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ORIGINAL ARTICLE

Acute Telogen Effluvium in Patients Recently Infected with SARS-CoV-2

Deflúvio Telógeno Agudo em Doentes Recentemente Infetados com SARS-CoV-2

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ABSTRACT – Introduction: The hair cycle is especially susceptible to endogenous and exogenous stimuli, including febrile states and emotional stress, which are a constant in this pandemic era. In this case series, we describe the clinical characteristics of patients recently diagnosed with SARS-CoV-2 infection who developed acute telogen effluvium.

Material and Methods: We performed a registry of patients with laboratory-confirmed SARS-CoV-2 infection who developed acute telogen effluvium and actively sought medical care at the Hair Unit of Dermatology Center of CUF Descobertas Hospital, from March 2020 to October 2020. Patient demographics, the month of SARS-CoV-2 infection diagnosis, COVID-19 associated symptoms, latency of telogen effluvium, duration of hair loss, and associated scalp symptoms were recorded.

Results: Twenty-seven patients recently diagnosed with SARS-CoV-2 infection presented with acute telogen effluvium. Of them, 5 (18.5%) patients mentioned trichodynia. The median time of latency of increased hair loss since SARS-CoV-2 infection diagnosis was 10 weeks. In a third of cases (n=9, 33.3%), hair loss occurred early (with a latency period of 3 weeks or less). The resolution of telogen effluvium was documented in 16 (59%) cases with a median duration of hair loss of 24.5 days. The most common symptoms of COVID-19 were fever (n=17, 63%), ageusia (n=8, 30%), cough (n=6, 22%), myalgia (n=5, 18.5%), anosmia (n=4, 15%), and thoracalgia (n=3, 11%). Four patients (15%) with SARS-CoV-2 infection were asymptomatic for COVID-19.

Discussion: Acute telogen effluvium corresponds to a delayed consequence of an abnormal shift in the hair cycle from anagen to telogen, which is responsible for premature hair shedding, occurring approximately two to three months after a triggering event. Viral illnesses and febrile states are known causes. Regarding SARS-CoV-2 infection, we hypothesize that viral cytopathic effects and inflammatory or immune responses may affect hair follicles and explain hair loss and trichodynia.

Conclusion: Our case series presents the first comprehensive collection of patients with acute telogen effluvium following SARS-CoV-2 infection. Interestingly, in a third of our cases, telogen effluvium developed within the first 3 weeks of SARS-CoV-2 infection. Based on these data, we propose that this finding should be considered in COVID-19, especially at the convalescent phase.

KEYWORDS – Alopecia; COVID-19; Coronavirus Infections; SARS-CoV-2.

RESUMO – Introdução: *O ciclo do cabelo é particularmente suscetível a estímulos endógenos e exógenos, como estados febris e stress emocional, que são uma constante nesta era pandémica. Nesta série de casos, descrevemos as características clínicas de doentes recentemente diagnosticados com infeção por SARS-CoV-2, que desenvolveram deflúvio telógeno agudo.*

Material e Métodos: *Realizámos o registo de doentes com infeção por SARS-CoV-2 confirmada laboratorialmente, que desenvolveram deflúvio telógeno agudo e foram observados na Unidade de Cabelo do Centro de Dermatologia do Hospital CUF Descobertas, entre março e outubro de 2020. Variáveis como características demográficas, o mês de diagnóstico de COVID-19, sintomas associados à COVID-19, período de latência do deflúvio telógeno, duração da queda de cabelo e sintomas do couro cabeludo foram analisadas.*

Resultados: *Vinte e sete doentes recentemente diagnosticados com infeção por SARS-CoV-2 desenvolveram deflúvio telógeno agudo. Destes, 5 (18,5%) doentes referiram tricodínia associada. A mediana do tempo de latência foi de 10 semanas. Num terço dos casos (n=9, 33,3%), a queda de cabelo ocorreu precocemente (com um período de latência de 3 semanas ou menos). Houve resolução do deflúvio telógeno em 16 (59%) casos com uma duração mediana de 24,5 dias. Os sintomas de COVID-19 mais comuns foram febre (n=17, 63%), ageusia (n=8, 30%), tosse (n=6, 22%), mialgias (n=5, 18,5%), anosmia (n=4, 15%) e toracalgia (n=3, 11%). Quatro doentes (15%) foram assintomáticos para a COVID-19.*

