

Covid Induced Telogen Effluvium (CITE): An Insight

Abstract

Hair loss is one of the most common post-covid symptoms observed during this severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. Pro-inflammatory cytokines, direct viral effect on hair follicles, and microthrombi are thought to be the pathogenic factors considered. Information regarding time of onset and severity is similar to other infection-induced acute telogen effluvium. It is reasonable to think that the evolution and prognosis are similar, and therefore, even without any specific treatment, full recovery of lost hair is expected.

Keywords: COVID 19, hair loss, SARS-CoV-2 infection, telogen effluvium

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread across the world leading an unexpected, serious global pandemic, since the emergence in the late of 2019. COVID-19 has been associated with varied skin manifestations like vesicular, maculopapular, urticarial, acro-ischemic lesions, and others.^[1]

Post-Covid Symptoms and Hair Loss

Numerous observational studies have of late assessed the persistent symptoms in hospitalized COVID-19 survivors beyond 3 months. In a study by Carfi A *et al.*,^[2] the predominant dermatologic complaint was hair loss, noted in approximately 20% of patients. Hair loss can possibly be attributed to telogen effluvium (TE) resulting from viral infection or a resultant stress response. Up to 80% of patients have symptoms lasting for 4–12 weeks or longer, post infection with COVID-19. Amongst the various diverse persistent symptoms, hair loss was an important symptom.^[3] According to the scientific report, out of the five most common symptoms, hair loss was seen in 25% of cases.^[4] Estiri *et al.*^[5] identified 33 phenotypes among different age/gender cohorts or time windows that were positively associated with past SARS-CoV-2 infection. Among these phenotypes, alopecia (OR 3.09, 95% CI [2.53–3.76]) was significant observation.

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Another study where, a total of 87 Japanese patients were studied, the most common chief complaint was general fatigue followed by dysosmia, dysgeusia, hair loss (18.4%), headache, and dyspnea.^[6]

Telogen Effluvium

TE is one of the most common forms of hair loss that is characterized by a diffuse hair loss and has many known triggers like stressful events, drugs, endocrine disease, major surgery, febrile illnesses, and nutritional deficiencies.^[1] It is characterized by diffuse hair loss within months of a significant systemic stress because of premature follicular transition from the anagen (active growth phase) to the telogen (resting phase). The telogen phase lasts approximately 3 months, after which excessive hair loss ensues.^[7]

Acute TE (ATE) is a non-scarring hair loss, usually occurs 3 months after the event that causes hair loss, and lasts up to 6 months, while chronic TE occurs after 6 months.^[1] Acute TE is a self-limited disease characterized by unusual hair shedding (>100 shed hair/day) as a consequence of an abrupt shift of the hair follicles from anagen to telogen phase.

Female preponderance is seen as females are more susceptible for stress commonly due to delivery, abortion, and others. Females are more disturbed by hair shedding than males and are therefore more likely to seek medical attention and

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long hair is more easily noticed by the females during hair shedding, while among males this is rarely reported as they have short hair.

Domínguez-Santás *et al.* were the first to report a case of acute TE, occurring 3 months after SARS-CoV-2 infection, and have been followed by additional authors, who described TE after COVID-19.^[8-10]

In our tertiary care hospital too, we saw a good number of post-covid TE in the early post-covid period (1–3 months) with classic TE like presentation [Figure 1]. The most common trichoscopic findings were decreased hair density, the presence of empty follicles, or short regrowing hair [Figure 2]. FotoFinder trichogram showed telogen hair root and shafts with lesser pigmentation and thickened root without angulations. It was club shaped, resembling an ear bud [Figure 3].

Pathogenic Mechanisms

TE is one of the most common forms of hair loss that is characterized by a diffuse hair loss and has many known triggers like stressful events, drugs, endocrine disease, major surgery, febrile illnesses, and nutritional deficiencies.^[11] Fever is a common symptom of COVID-19. A few months after having a high fever or recovering from an illness, many people see noticeable hair loss. Even if you never developed a fever or COVID-19, you may still see hair shedding. Emotional stress can also force more hairs than normal into the shedding phase.

