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Androgenetic alopecia in women and men is not related to COVID-19 infection severity: a prospective cohort study of hospitalized COVID-19 patients

To the Editor,

The ongoing outbreak of COVID-19 has posed significant threats to international health. The first biologic step of potential infectivity of COVID-19 is the priming of the spike proteins by transmembrane protease, serine 2 (TMPRSS2). TMPRSS2 cleave angiotensin converting enzyme 2 for augmented viral entry and thus is regarded as essential for viral spread and pathogenesis in the infected hosts.[1,2] Androgen receptor activity is considered as a requirement for the transcription of the TMPRSS2 gene and no other regulatory element of the TMPRSS2 promoter has been described in human to date.[3] Thus, this led us to hypothesize that variations in the androgen receptor gene may predispose male COVID-19 patients to increased disease severity.

Through a prospective study, 116 hospitalized patients due to severe COVID-19 infection (confirmed with viral nucleic acid testing) were involved in the study. Lung high-resolution computed tomography (HRCT) findings as well as laboratory data, and disease outcome including discharge, intensive care unit (ICU) care, intubation and death, were recorded for each patient. hyper-androgenic skin manifestations including androgenetic alopecia (AGA), acne severity, seborrheic dermatitis and hirsutism were examined by a dermatologist. Severity of AGA was assessed using Hamilton scale and Ludwig scale for male and female patients, respectively. Patients with immunosuppressive conditions and anti-androgenic medication were excluded. Analyses were carried out by Statistical Package for Social Sciences computer software (SPSS version 16, Chicago, IL, USA).

Totally, 118 confirmed COVID-19 patients including 61 men (51.7%) and 57 women (48.3%) with mean age of 60.45 ± 15.99 (ranging 18–100) years were investigated. All the patients were symptomatic. Triad of dyspnoea, cough and fatigue were the most common symptoms that were recorded in 100 (84.7%), 78 (66.1%) and 57 (48.3%) patients, respectively. Twenty-nine patients (24.4%) had all the symptoms of the triad (Table 1).

Chest HRCT showed abnormalities in 115 patients (97.4%) whom all of them had more than one involved lobe. Lesions were inclined to distribute in the lower lobes. Right inferior (92.3%) and right middle lobes (61.0%) were the most and the least affected lobes, respectively. Combination of ground glass opacification and consolidation which was presented in 65 patients (55.1%) was the most involved pattern.

Androgenetic alopecia was present in 45 men out of 61 (73.7%) including 13 (28.8%) severe AGA (Hamilton scale >5), 22 (48.8%), moderate AGA (Hamilton scale 3–4) and 10 (22.2%) mild AGA (Hamilton scale 1–2). In total, 32 women out of 57 (56.1%) had AGA including 2 (6.2%) severe AGA (Ludwig score advanced and frontal), 14 (43.7%) moderate AGA (Ludwig score 2–3) and 16 (50.0%) mild AGA (Ludwig score 1). Both the mortality rate and AGA severity were significantly higher in patients over 60 years old ($P = 0.003$ and 0.020, respectively). AGA was significantly higher in men than women ($P = 0.045$). AGA severity did not show any significant correlation with HRCT severity, neither with patients' ICU care, intubation and expire in both genders. Similarly, other hyperandrogenic manifestations did not significantly correlate with disease outcome and HRCT severity (Table 2).

Among disease outcomes, ICU care, intubation and death were recorded in 48 patients (40.7%), 16 (13.6%) and 22 (18.6%) patients, respectively. Mortality rate was 18.0% among males (11 patients) and 19.3% among women (11 patients). No

Table 1 Demographic characteristics, clinical history, symptoms and signs of 118 patients admitted to hospitals with confirmed COVID-19 infection

