission revealed an increased erythrocyte sedimentation rate (ESR) of 52 mm/h. Erythrocyte, leukocyte (including lymphocyte), and platelet counts were within reference values (Table 1).

The patient's blood biochemical parameters were characterized by increased levels of alanine aminotransferase, aspartate aminotransferase, urea, creatinine, C-reactive protein (CRP), and fibrinogen. Hyperglycemia (Tables 2, 3) was revealed for the first time.

The improvement of the primary disease was noted due to the administered treatment (intravenous infusions of Ceftriaxone 2.0 g, Dexamethasone 8 mg, insulin therapy, subcutaneous injections of Enoxaparin 0.8 mg, oral administration of Azithromycin 500 mg/day, Hydroxyquinoline 200 mg 2 times a day for 5 days, Ambroxol 30 mg three times a day, Omeprazole 20 mg twice a day). Patient's body type normalized and saturation increased to 96%. The patient's ESR decreased to 48 mm/h, and her CRP level was 36 g/l

Table 3. Hemostatic indicators of patient G.I.F. (age, 39 years)

Parameters	Date				
	12.10	02.11	18.11	24.11	02.12
International Normalized Ratio	1.24	0.88	—	0.96	0.91
Fibrinogen, g/l	7.5	5.4	3.7	8.85	3.11
Prothrombin index,%	80	103	102	105.9	118.2

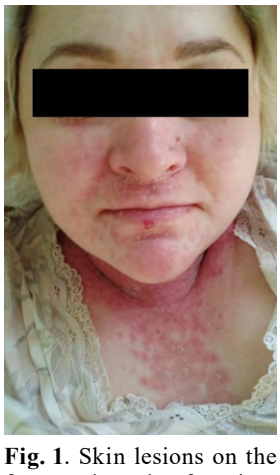

Fig. 1. Skin lesions on the face and neck of patient G.I.F. diagnosed with exfoliative dermatitis.

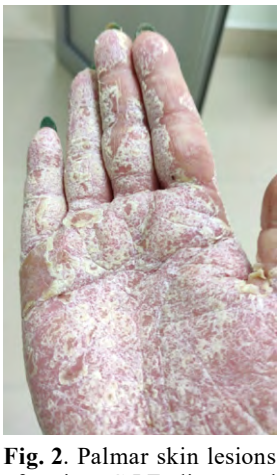

Fig. 2. Palmar skin lesions of patient G.I.F. diagnosed with exfoliative dermatitis.

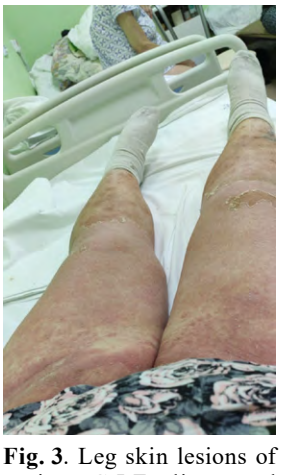

Fig. 3. Leg skin lesions of patient G.I.F. diagnosed with exfoliative dermatitis.

(Tables 1, 2). Compared with the CT data from 20.10.2020, a significant decrease in the intensity and size of pneumonia foci to CT 1 (25%) was observed. Repeated polymerase chain reaction tests to detect SARS-COV2 RNA via nasal and oropharyngeal swabs dated 24.10.2020 and 27.10.2020 yielded negative results.

However, 12 days from the start of COVID19 therapy (22.10.2020), skin rashes appeared on the face of the patient in the form of bright-pink erythema with unclear contours, moderate edema, and minor peeling. The patient was disturbed by itching and a tingling sensation. The prescribed therapy of intramuscular injections of chloropiramine (1.0 ml) and application of cream containing a topical glucocorticoid, an antibiotic, and antimycotic (twice a day) was ineffective. The pathological process spread to the skin of the neck, body, and limbs over the course of several days.

The patient was hospitalized on 05.11.2020 at a branch of the SAHI Republican Clinical Skin-Venereological Dispensary of Naberezhnye Chelny with a main diagnosis of generalized skin rash induced by drugs and medicines.

Therapy with intravenous administration of prednisolone (90 mg), followed by a decrease in dose and transition to the tableted form, for 12 days, intramuscular injection of calcium gluconate and chloropyramine, and application of topical glucocorticoids to the foci was conducted, but the patient's skin process did not resolve. Diabetes decompensation occurred as well.

The patient was transferred to the therapeutic department of the Zainsk Central District Hospital on 18.11.2020. At the time of transfer, the patient's skin process showed generalized characteristics, including extensive hyperemia of the skin of the scalp, face, neck, torso, and upper and lower extremities with infiltration and widespread peeling. On the abdominal skin multiple pustules, prone to confluence are found. The patient also reported soreness of the skin (Fig. 1–3).

The patient was examined by a dermatologist on 20.11.2020 and diagnosed for the first time as exfoliative erythrodermia complicated by piederma. Treatment with cefepim (2 g) and topical glucocorticoids was recommended. In the following days (November 21-22, 2020), a sharp deterioration in the patient's overall state was noted, shivers appeared again and her body temperature rose to 39 °C.