Discussão: *O deflúvio telógeno agudo corresponde a uma consequência tardia de uma mudança anormal no ciclo do cabelo da anagénese para a telogénese. Esta alteração é responsável pela queda prematura de cabelo, que ocorre aproximadamente 2 a 3 meses após o evento desencadeante. As infeções virais e as doenças febris são causas conhecidas de deflúvio telógeno agudo. Relativamente à infeção por SARS-CoV-2, consideramos hipoteticamente que efeitos citopáticos virais e respostas inflamatórias ou imunes possam afetar os folículos pilosos e explicar a queda de cabelo e a tricodínia.*

Conclusão: *Esta série de casos representa a primeira descrição de eflúvio telógeno agudo após o diagnóstico de infeção por SARS-CoV-2. Curiosamente, num terço dos casos, o deflúvio telógeno manifestou-se nas primeiras 3 semanas da infecção. Com base nestes dados, propomos que este achado seja considerado na COVID-19, nomeadamente na fase de convalescença.*

PALAVRAS-CHAVE – *Alopecia; COVID-19; Infecções por Coronavírus; SARS-CoV-2.*

INTRODUCTION

A novel virus of the Coronaviridae family, designated "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2), was identified in Wuhan, China, in December 2019. The infection caused by SARS-CoV-2, also known as COronaVIrus Disease-19 (COVID-19), has rapidly spread throughout the world, becoming pandemic in early March 2020, with significant health, social, and economic impact.[1] To date, more than 55.6 million people have been infected by SARS--CoV-2 worldwide.[2]

The clinical spectrum of COVID-19 is heterogeneous, ranging from asymptomatic or mild symptoms to severe and fatal illness. Over the course of the disease, diverse organs and systems can be affected. In the skin, several clinical manifestations have been associated with COVID-19. Urticarial, morbilliform, and varicelliform eruptions, pernio-like lesions, purpuric lesions, acro-ischemic lesions, and retiform purpura, may occur early and their identification may be relevant for the initial diagnosis of SARS-CoV-2 infection.[1,3-7] However, delayed dermatological manifestations of the infection can also hypothetically be expected, similar to what is observed with other viral diseases.

The hair cycle is especially susceptible to endogenous and exogenous stimuli, including febrile states and emotional stress,[8-11] which are a constant in this pandemic era.[12]

In this case series, we describe the clinical characteristics of patients with a recent history of SARS-CoV-2 infection who presented in our Hair Consultation due to acute telogen effluvium (TE). Our objectives were to assess the timing and duration of the hair loss and the presence of scalp symptoms after the diagnosis of SARS-CoV-2 infection.

MATERIAL AND METHODS

We performed a registry of patients with laboratory-confirmed SARS-CoV-2 infection who developed acute TE and actively sought medical care at the Hair Unit of Dermatology Center of CUF Descobertas Hospital, from March 2020 to October 2020. Patient demographics, the month of SARS-CoV-2 infection diagnosis by polymerase chain reaction of nasopharyngeal swab test, COVID-19 associated symptoms, latency and duration of hair loss, associated scalp symptoms, and local of hair loss (scalp, body) were recorded. The anonymized patient data were analyzed using SPSS Statistics, 23rd version.

RESULTS

From March 2020, we observed 27 patients with acute TE following SARS-CoV-2 infection. The mean age was 45 (± 16) years. There was a female preponderance with a female to male ratio of 6.75:1.

Of the 27 patients with acute TE, 5 (18.5%) patients also referred trichodynia. The median time of latency of increased hair loss since SARS-CoV-2 infection diagnosis was 10 weeks. In a third of cases (n=9, 33.3%), hair loss occurred early (with a latency of 3 weeks or less).

Overall, the clinical picture of acute TE was characterized by diffuse hair loss with a bitemporal recession of the hairline. The pull test was highly and diffusely positive. Trichoscopy revealed empty follicles and numerous short regrowing hairs of normal thickness. No signs of peripilar inflammation were observed. In 3 (11%) patients, hair loss involved not only the scalp but also the body. TE resolution was documented in 16 (59%) cases with a median duration of hair loss of 24.5 days.

Figure 1 - Acute telogen effluvium after SARS-CoV-2 infection diagnosis. Clinical picture showing temporal recession.