Characteristics (Unit)	Results (Mean ± SD) *N* (%)	Characteristics (Unit)	Results (Mean ± SD) *N* (%)	Characteristics (Unit)	Results (Mean ± SD) *N* (%)	Characteristics (Unit)	Results (Mean ± SD) *N* (%)
Demography		**History**		**Symptoms**		**Signs**	
Gender					100 (84.7%)	Oral temperature ©	
Men	61 (51.7%)	Smoking	30 (25.4)	Dyspnoea		≥ 38	42 (35.6%)
Women	57 (48.3%)					< 38	76 (64.4%)
Age	60.45 ± 15.99	Alcohol consumption	4 (3.4%)	Cough	78 (66.1%)	Percutaneous O_2 saturation (%)	31 (26.2%)
						>90	
Men	58.36 ± 17.04					80–90	65 (55.0%)
Women	64.82 ± 13.60					<80	22 (18.6%)
Height (cm)	166.89 ± 9.59	Opium consumption	24 (20.3%)	Fatigue	57 (48.3)	Respiratory rate	
						≥20	101 (85.6%)
						<20	17 (14.4%)
Weight (kg)	72.92 ± 12.53	Hypertension	40 (33.8%)	Fever	42 (35.6%)		
BMI (kg/m^2)	26.17 ± 4.00	Diabetes mellitus	32 (27.1%)	Muscle pain	40 (33.9%)		
Educational status		Ischemic heart disease	18 (15.2%)				
Illiterate	52 (44.1%)			Chest pain	36 (30.5%)		
Less than 11 years	46 (39.0%)						
More than 11 years	20 (16.9%)						
Job status		Family history of COVID-19 infection	12 (10.2%)	Loss of appetite	26 (22.0%)		
Employee	18 (15.3%)						
Self employed	28 (23.7%)						
Retired and unemployed	20 (16.9%)						
Housewife	52 (44.1%)						
Location		Days from symptom onset to admission		Chilling	26 (22.0%)		
Urban	85 (72.0%)						
Rural	33 (28.0%)						
Marital status				Sputum	20 (16.9%)		
Single	11 (9.3%)						
Married	107 (90.7%)						
				Sore throat	10 (8.5%)		

Table 2 Lung HRCT findings vs. hyper-androgenic finding in 118 patients admitted to hospitals with confirmed COVID-19 infection

HRCT findings	*N* (%)	Hyper-androgenic findings	*N* (%)
Number of involved lobes (>5%)		**Both genders (*N* = 118)**	
0	3 (2.5%)	History of acne	18 (15.3%)
1	0 (0.0%)		
2	16 (13.6%)	Current acne	7 (5.9%)
3	21 (17.8%)	Mild	3 (2.5%)
4	31 (26.3%)	Moderate	4 (3.4%)
5	47 (39.8)	Severe	0 (0.0%)
Lobe of lesion distribution (>5%)		History of greasy skin	38 (32.2%)
Left upper lobe	90 (76.2%)		
Left lower lobe	105 (8.9%)		
Right upper lobe	78 (66.1%)	Current greasy skin	23 (19.5%)
Right middle lobe	72 (61.0%)		
Right lower lobe	109 (92.3%)	History of seborrheic dermatitis	20 (16.9%)
Bilateral upper lobes	70 (59.3%)		
Bilateral lower lobes	99 (83.9%)		
Pattern of the lesion		Current seborrheic dermatitis	6 (5.1%)
Ground glass opacification	30 (25.4%)	**Male (*N* = 61)**	
Consolidation	2 (1.7%)	Androgenic alopecia (Hamilton-Norwood scale)	45 (73.7%)
Crazy paving	1 (0.8%)	Mild	10 (22.2%)
Ground glass and Consolidation	65 (55.1%)	Moderate	22 (48.8%)
All the three patterns	20 (16.9%)	Severe	13 (28.8%)
		Excess hair	24 (39.3%)
		Face	21 (87.5%)
		Ear	23 (95.8%)
		Chest	6 (25.0%)
Pleural effusion	21 (17.8%)	Pre-puberty	0 (0.0%)
Pericardial effusion	1 (0.8%)	**Female (*N* = 57)**	
Cavitation	0 (0.0%)	Androgenic alopecia (Ludwig scale)	32 (56.1%)
		Mild	16 (50.0%)
		Moderate	14 (43.7%)
		Severe	2 (6.2%)
		History of infertility	2 (3.5%)
		Dysmenorrhea	11 (19.3%)
		History of hirsutism	15 (26.3%)
		Current hirsutism	19 (33.3%)
		Face	17 (89.4%)
		Nipple	9 (47.3%)

significant difference was observed between the two genders in terms of disease outcome.