Recently, the percentage of ATE among other forms of hair loss is increased in comparison with the previous years; this could be attributed to the pandemic of COVID-19 during this period.



Figure 1: A 55-year-old female, in post-Covid-19 period with hair shedding since 3 months with diffuse thinning of scalp hair and prominent temporal thinning (Arrows depict parting of hair)

The exact mechanisms by which this virus induces hair loss are not well known, but the most acceptable ones would be: pro-inflammatory cytokines, direct viral damage to hair follicles (antibody-dependent enhancement [ADE phenomenon]), and coagulation cascade with microthrombi formation.

Pro-inflammatory cytokines: First of all, acute TE may be induced by the intense release of pro-inflammatory cytokines as a consequence of viral infections. SARS-CoV-2 and other viruses elicit strong antiviral responses, especially via interferon, which is a well-known TE-inducer molecule.^[12] Interleukin (IL)-6 is a pro-inflammatory cytokine, it has a critical role in severe COVID-19. High levels of IL-6 act on the hair follicle (HF), causes collapse of immune privilege and induces the catagen phase as well as causes local inflammation. High levels of IL-4, which are typical of COVID-19 in the elderly, also regulate keratinocyte apoptosis in HF.^[13] Additional molecules showing high levels in COVID-19 are metalloproteinase 1 and 3 and IL-1 β , which may inhibit the HF growth.^[14]

Cytokine storm can initiate the development of TE by damaging the matrix cells usually, the high levels of interferon have already been confirmed to be associated with ATE. Monocytes and macrophages infected by SARS-CoV-2 can produce pro-inflammatory cytokines that play a crucial role in the development of COVID-19-related complications. The role of monocytes on the hair follicles may be one of the responsible mechanisms.^[15] The role of pro-inflammatory cytokines in TE is depicted diagrammatically in Figure 4.

Direct viral damage to hair follicles (ADE phenomenon): Figure 5 details the direct viral damage to HFs which may be hypothesized in COVID-19 TE owing to the early onset of TE after SARS-CoV-2 infection. Initially it is due to the superficial spike glycoproteins characteristic of SARS-CoV-2, which binds to angiotensin I-converting enzyme-2 on host cells, allowing pathogen entry. Later it

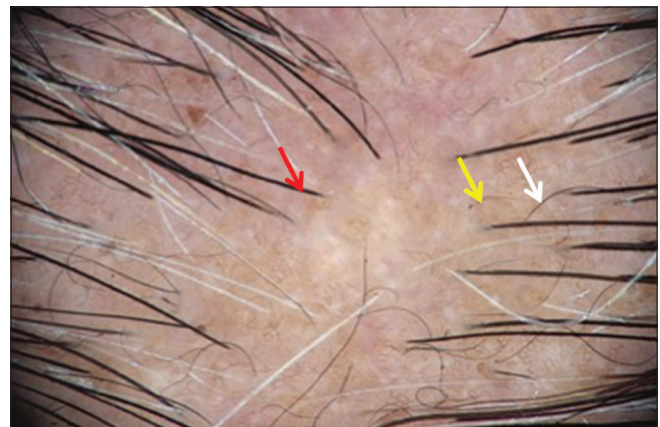


Figure 2: Trichoscopic findings showing diffuse thinning of scalp hair, terminal hair (red), and vellus hairs (yellow) with upright regrowing hair (white) (Dermalite 4, 10x magnification, polarised) [Courtesy: Prof. B S Ankad, SNMC Bagalkot]

is due to the presence of non-neutralizing virus-specific antibodies (NAb). NABs are present in patients with SARS-CoV-2 infection and are able to promote virus entry into host cells through interaction with Fcγ and/or complement receptors.^[16] Rossi *et al.*^[17] hypothesized that SARS-CoV-2 may determine direct effects on the HF via the ADE phenomenon as previously reported for dengue virus. ADE phenomenon has also been reported in coronaviruses, including SARS-CoV and Middle East Respiratory Syndrome Coronavirus (MERS-CoV).^[18]