Regarding SARS-CoV-2 infection, the great majority of patients (n=23, 85%) had symptoms and 4 (15%) patients were asymptomatic. The most common symptoms were fever (n=17, 63%), ageusia (n=8, 30%), cough (n=6, 22%), myalgia (n=5, 18.5%), anosmia (n=4, 15%), and thoracalgia (n=3, 11%). Two patients also reported cutaneous manifestations, such as pernio-like lesions (n=1) and maculopapular eruption (n=1). Most symptomatic cases of COVID-19 were mild in severity and only 3 (11%) patients required hospitalization. None of them needed admission to the intensive care unit.

Figures 1, 2 and 3 illustrate the clinical and trichoscopic features of one of the patients with acute TE following SARS-CoV-2 infection.

Patients' data are summarized in Table 1.

Figure 2 - Acute telogen effluvium after SARS-CoV-2 infection diagnosis. Trichoscopy showing decreased hair density with the presence of empty follicles and short regrowing hairs.

Figure 3 - Acute telogen effluvium after SARS-CoV-2 infection diagnosis. Amount of hair shed on a wash day showing stage 6 of hair loss severity (about 750 hairs).

DISCUSSION

In this case series, we observed 27 patients with acute TE developed after SARS-CoV-2 infection diagnosis. There was a female predominance, as usually occurs in TE. Possible explanations include a higher vulnerability of female hair follicles, easier recognition of hair loss due to longer hairs, and the higher impact of hair loss in women.[8,9]

In this study, the median latency between the diagnosis of SARS-CoV-2 infection and the development of hair loss was 10 weeks. TE corresponds to a delayed consequence of an abnormal shift in the hair cycle from anagen to telogen, which is responsible for premature shedding of hair, occurring approximately two to three months after a triggering event. Different endogenous and exogenous factors may disrupt the balance of the hair cycle and induce TE, including febrile states.[8-11] In our case series, fever was the most frequent symptom of COVID-19, present in 63% of cases. Even so, 15% of patients had asymptomatic SARS-CoV-2 infection. Similar to our observations, hair

Table 1 - Summary of patients with acute telogen effluvium after SARS-CoV-2 infection diagnosis.

Patients	Gender	Age	SARS-CoV-2 infection		Trichodynia	Telogen effluvium			
			Month of diagnosis	Systemic symptoms		Latency period (weeks)	Local of hair loss	Resolution	Duration of hair loss (days)
1	M	45	March	Fever, thoracalgia	Yes (pain)	9	Scalp	Yes	8
2	F	60	March	Fever, cough, headache, diarrhea	Yes (burning sensation)	11	Scalp	Yes	10
3	F	41	March	No	No	11	Scalp	Still active	-
4	F	18	March	Ageusia	No	14	Scalp	Yes	28
5	F	31	April	Fever, cough, anosmia	No	13	Scalp and body	Yes	56
6	F	63	April	No	No	10	Scalp	Yes	84
7	F	50	April	Cough, ageusia	No	3	Scalp	Yes	21
8	F	53	April	Fever, myalgia	No	12	Scalp	Yes	21
9	F	39	April	Fever	No	14	Scalp	Yes	28
10	F	26	April	Fever, anosmia, ageusia, pernio-like lesions	No	11	Scalp	Yes	35
11	F	58	April	No	No	11	Scalp	Yes	21
12	F	24	April	Fever, cough, ageusia	No	5	Scalp	Still active	-
13	F	23	April	Ageusia	No	12	Scalp	Still active	-
14	M	48	April	Fever, thoracalgia, myalgia	No	12	Scalp	Yes	90
15	M	26	May	Fever, maculopapular eruption	No	2	Scalp	Yes	28
16	F	61	May	No	No	10	Scalp	Yes	13
17	F	29	May	Fever, myalgia, abdominal pain	No	3	Scalp and body	Yes	28
18	F	27	June	Fever, thoracalgia, dyspnea	No	2	Scalp and body	Yes	21
19	F	62	June	Fever, myalgia	No	0	Scalp	Still active	-
20	F	48	June	Fever, cough, myalgia	No	8	Scalp	Still active	-
21	F	41	July	Fever	Yes (pain)	3	Scalp	Still active	-
22	F	76	July	Anosmia, ageusia	No	11	Scalp	Yes	14
23	F	61	August	Sore throat	Yes (pain, burning sensation)	2	Scalp	Still active	-
24	F	53	August	Fever, ageusia	No	10	Scalp	Still active	-
25	F	72	August	Fever, sore throat	No	12	Scalp	Still active	-
26	M	37	September	Cough	No	3	Scalp	Still active	-
27	F	48	October	Fever, anosmia, ageusia, arthralgia	Yes (pain)	1	Scalp	Still active	-

