Dermatology Practical & Conceptual

The Difference Between SARS-CoV-2 Associated Telogen Effluvium and Telogen Effluvium Due to Other Causes

Didem Kazan[1,2], Defne Özkoca[3], Nazlı Dizen Namdar[1]

1 Kutahya Health Science University, Evliya Celebi Training and Research Hospital, Dermatology and Venerology Clinic, Kutahya, Turkey
2 Istanbul Arel University, Department of Dermatology and Venerology, Istanbul, Turkey
3 Zonguldak Atatürk State Hospital, Dermatology and Venerology Clinic, Zonguldak, Turkey

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Corresponding Author: Didem Kazan, Kutahya Health Science University, Evliya Celebi Training and Research Hospital, Dermatology and Venerology Clinic,Kütahya; Istanbul Arel University, Department of Dermatology and Venerology, Istanbul, Turkey. Bussiness tel: +902742236053, E-mail: didem.senses_343@hotmail.com

ABSTRACT

Introduction: Telogen effluvium (TE) is a common type of non-cicatricial alopecia, and it is reported frequently in patients with SARS-CoV-2 infection.

Objectives: Herein, we aimed to examine the demographic, dermoscopic, and laboratory features of the patients with SARS-CoV-2 associated TE (CATE) and compare them with TE due to other causes (TEDOC) according to these features.

Methods: In this retrospective case-control study we evaluated the patients who were diagnosed with TE and were above 18 years of age between April and June 2022. The patients were divided into two groups based on their medical history and SARS-CoV-2 PCR positivity. The first group included patients with CATE and positive SARS-CoV-2 PCR test results in the last 3 months. The second group consisted of patients with TEDOC. Patients gender, age, disease duration, additional systemic disease, dermoscopic findings, and laboratory results were recorded.

Results: A total of 92 patients, 86 (93.5%) females, and 6 (6.5%) males, were included in the study. CATE was detected in 52 (56.5%) patients whereas 40 (44.5%) patients had TEDOC. The mean time between the onset of SARS-CoV-2 infection and hair loss complaint was calculated as 64.8 + 25.6 days, and this time was significantly shorter than patients with TEDOC (P = 0.003). The dermoscopic evaluation showed that empty follicular openings and yellow dots were statistically higher in patients with CATE, whereas short regrowing hair were markedly higher in patients with TEDOC (P = 0.001, P = 0.001, and P = 0.001, respectively)

Conclusions: CATE is characterized by excessive hair-shedding that begins sooner after infection than classic TE. Dermoscopic findings can assist clinicians in diagnosis.

Introduction

Telogen effluvium (TE) is a type of diffuse non-cicatricial alopecia that develops as a result of a disturbance in the growth cycle of the hair follicle. There are five functional types of TE, which are classified according to alterations in specific phases of the follicular cycle: immediate or delayed anagen release, short anagen syndrome, and rapid or delayed telogen release. This results in intense hair shedding, which can be acute or chronic. Acute TE usually resolves within 3-6 months, while chronic TE persists for more than 6 months. TE is often triggered by underlying emotional stress, febrile illness, the postpartum period, weight loss, systemic disease, systemic drug use, or surgery [1].

Numerous studies reported many patients with TE after SARS-CoV-2 infection and as well as after receiving its vaccines [2-4]. The development of TE has been linked to the release of proinflammatory cytokines due to systemic inflammation, the occlusion of the vascular system of the hair follicle, and direct infection of the hair follicle by the virus [5-7]. Emotional and psychological stress, fever, weight loss, nutritional deficiency, and systemic medications may also increase the prevalence and severity of TE during SARS-CoV-2 infection [8].

Objectives

In this study, we planned to examine the demographic, dermoscopic, and laboratory features of the patients with SARS-CoV-2 -associated TE (CATE) and compare them with TE due to other causes (TEDOC) according to these features.

Methods

This study is a descriptive, retrospective and case-control study. It was conducted in a tertiary dermatology center after approval from the ethics committee according to the Declaration of Helsinki (Approval date: August 2023, approval number:2023/09-31).

Study Population

The study included patients who visited our dermatology clinic between April and June 2022 due to excessive hair loss, had a positive hair-pulling test, were diagnosed with TE based on the clinic and dermoscopic features, and were over 18 years old.

The patients reported that their hair loss started after contracting SARS-CoV-2 infection and had SARS-CoV-2 PCR positivity in the last 3 months in our hospital recording system were categorized as CATE, on the other hand, patients who did not link their hair loss to SARS-CoV-2 infection and had no records of SARS-CoV-2 positivity in the last three months were classified as TE due to other causes (TEDOC). All patients provided informed consent forms before participating in the study.

Data Collection

Patients gender, age, disease duration, accompanying systemic disease, dermoscopic findings, and laboratory results were recorded. All dermoscopic examinations were performed using a hand-held dermoscop (Plusmed) and data were collected from hospital records.

