of developing severe, symptomatic forms of COVID-19 through an androgen-mediated vulnerability to SARS-CoV-2.[4-6] Sensitivity to androgen hormones is determined by genetic variants of the androgen receptor (AR). X-linked genetic polymorphisms that have been associated with androgenetic alopecia, benign prostatic hyperplasia, prostate cancer,[7] and polycystic ovary syndrome[8] may be responsible for an increase in host susceptibility, with AR being the only known promoter of transmembrane protease serine 2 (TMPRSS2). TMPRSS2 is an enzyme involved in SARS-CoV-2 infectivity by initiating the virus' spike protein, a key step in viral replication and cell–virus fusion.[5] In addition to theoretical molecular and epidemiological mechanisms, several studies have reported high rates of androgenetic alopecia in patients hospitalised with severe forms of COVID-19.[2,4-6,9,10]

CONCLUSION

The mechanism of regulation of TMPRSS2 by androgen hormones may explain the increased susceptibility of males to COVID-19. This pathophysiological process can also motivate the less symptomatic forms of children, given their reduced AR expression.[5] The investigation of the potential association between androgens and the severity of COVID-19 disease is justified in view of evaluating androgen suppression therapy as a potential treatment for COVID-19 infection. ■

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Histopathological Findings in COVID-19 Necrotic Lesions

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Disclosure: The authors have declared no conflicts of interest.

Acknowledgements: The patient in this case has given informed consent to publication of their images and case details.

Keywords: COVID-19, histopathology, necrotic lesion, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), skin.

Citation: EMJ Dermatol. 2021;9[1]:52-54. Abstract Review No. AR2.

BACKGROUND

One year after the identification of the novel severe acute respiratory syndrome 2 (SARS-CoV-2) infection in Wuhan, China, and the outbreak of the virus worldwide, the pandemic state persists, and the management of COVID-19 remains burdensome, with the number of people infected daily increasing progressively in most countries and the death rate being alarmingly elevated.[1] Since the elevated rate of infectivity of the virus, the authorisation of histological examination has been a harsh process, with high-risk of contagiousness even in qualified medical personnel.[2] However, thanks to the recently published histological reports, more about the pathogenic mechanism underlying viral-derived tissue damage has been understood. In this report, the authors describe a patient hospitalised for COVID-19 who developed necrotic acral lesions that were biopsied.

CASE REPORT

An 83-year-old female came to the emergency department because of acute respiratory distress, which required oxygen therapy. An oronasal swab was performed to identify SARS-CoV-2 RNA and the test resulted positive. Due to her rapidly deteriorating clinical condition, the patient was admitted to the infectious disease ward. Five days after her inpatient stay, she developed vesicular lesions on the lower

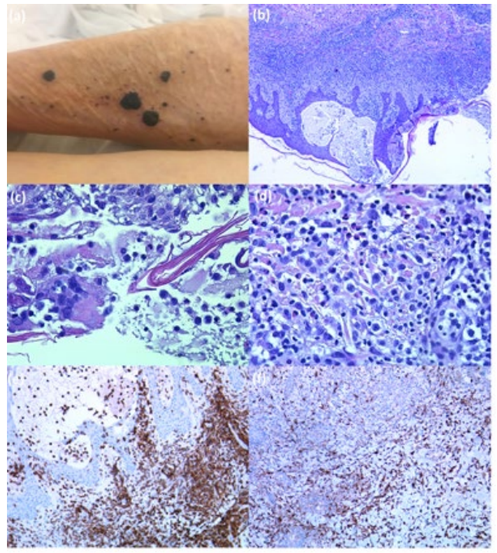

Figure 1: Gross and microscopy appearance of the necrotic lesions of a patient with COVID-19.

A) Multiple necrotic lesions on the lower limb of the patient. There are four main lesions and numerous other lesions with smaller diameters. **B)** Histological examination showing an intraepidermal vesicle and dense inflammatory infiltrate within the dermis (H&E 10x). **C)** Histology of the necrotic lesions. The lumen of the blister contains histiocytes and multinucleated giant cells (H&E 40x). **D)** Histology of the necrotic lesions. Many eosinophils associated with lymphocytes and histiocytes in the superficial dermis (H&E 40x). **E)** Numerous dermal and intraepidermal inflammatory cells are T lymphocytes as demonstrated with anti-CD3 rabbit monoclonal primary antibody 2GV6 (100x immunohistochemistry with haematoxylin counterstain using Ventana Ultraview DAB detection Kit in a Ventana BenchMark Ultra Processor® [Ventana Medical Systems, Tuscon, Arizona, USA). **F)** Histology of the necrotic lesions. The lymphocytes are mixed with numerous macrophages as demonstrated with anti-CD68 (KP-1) antibody (100x immunohistochemistry with haematoxylin counterstain using Ventana Ultraview DAB detection Kit in a Ventana BenchMark Ultra Processor®).
CD: cluster of differentiation; H&E: haematoxylin and eosin staining.

limbs, which quickly became necrotic (Figure 1). A skin biopsy was performed, and the histopathology report evidenced a dermal-epidermal inflammatory infiltrate made of lymphocytes, histiocytes, neutrophils, and eosinophils, which displayed either an interstitial and periannexial distribution or a perivascular one with endothelial swelling and detachment.