F: female. M: male.

loss had been a common condition during the 1918 influenza pandemic (also known as Spanish flu), developing 2 to 6 weeks after the onset of the fever, according to historical descriptions.[10] Other infectious illnesses have also been associated with TE, such as other viral infections (e.g.: dengue, HIV infection), typhoid, malaria, and tuberculosis.[8,13,14]

Among patients with acute TE herein described, 18.5% also referred trichodynia. Trichodynia corresponds to a complex symptom that includes pain, pruritus and/or a burning sensation, most commonly associated with hair loss, which occurs in about 20% of patients with TE, according to the literature. It is generally considered a sign of severity and, in some cases, it may be a warning symptom of imminent hair shedding, which may occur after the trichodynia onset.[15]

Pathophysiological mechanisms of hair loss in TE and trichodynia are complex and not fully understood.[8,10] Substance P, a proinflammatory mediator synthesized by neuronal cells and released by cutaneous peripheral nerve terminals, seems to play a major role in trichodynia.[15] Inflammation of the small papillary or peripapillary vessels is possibly involved in both TE and trichodynia. Furthermore, some authors suggest that post febrile TE may be secondary to circulating immunocomplexes. Unfortunately, the histopathological examination fails to demonstrate signs of perifollicular inflammation in TE scalp biopsies. This may be due to a deferred biopsy, done when the injurious event is no longer active.[10] In our cases, scalp biopsies were not performed. Interestingly, in a third of our cases, increased hair loss developed within the first 3 weeks of SARS-CoV-2 infection. This aspect is comparable to the reports concerning hair loss in dengue,[13,16] in which hair shedding occurred as early as the first month after acute infection. These descriptions made the authors suggest that the dengue virus may primarily infect human hair follicle dermal papilla cells.[16] Regarding COVID-19, multifactorial pathogenesis may explain dermatological conditions associated with SARS-CoV-2 infection.[17,18] Among them, viral cytopathic effects and inflammatory or immune responses, including stimulation by cytokines and deposition of immunocomplexes,[17,18] which may also affect hair follicles and induce hair loss.

Generally, TE is a reactive and self-limiting condition. In our case series, TE resolution occurred in the majority of patients and the median duration of the hair loss was 24.5 days. However, the number of days referring to hair loss is an approximate number and should be regarded as a subjective assessment of patients. In fact, if the triggering factor spontaneously resolves or is treated, patients normally experience hair shedding for 2-3 months and a significant cosmetic improvement is expected with full hair restoration after 6-12 months.[8]

Limitations of this case series include the small size sample and impossibility to estimate the incidence or prevalence of this condition in patients diagnosed with SARS-CoV-2 infection. Furthermore, we cannot exclude an epiphenomenon. The emotional stress involved in the pandemic, even in non-infected people, might also significantly contribute to TE and should not be ignored.[19] In addition, the confinement recommended by the authorities has led to changes in lifestyle, including eating habits, sleep, outdoor activities, and social life, which may also influence the hair cycle. Further studies are necessary to establish causality between SARS-CoV-2 infection and TE.

CONCLUSION

Our case series presents the first comprehensive collection of patients with acute TE after SARS-CoV-2 infection. Interestingly, in a third of our cases, TE developed within the first 3 weeks of SARS-CoV-2 infection. Based on these data, we propose that this finding should be considered in COVID-19, especially at the convalescent phase. Despite being a common, reactive, and self-limiting cause of diffuse, nonscarring alopecia, acute TE may manifest as a cataclysmic and alarming phenomenon. Even not progressing to complete baldness, patients who seek medical care are often very concerned about becoming bald.[8] Therefore, TE may be a source of significant psychological and emotional distress, which is essential to recognize and reassure patients.[8,20]

Future studies are necessary to clarify the possible association between SARS-CoV-2 infection and TE, to understand involved pathophysiological mechanisms, and to assess the real incidence of hair loss and trichodynia in patients recently infected with SARS-CoV-2.

Conflicts of Interest: The authors have no conflicts of interest to declare. **Financing Support**: This work has not received any contribution, grant or scholarship. **Confidentiality of Data**: The authors declare that they have followed the protocols of their work center on the publication of data from patients. **Protection of Human and Animal Subjects**: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki). **Provenance and Peer Review**: Not commissioned; externally peer reviewed.

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