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RESEARCH ARTICLE

CUTANEOUS ERUPTION IN COVID-19 IN TWO CASES: SIDE EFFECTS DRUGS OR VIRAL MANIFESTATION?

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Abstract

It has been documented that COVID-19 can induce a significant systemic inflammatory response, potentially attending organ injury. The integumentary system may be similarly affected. The cutaneous manifestations in COVID-19 are largely unknown but case reports and studies will aid further understanding the association of COVID-19 disease progression and dermatological manifestations. Here we report two cases of patients, Hospitalized in pediatric department of Center hospital university of Mohamed VI, Marrakesh, Morocco; presenting cutaneous eruptions after SARS-CoV-2 infection treated with chloroquine and azithromycin and literature review.

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Introduction:-

The Coronavirus infection Disease-19 (COVID-19) is making many health management challenges with multiple uncertainties. The most of them is the treatment; the combination therapy (Hydroxychloroquine or chloroquine and azithromycin) have been increasingly proposed and used in Moroccan program to fight against COVID-19 as an effective treatment.

The other challenge is the various clinical presentations including fever, cough, and shortness of breath. Other symptoms, such as cutaneous manifestations have been reported.

The purpose of this article is to report two relevant cases and provide a literature review of cutaneous eruption in patients with COVID-19 treated with the association chloroquine and azithromycin.

Case Reports:

Case 1:

A 33-year-old woman presented on March 27, 2020 to our department, complaining of fever, dry cough and rhinorrhea which started one week before. The patient was otherwise healthy with no previous adverse drug reactions or no co-morbidities except hypothyroidism treated with Levothyroxine at 50mg/day since 5 years. She was living with her husband, who was diagnosed with COVID-19. The vital signs were as follows: pulse rate 72/minute, respiratory rate 22/minute, temperature 37°C, and SpO₂ 99% on room air.

Laboratory tests revealed a normal white blood cells and platelet count (WBC 5690/mm, PLT 207.000/mmc), normal liver and kidney function, normal C-reactive protein (2.26 mg/L) and procalcitonin, an increased thyroid-

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stimulation hormone level to 18.84 mUI/L with Thyroxine test normal at 15.1 uml/L adjust with increasing her daily dose at 75 mg/day. Prothrombin level at 76 % and activated cephalin time at 27.7 sec.

Naso-pharyngeal swab tested for SARSCoV-2 RNA amplification resulted positive. She was admitted to our department with her children who were diagnosed also with COVID-19 and started off-label antibiotic therapy with azithromycin and chloroquine, following Moroccan protocol of COVID-19 treatment. Other drugs administered during hospitalization were: paracetamol, metoclopramide and subcutaneous low molecular weight heparin.

In the subsequent days, she promptly recovered: she never had fever, chloroquine and antibiotic therapies were continued. At the 9th days of treatment, she presented erythematous lesions on the anterior aspect of both legs. She noticed pruritus and a burning sensation on both legs. Examination revealed multiple, sharply demarcated erythematous eruptions from the surrounding skin of varying sizes on both legs resolving with hyperpigmentation. We conducted to a fixed drug eruption. The eruption has disappeared 5 days later (Figure 1).

Case 2:

A 25-year-old woman, was admitted to our department on April 11, 2020 with presenting symptoms including fever, anosmia, myalgia and diarrhea. Her RT-PCR for COVID was positive on April 11, 2020 therefore she was diagnosed with COVID-19. The vital signs were as follows: pulse rate 83/minute, respiratory rate 24/minute, temperature 36.5°C, and SpO2 98% on room air. The result of the laboratory finding on admission as follows: normal haemoglobin (13.9 g/dL), white blood cell count (6.76×10^3 L), platelet count (219×10^3 L), Ferritin (27 ng/ml), CRP (2.69 mg/dL). The patient was treated with azithromycin and hydroxychloroquine, following Moroccan protocol of COVID-19 treatment associated to other drugs zinc sulfate, vitamin C and subcutaneous low molecular weight heparin. On day 5 of hospitalization, suddenly the patient presents with sudden onset of multiple violaceous to hyperpigmented round to oval plaques on lateral aspects of both legs, the treatment was stopped and the lesions subsided after 2 weeks without any medication. There was no significant past history of any personal drug allergy or in family members.

Discussion:-

The SARS-CoV-2 infection has yet to reveal all of its mysteries. As the number of COVID-19 cases increases, new, rather atypical symptoms are identified. After anosmia and ageusia, digestive disorders or conjunctivitis, urticaria, vasculitis and others dermatological eruptions has been reported in several case reports and series (1). In fact, cutaneous manifestations, such as erythematous rash, localized or widespread urticaria reported as atypical symptom (2), seem to be the most common manifestations in acute severe cases, however, it can be difficult to discriminate the underlying cause (viral infection or medication prescribed)(3).

Recalcati et al (3) conducted study of cutaneous manifestations of COVID-19 including 88 patients (18 patients confirmed COVID-19 and presenting cutaneous manifestation) and they found that the most presentation reported were erythematous rash (77.8% or 14/18) with few cases of urticaria (16.7% or 3/18) and vesicle formation (5.6% or 1/18).

Among the drugs used for prophylaxis against COVID-19 we cite chloroquine (CQ) or hydroxychloroquine (H-CQ) and azithromycin (4). It has been found that this drugs have a potential dermatological side-effects, but the combination (CQ or H-CQ + azithromycin) has been associated with positive patient outcomes according to the low-powered France study (5) with few publications of the combination's side-effects .

The side effects of azithromycin are febrile cutaneous severe skin reaction, burning in eyes, angioedema, skin pain, blistering, toxic pustuloderma, anaphylaxis, generalized red or purple skin rash, cutaneous leukocytoclastic vasculitis, and DRESS syndrome, reported in the publication of Prof Dr Ümit TÜRSEN (6). These eruptions occur in also COVID infection's findings. The other side-effects of azithromycin is the Fixed Drug Eruptions (FDE) which has been reported in many case reports and clinicians should be aware of this eruption (7, 8).

Umeshchandra C. H and all (9) reported also that the FDE is a side effects of Azithromycin through a case report of man suffering from pharyngitis, treated with Azithromycin 500mg once in a day for 5 days.

Concerning the side effects of antimalarials used in the treatment of many pathology such as discoid lupus erythematosus, cutaneous eruptions linked to the treatment such as dry skin, rashes, Stevens-Johnson-like

syndrome, acute generalized exanthematous pustulosis, mucocutaneous dyspigmentation, urticaria, pruritus, flares of psoriasis and exfoliating lesions has been also reported by other author(6).

In our two cases report the diagnosis of erythema nodosum was suspected as viral manifestation of COVID-19 infection caused by an inflammatory disorder affecting subcutaneous fat, furthermore the eruption may oriented to the FDE which may be due to the utilization of azithromycin or CQ/H-CQ.

However, more researches are required to elucidate cutaneous manifestations related to COVID-19 so that we cannot correlate these eruptions to the possibility of dermatologic side effects experienced from medications.

Conflict of interest:

None.

Author's contributions:

All authors have read and contribute to the final version of this article.

Consent for publication:

Written informed consent was obtained from the two patients for publication of this case report and any accompanying images.

Figure:



Figure 1:- Multiple sharply demarcated erythematous eruptions on the anterior aspect of both legs.

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