doi:10.1111/imj.15261

LETTER TO THE EDITOR

General correspondence

Late unexpected consequences of COVID-19 infection in survivors of acute hypoxic respiratory failure

In the literature, the onset of alopecia occurring after multisystem illnesses, psychological distress, fever and intensive care unit (ICU) admission is described. The highest percentage of alopecia described in patients after ICU admission is 35%.[1,2] During the COVID-19 pandemic some studies reported patients suffering from androgenic alopecia and alopecia areata.[3] The first seems to be supported by an androgen-regulated pathway based on the transcription of the transmembrane protease serine 2 (TMPRSS2), required for COVID-19 cells' infection included in the lung tissue.[4,5] We conducted a prospective single-centre study (number 6380) from May to July 2020. All 38 patients enrolled were COVID-19 survivors of severe hypoxic respiratory failure who had been admitted to respiratory intermediate ICU needing respiratory support. They were all re-evaluated via a dermatologic assessment as they were all complaining to their general physicians of persistent alopecia. Within 3 months after discharge in 71% of this patient cohort the onset of telogen effluvium (TE) alopecia phenotype was reported (Table 1). TE is a scalp disorder characterised by excessive shedding and thinning of hair. Among the principal factors related to its development, drugs, trauma and emotional and physiological stress are encountered. Patient characteristics and demographics are shown in Table 1. Usual known aetiologies of TE are fever, systemic illnesses, childbirth, major surgery and emotional strain. Furthermore, major potential pathological

Table 1 Patients' characteristics and demographics

Patients, *n* = 38	Patients with alopecia	Patients without alopecia	*P*-value
n (%)	27 (71)	11 (29)	0.0002
Age, mean ± SD (years)	60 ± 10	63 ± 9	0.12
Male, *n* (%)	17 (63)	10 (90)	0.49
TE alone, *n* (%)	8 (30)		
AGA alone, *n* (%)	5 (19)		
TE/AGA combined, *n* (%)	13 (48)		
TE/AA combined, *n* (%)	1 (4)		
At admission			
PCR, mean ± SD	104.0 ± 64.3.0	80.0 ± 53.2	0.09
Ferritin, mean ± SD	593.0 ± 347.0	724.3 ± 463.2	0.14
PaO_2/FiO_2 ratio, mean ± SD	218.0 ± 80.0	237.0 ± 84.8	0.45
Prior to admission			
Any hair problem, *n* (%)	9 (33)	0	0.21
Dysthyroidism, *n* (%)	6 (22)	0	0.42
During admission			
On therapeutic doses of low-fraction anti-coagulation, *n* (%)	18 (66)	8 (72)	0.87
On prophylactic doses of low-fraction anti-coagulation, *n* (%)	6 (22)	2 (18)	0.82
Oral or intravenous corticosteroids, *n* (%)	7 (26)	2(18)	0.68
On antibiotics, *n* (%)	27 (100)	11 (100)	1
On respiratory support and O_2 supplementation, *n* (%)	27 (100)	11 (100)	1
Non-invasive respiratory support			
HFNC, *n* (%)	1 (4)	2 (18)	0.17
CPAP, *n* (%)	22 (81)	9 (81)	0.99
NIV, *n* (%)	4 (15)	1 (9)	0.67
After admission			
On non-vitamin K oral anti-coagulants, *n* (%)	8 (30)	5 (45)	0.52
On cardio-aspirin, *n* (%)	5 (19)	0	0.53

AA, alopecia areata; AGA, androgenic alopecia; CPAP, continuous positive airway pressure; HFNC, high-flow nasal cannula; NIV, non-invasive ventilation; PCR, polymerase chain reaction; SD, standard deviation; TE, telogen effluvium.

background described in the literature include: (i) premature hair teloptosis, usually related to topic scalp treatment; (ii) collective teloptosis, often caused by an external insult that predisposes hairs to synchronise their life cycle and to start falling together; and (iii) premature telogen, in which hairs commonly quicken their growth progression and rapidly displace. Usually, options (ii) and (iii) are drug related (e.g. anti-coagulants). Autoimmune diseases, thyroid dysfunctions or emotional stress may also predispose patients to suffer from TE.[6] All followed-up patients presenting with TE were on anti-coagulants during admission, a few were affected by dysthyroidisms (Table 1), and all experienced emotional distress due to the severity of the disease's clinical manifestations: all potential TE promoters. However, the most important pathophysiologic pathway that might have predisposed patients to TE onset may be found in the prolonged persistent severe hypoxia these patients experienced, which may be responsible for a lower or insufficient blood supply to the scalp tissues, leading to TE alopecia. Furthermore, the use of tight mask head support for many consecutive hours or sometimes days, may have also contributed to the drop in scalp oxygenation and the normal vital cycle of hair. To the best of our knowledge, no other reports have described this potential correlation. In conclusion, this study found that 71% of survivors of hypoxaemic ARF secondary to severe COVID-19 infection were affected by TE alopecia. The pathophysiologic mechanisms responsible for its onset may be prioritised as follows: (i) severe prolonged hypoxia; (ii) increased androgen receptor related pathway; (iii) drugs used during admission; (iv) stress; and (v) autoimmune disease. Further studies will be warranted to clarify better each of those hypothesised mechanisms or the potential correlations among them.

Received 16 January 2021; accepted 21 February 2021.

Lucrezia De Michele,[1] Paola Pierucci,[2] Giovanna E. Carpagnano,[2] Domenico Bonamonte,[3] Francesca Ambrogio,[3] Guido Giovannetti,[1] Michela Dimitri[2] and Carlo D'Agostino[1]

[1]Cardio Thoracic Department, Cardiology Unit, Policlinico di Bari, [2]Cardio Thoracic Department, Respiratory and Sleep Disorders Unit, Policlinico di Bari, 'Aldo Moro' Bari University, and [3]Department of Biomedical Science and Human Oncology, Dermatology Unit, University of Bari Medical School, Bari, Italy

References

1 Battle CE, James K, Paul Temblett J. Alopecia in survivors of critical illness. *J Intensive Care Soc* 2016; **17**: 270.

2 Scott T, Davies M, Dutton C, Cummings I, Burden B, England K *et al*. Intensive care followup in UK military casualties: a one year pilot. *J Intensive Care Soc* 2014; **15**: 113–16.

3 Wambier CG, Vaño-Galván S, McCoy J, Gomez-Zubiaur A, Herrera S, Hermosa-Gelbard Á *et al*. Androgenetic alopecia present in the majority of patients hospitalized with COVID-19: the 'Gabrin sign'. *J Am Acad Dermatol* 2020; **83**: 680–2.

4 Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S *et al*. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell* 2020; **181**: 271–80.e8.

5 Mikkonen L, Pihlajamaa P, Sahu B, Zhang F-P, Jänne OA. Androgen receptor and androgen-dependent gene expression in lung. *Mol Cell Endocrinol* 2010; **317**: 14–24.

6 Rebora A. Telogen effluvium: a comprehensive review. *Clin Cosmet Investig Dermatol* 2019; **12**: 583–90.