The epidermis demonstrated spongiosis, erosion, and vesicles with mild keratinocyte acantholysis, and inflammatory cells (lymphocytes, histiocytes, and multinucleate giant cells [Figure 1]).

The inflammatory infiltrate was composed mainly by T cells (CD3+, CD4+, and CD8+), histiocytes (CD68+), with rare B cells (CD20+) and activated blasts (CD30+) (10–20%). Moreover, many mitotic figures were evident (Ki67). No natural killer cells were detected (CD56+) and no Epstein–Barr virus-LMP1 viral protein was present. In addition, myeloperoxidase, CD34, and Mart1 were negative. This morphologic report led to the identification of the lesions as SARS-CoV-2-related papulovesicular eruptions.

DISCUSSION AND CONCLUSIONS

Mounting scientific evidence has emerged regarding the manifestations of SARS-CoV-2 infection on the skin. Regarding histological reports, while several cases of cutaneous manifestations have been described, relatively few cases were subjected to biopsy because of the numerous limitations imposed in medical centres. Current data reports different histological pictures related to specific clinical aspects.[3]

The maculopapular lesions show lymphocytic exocytosis, with thrombosed vessels filled with neutrophils and eosinophils; conversely, dermatitis is characterised by infiltrated perivascular lymphocyte, focal elements of suprabasal acantholysis, dyskeratotic cells, and swollen vessels with mixed lymphocyte infiltration in the dermis.[3] Vesicular (varicella-like) eruptions show dyskeratotic cells with acantholysis, intraepidermal vesicles, and suspected viral inclusions within multinucleate cells.[3]

Compellingly, a retrospective analysis carried out on 23 patients with COVID-19 and with cutaneous manifestations showed that, at histopathological level, microvascular and endothelial damage were evident. Infiltrating perivascular lymphocytes, thrombosis, and swollen vessels were present and C5b deposits were predominant.[4] Of note, the activation of the complement system and coagulation cascade had already been identified as responsible for vascular clinical manifestations such as thrombosis and necrosis. However, in the authors' case, the presence of abundant infiltrating lymphocyte, dilated vessels, and epidermal vesicles filled with inflammatory infiltrators without obvious elements of thrombosis may suggest a combination of direct viral and immune mediated damage.

Further studies are needed to better understand the skin involvement in COVID-19, in terms of clinical characteristics, evolution, and correlation with the severity of the disease, and the pathological mechanism responsible for cutaneous damage. From the data published so far, it can be assumed that the visible skin lesions are the result of a combination of the direct action of the virus and the immune signalling cascade induced by it. ■

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Sexually Transmitted Infections in Northern Greece During the COVID-19 Pandemic

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Disclosure: The authors have declared no conflicts of interest.

Keywords: COVID-19 pandemic, gonorrhoea, sexually transmitted infections, syphilis.

Citation: EMJ Dermatol. 2021;9[1]:55-56. Abstract Review No. AR3.

BACKGROUND

During the COVID-19 outbreak, many countries imposed restrictive measures that resulted in unprecedented modifications in healthcare services.[1] In several countries, including Greece, most of the public hospitals were practically transformed into COVID-19 units. In addition, public and health authorities repeatedly advised the population to avoid visiting hospitals during the pandemic outbreak. Moreover, social and sexual behaviour dramatically altered as a result of the strict social distancing measures.

Sexually transmitted diseases (STDs), though generally deemed as a major social health problem, rarely end up as an urgent life-threatening condition.[2] Therefore, it is not surprising that the findings of studies from several countries reported a reduced number of STDs diagnosed in 2020 as compared with previous years.[3]

MATERIALS AND METHODS

The authors reviewed records of the STDs clinic of the State Hospital of Skin and Venereal Diseases, Thessaloniki, Greece, to identify newly diagnosed cases of gonorrhoea and syphilis from 1st March–30th October, 2020 and compared it with the respective numbers of the same period in 2019.

RESULTS

The total number of new diagnoses of syphilis and gonorrhoea in 2020 was 91, whereas in 2019 it was 108. The number of newly diagnosed cases of syphilis in 2020 was 72, slightly lower than the 85 cases of 2019 (p=0.943). Similarly, 19 patients were diagnosed in 2020 with gonorrhoea, fewer than the 23 diagnosed in 2019 (p=0.943). Regarding sexual preference, the percentage of heterosexual individuals was significantly lower in 2020, while the percentage of homosexual individuals was higher. The ratio of native Greek patients to foreign patients was comparable in 2020 and 2019. Results are summarised in Table 1.

DISCUSSION

A reduction in newly diagnosed STDs was reported in several other countries during the COVID-19 outbreak. The most remarkable reduction was recorded in Madrid, Spain, where researchers reported a reduction of new syphilis and gonorrhoea cases in the first 26 weeks of 2020 by 73.2% and 81.4%, respectively, as compared with the same period of 2019.[4] In Switzerland, syphilis diagnoses were reduced by 84.8% and gonorrhoea diagnoses reduced by 16.5% in 2020, as compared with 2019.[5] In China, new syphilis diagnoses in 2020 were reduced by 8.2% as compared with 2019.[6]

A direct comparison of these percentages in the authors' hospital is significantly limited by the heterogeneity of used data in terms of collection and reporting. In Greece, the authors' hospital maintained, uninterruptedly, its function throughout the year and was never involved in hospitalising patients with COVID-19. Therefore, the impact of restricted access on the number of newly diagnosed STDs should, reasonably, be less