Statistical Analysis

Statistical analysis was done with the IBM SPSS 20.0 (IBM Corp.) package program. Numerical variables were given as mean ± standard deviation or median (25th-75th percentile). Categorical variables were given as frequency (percentage). Relationships between categorical variables were evaluated by chi-square analysis. Two samples Student t-test was used to compare mean values of normally distributed quantitative variables. In the testing of two-sided hypotheses, $P < 0.05$ was considered sufficient for statistical significance.

Results

A total of 92 patients, 86 (93.5%) females, and 6 (6.5%) males, were included in the study. Previous SARS-CoV-2 infection before hair shedding was detected in 52 (56.5%) patients whereas 40 (44.5%) patients had TEDOC. Female dominance was detected in both groups, however, there was no statistically significant difference between the groups ($P = 0.197$). The mean age of the patients with CATE was 30.3 + 10.7 years. The mean duration of the disease was 102.5 + 35.2 days. As a result of that, acute TE was found to be higher in patients with CATE ($P = 0.001$). In terms of the mean age of the patients and the mean duration of the disease, there was no significant difference between the groups ($P = 0.888$, $P = 0.077$, respectively). However, the mean time between the onset of trigger and hair loss complaint was calculated as 64.8 + 25.6 days, and this time was markedly shorter than patients with TEDOC ($P = 0.003$).

Evaluation of the additional systemic diseases revealed that 2 (3.8%) patients had hypertension in patients with CATE, whereas 4 (10%) patients had Hashimoto thyroiditis, 3 (7.5%) patients had diabetes mellitus, and 1 (2.5%) patient had chronic hepatitis due to hepatitis B virus in patients with TEDOC, and there was no statistically significant difference between the groups ($P = 0.073$).

Reduced hair density was detected in all patients with CATE and/or TEDOC. After evaluating in terms of the difference in dermoscopic examination, empty follicular openings and yellow dots were significantly higher in patients with CATE (respectively $P = 0.001$ and $P = 0.001$), whereas

short regrowing hair were higher in patients with TEDOC (P = 0.001).

Iron deficiency was the most common laboratory finding in 54 (58.6%) of total patients. Among all CATE patients with accompanying anemia, vitamin B12 deficiency and 25-OH-vitamin D deficiency, these deficiencies were present before SARS-CoV-2 infection and were not related to hair loss. Iron deficiency and hypothyroidism were found statistically higher in patients with TEDOC (P = 0.005, P = 0.03, respectively)

Conclusions

In this study, we retrospectively evaluated 92 patients with TE between April and June 2022. Among 92 patients, 52 (56.5%) had CATE and 40 (44.5%) had TEDOC. The mean time between the onset of trigger and hair loss complaint was statistically shorter in patients with CATE than patients with TEDOC. We found empty follicular openings and yellow dots significantly higher in patients with CATE, whereas short regrowing hair markedly higher in patients with TEDOC. Iron deficiency and hypothyroidism were also higher in patients with TEDOC.

TE was reported as the most common hair disease in patients with SARS-CoV-2 infection in many studies in the literature [5-7]. The main pathogenesis of CATE was still not fully understood, however, several factors were implicated. Recent studies reported that proinflammatory cytokines such as interleukin 1β, interleukin 6, tumor necrosis factor α, type 1 and type 2 interferon, and metalloproteinases 1 and 3 affect matrix cells of the follicle [7-9]. Metalloproteinases 1 and 3, and interleukin 1β inhibit hair follicle growth, and interleukin 6 induces the catagen phase [10,11]. In addition, this systemic cytokine storm may mediate microvascular inflammation and the activation of the coagulation cascade and decrease the concentration of anticoagulant proteins. This process may end with capillary thrombosis and dermal fibrosis [12-14]. Another hypothesized mechanism was Fcγ-mediated virus entry into the host cells because of non-neutralizing virus-specific antibodies (NAb) [15]. Therefore, CATE develops because of the early-onset telogen phase, namely, dystrophic anagen effluvium. Thus, patients with CATE have a shorter time of onset, typically 1–2 months instead of 3 months compared with TEDOC [16]. In our study, we found shorter time between the onset of trigger and hair loss complaint in patients with CATE than in patients with TEDOC.

Common dermoscopic findings of the patients with TE are reduced hair density, one emerging hair on the follicle, etc [17]. Unfortunately, these findings were not specific and could be seen in CATE and/or TEDOC.[18] However, Lv et al reported a case with CATE had scalp capillary ectasia without any inflammatory scalp disease because of medium to small vessel dilatation due to the inflammatory stimulus of SARS-CoV-2. [19]. They also declared that this dermoscopic finding was regressed at 3rd month of control. Saber et al. suggested scalp capillary ectasia as a trichoscopic sign and a diagnostic clue for patients with CATE [20]. We did not observe this dermoscopic finding in our patients with CATE because our patients applied to the hospital when the mean disease duration was 102.5 + 35.2 days. However, empty follicular openings and yellow dots were statistically higher in patients with CATE, whereas short regrowing hair were significantly higher in patients with TEDOC. This result could be explained by the fact that CATE patients were more in acute TE, while TEDOC patients were more in chronic TE.