The patient was transferred to the pulmonology department of the Republican Clinical Hospital, where the following laboratory findings were recorded: CRP of 161.7 mg/l, fibrinogen of 8.85 g/l, accelerated ESR (39 mm/h), leukocytosis, banded neutrophil shift and dysproteinemia (hypoalbuminemia and increased number of α-globulins) (Table4, see Tables 1–3).

Table 4. Proteinogram of patient G.I.F. (age, 39 years) conducted on 25.11.2020

Albumin, %	α_1-Globulins, %	α_2-Globulins, %	β_1-Globulins, %	β_2-Globulins, %	γ-Globulins, %
50.2	8.0	16.5	7.7	5.5	12.1

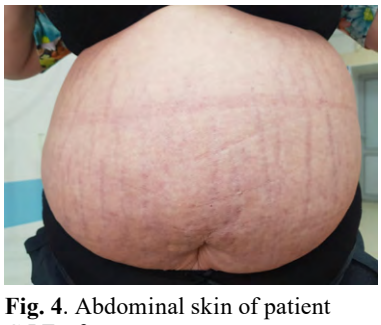

Fig. 4. Abdominal skin of patient G.I.F. after treatment.

Fig. 5. Face and neck skin of patient G.I.F. after treatment.

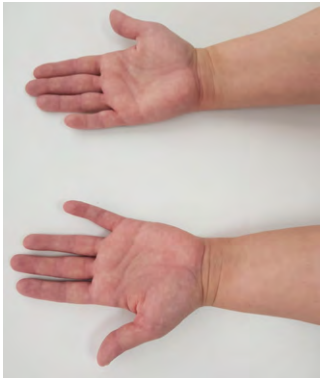

Fig. 6. Palm skin of patient G.I.F. after treatment.

During examination, an acute infectious and somatic pathology was excluded; thus, the patient's recent febrile fever (39 °C) and inflammatory blood changes were associated with a generalized skin process (erythrodermia). Treatment by intravenous infusion of prednisolone (120 mg for 2 days), followed by a decrease in dose and transition to the tableted form, intramuscular injection of chloropiramine (1.0 ml), infusion of enoxiparin (1.2 mg), and application of topical glucocorticoids, Unna cream, and salicylic acid was initiated. Correction of the concomitant pathology was performed with insulin therapy, levofloxacin, fluconazole, and omeprazole.

During the patient's hospital stay, mild hypertensive disease and anemia were detected. Thus, angiotensin II receptor antagonist and oral iron (III) preparation, polymaltosate hydroxide, were prescribed.

The patient was discharged on 14/04/2020 in satisfactory condition with a final diagnosis of "Exfoliative dermatitis. Interstitial lung fibrosis in the outcome of viral lesion of lungs. RF0. State after past novel coronavirus infection. Hypertension of the 2nd stage, risk 2. Chronic heart failure 1, functional class 2. Type 2 diabetes mellitus, insulin-dependent, subcompensated. Target glycated hemoglobin less than 7.5%. Obesity of the 3rd degree of exogenous-constitutional genesis (body mass index 46.87 kg/m^2). Mild anemia."

One month after discharge, the patient was actively visited at home to assess her condition. Hyperglycemia correction, including subcutaneous insulin injections, oral anticoagulants, and antihypertensive drugs, was recommended according to data on discharge. Local therapy, including the use of moisturizing and softening skin care products, was also recommended. The patient accepted these recommendations with good treatment tolerance. At the time of examination, the patient's condition was satisfactory, and complete resolution of exfoliation was recorded (Fig. 4–6).

In the clinical case considered in this report, the pathological skin process began as COVID19-associated toxidermia complicated by exfoliative dermatitis. The patient had a generalized course of erythrodermia against the background of moderate viral pneumonia. The etiological factor of exfoliative dermatitis was presumably the sensitization caused by the simultaneous acceptance of several groups of medicines associated with a high frequency of drug allergy development (e.g., ceftriaxone, hydroxyquinolone). The accompanying metabolic syndromes (i.e., type 2 diabetes, obesity, hypertensive disease) were also aggressive factors contributing to the transfer of toxidermia in exfoliative dermatitis.

This assumption was confirmed by the fact that the skin process could not be resolved without the correction of the patient's hyperglycemia and hemostatic disorders. Deterioration of the patient's clinical laboratory parameters was evident over the course of exfoliative dermatitis but was not an infectious process in the lungs.

Improvement of the patient's condition occurred after administration of complex anti-inflammatory, hypoglycemic, and antithrombotic therapy. Exfoliative dermatitis has a benign course and is characterized by relatively rapid resolution following the use of systemic glucocorticoids and correction of the concomitant pathology.

Conclusion. A description of exfoliative dermatitis associated with COVID19 infection is relevant

for dermatovenenerologists and physician-specialists involved in the treatment of COVID-19. The possibility of developing severe forms of drug toxidermia in patients with novel coronavirus infection and the related somatic pathology should be taken into account during clinical practice. Patient management may require an integrated approach to treat the underlying disease, its related pathology, and emerging complications.

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