The precise prevalence of AGA among healthy Iranian population is unknown; however, based on literature, prevalence of age-matched AGA in a similar white population is estimated 31–53% in men and up to 38% in women.[4] Our results indicated substantial proportion of AGA in hospitalized COVID-19 patients considering estimated age-matched AGA in healthy population. Moreover, hyper-androgenic phenotypes have been recently observed by some authors to have correlation with severe forms of COVID-19.[5–8] However, the results of this study revealed that AGA as well as other skin hyper-androgenic manifestations are not related risk of severe COVID-19 infection. Additional large-scale prospective studies are recommended.

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Conflict of interest

None declared.

Disclosure statements

Nothing to disclose.

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Detection of a second outbreak of chilblain-like lesions during COVID-19 pandemic through teledermatology

Editor

Teledermatology (TD) was previously described as an efficient substitute for in-person visits for COVID-19-associated lesions.[1] During the first COVID-19 wave, chilblain-like lesions (CLLs) were the most reported dermatological manifestation.[2–4] Although SARS-CoV-2 infection polymerase chain reaction and serology testing were negative for most cases, this unexpected outbreak of chilblains like lesions remained remarkable.[5]

To date, it is unclear whether CLL outbreak reported during the first COVID-19 pandemic is related to media release of this particular sign right after the wave or whether observed CLLs are truly associated with COVID-19 disease.[6] Therefore, we aimed to evaluate the prevalence of request with the stated diagnosis of CLLs observed in two TD networks (store and forward requests addressed by either general practitioner dermatologists or institutions) between January and December 2020 and to compare this prevalence to that observed between January and December 2019 in one of the two TD centres. In 2020, the monthly number of COVID-19 deaths and CLLs was visualized on the same graph. Continuous variables were compared using Wilcoxon test and categorical variable using chi-square test.

In 2020, out of 4493 TD requests, 137 were for CLLs (3%). In 2019, out of 3554 requests, 11 were for CLLs (0.3%). Between 2019 and 2020, the number of requests for CLLs increased up to ten times. Two peaks of CLL prevalence were identified in 2020, one in March/April (period 1) and another in November/December (period 2); these two periods fitted perfectly the COVID-19 peaks of deaths in France (Fig. 1). The characteristics of the requests during the COVID-19 pandemic are summarized in Table 1. Most of the requesting physicians were general practitioners (n = 71 (86%) and n = 29 (97%) for the periods 1 and 2, respectively). Neither patients' median age nor sex ratio significantly differed between the two time periods. A minority of patients had COVID-19 symptoms or a recent COVID-19 contact: 41% during the first period vs 23% during the second period. During the second period, more than half of physicians associated observed CLLs to COVID-19. The PCR and serology results were not available.

Our results highlight the following: (1) an increase in the number of TD requests for CLLs between 2019 and 2020, (2) two peaks of TD requests for CLLs concomitant with peaks of COVID-19 deaths in 2020 and (3) general practitioners as major requesting physicians.

The causal link between chilblain-like lesion and COVID-19 is highly controversial.[7] Similar to the first CLL outbreak, which was observed away from cold weather, TD networks also enabled the detection of a second CLL outbreak before the cold weather of winter and concomitant with the second peak of COVID-19 deaths in France. These findings confirmed the second wave of CLLs previously described by Piccolo et *al*.[8] The clinical and histopathological features of COVID-19-associated CLLs have been described as similar to non-COVID-19-associated CLLs. Histological studies showed a mild interface dermatitis featuring vacuolar degeneration of