Because of having more stressful events such as delivery, abortion, lactation, etc, TE is more commonly seen in

Table 1. Demografic features of the patients

Demografic features of the patients	SARS-CoV-2 associated TE N = 52 (%)	TE due to other causes N = 40 (%)	P value
Gender Female Male	 46 (88.5%) 6 (11.5%)	 37(92.5%) 3 (7.5%)	 0.197
Mean age of the patients (+ SD) (year)	30.3 + 10.7	27.9 + 10.7	0.888
Mean duration of disease (+ SD) (day)	102.5 + 35.2	249.7 + 109.3	0.077
Mean time between the onset of trigger and hair loss complaint (day)	64.8 + 25.6	133.5 + 5.8	0.003
Acute TE Chronic TE	48 (92.3%) 4 (7.7%)	19 (47.5%) 21 (52.5%)	0.001
Accompanying systemic disease Present Absent	 3 (5.8%) 49 (94.2%)	 7 (17.5%) 33 (82.5%)	 0.073

SD = standard deviation; TE = Telogen effluvium.

Table 2. Dermoscopic features of the patients

Dermoscopic findings	SARS-CoV-2 associated TE N = 52 (%)	TE due to other causes N = 40 (%)	P value
Empty follicular opening			
Present	40 (76.9%)	4 (10%)	
Absent	12 (23.1%)	36 (90%)	0.001
Yellow dots			
Present	29 (55.8%)	3 (7.5%)	
Absent	23 (44.2%)	37 (92.5%)	0.001
Short regrowing hair			
Present	10 (10.2%)	30 (75%)	
Absent	42 (80.8%)	10 (25%)	0.001
One emerging hair shaft on the follicle			
Present	8 (15.4%)	8 (20%)	
Absent	44 (84.6%)	32 (80%)	0.563

TE = Telogen effluvium.

Table 3. Laboratory findings of the patients

Laboratory findings	SARS-CoV-2 associated TE N = 52 (%)	TE due to other causes N = 40 (%)	P value
Iron deficiency			
Present	24 (46.2%)	30 (75%)	
Absent	28 (53.8%)	10 (25%)	0.005
Hypothyroditis			
Present	0	4 (10%)	
Absent	52 (100%)	36 (90%)	0.033
Vitamin B12 deficiency			
Present	14 (26.9%)	11 (27.5%)	
Absent	38 (73.1%)	29 (72.5%)	0.951
25-OH-vitamin D deficiency			
Present	10 (19.2%)	8 (20%)	
Absent	42 (80.8%)	32 (80%)	0.927
Folic acid deficiency			
Present	0	2 (5%)	
Absent	52(100%)	38 (95%)	0.186

TE = Telogen effluvium.

females. In addition, females are prone to be more affected emotionally by hair shedding, and having longer hair makes them think of having more hair loss. Therefore, they are more likely to seek medical attention [21]. Numerous studies in the literature also reported female dominance in patients with CATE [2,5-8]. We also found female dominance in both groups in our study. However, the exact mechanism under this situation was still not understood. Estrogens and progesterone are known to be immunomodulatory, anti-inflammatory, and work protectively at hair follicles. The reduction of estrogen and progesterone levels at blood due to systemic inflammation could cause hair loss in female patients with SARS-CoV-2 [22]. However, we need further studies to enlighten the relationship between hair loss and SARS-CoV-2.

CATE is characterized by excessive hair loss, positive hair pull test, not having anisotrichosis in dermoscopic examination and not having underlying other common TE causes. However, lots of patients could have systemic comorbidities and SARS-CoV-2 infection at the same time. They could also have CATE after infection. At this situation, the exact time of the onset of the complaint was taken as basis. If the complaints started after SARS-CoV-2 infection immediately, it is categorized as CATE [23]. In our study, 24 (46.2%) patients had iron deficiency, 14 (26.9%) patients had vitamin B12 deficiency, and 10 (19.2%) patients had 25-OH-vitamin D deficiency in CATE group. However, statistical analysis showed that TE-DOC patients had significantly more iron and vitamin B12 deficiency. Therefore, we should think that patients prone to the development of TE could facilitate the development of CATE.

The main limitation of the study is its retrospective design. The effects of systemic drugs and SARS-CoV-2 vaccines on CATE and disease severity have not been evaluated. On the other hand, some patients could associate different triggers of TE at the same time. Different trigger factors could facilitate hair loss and affect clinical and dermoscopic findings.

In conclusion, CATE is a common disease in patients with SARS-CoV-2, and the clinical presentation of CATE is more acute than the other reasons for TE. Dermoscopic findings such as empty follicular openings and yellow dots may help clinicians in diagnosis.

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