Coagulation cascade with microthrombi formation. Those with more severe COVID-19 infections had higher levels of pro-inflammatory cytokines. They may correlate to a higher risk of TE given the pro-inflammatory state, additional mechanism by which TE can be provoked is the activated coagulation cascade in response to COVID-19 infection. There will be decreased concentration of anticoagulant proteins due to decreased production and increased consumption.^[19] These factors can lead to microthrombi formation, which may occlude hair follicle blood supply. Microthrombi and systemic inflammation

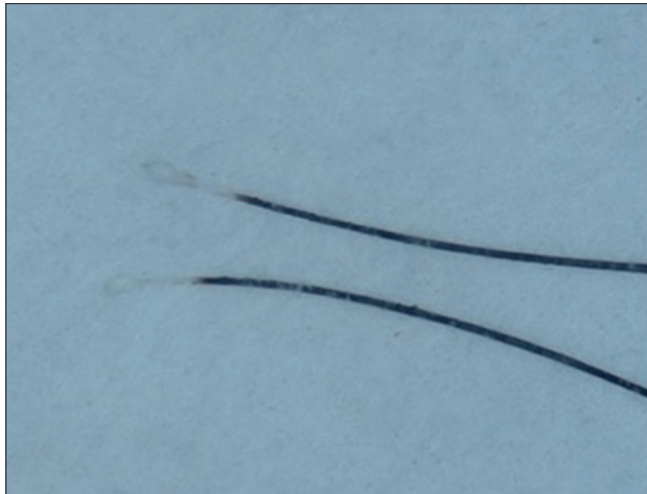


Figure 3: Trichogram by FotoFinder showed telogen hair root and shafts with lesser pigmentation and thickened root without angulations. Club shaped resembling an ear bud. [Courtesy: Prof. B S Ankad, SNMC Bagalkot]

represent two possible mechanisms to explain how COVID-19 infection could provoke TE [Figure 6].

Certain speculative things in causation can also be thought: whether androgens and their receptor, which regulate the HF cycle and have a key role in TE, could facilitate a direct effect of SARS-CoV-2 on the HF?. Therapies administered for COVID-19 in patients or psychological distress was unlikely a trigger of hair loss, since the timing of onset of TE is not compatible with drug-related or stress-related TE, which commonly occurs 3–4 months after the triggering event and drugs like heparinoids are known to cause hair loss.

Management

When the cause of your hair shedding is due to a fever, illness, or stress, hair tends to return to normal on its own. You just have to give it time.

Most people see their hair regain its normal fullness within 6–9 months.

- Information regarding time of onset and severity is similar to other infection-induced ATE, it is reasonable to think that the evolution and prognosis are similar, and therefore, even without any specific treatment, full recovery of lost hair is expected.
- Topical minoxidil is prescribed in many reported

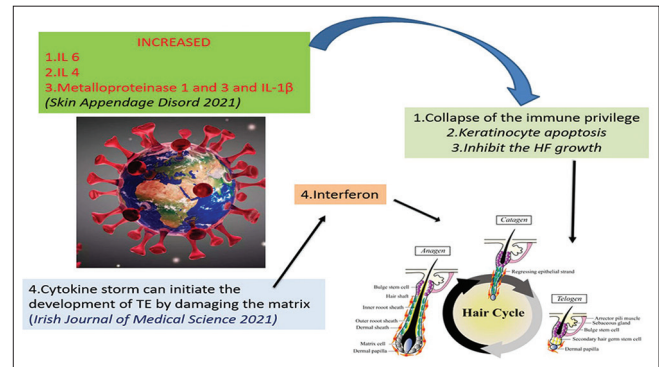


Figure 4: Mechanism of Pro-inflammatory cytokines causing CITE

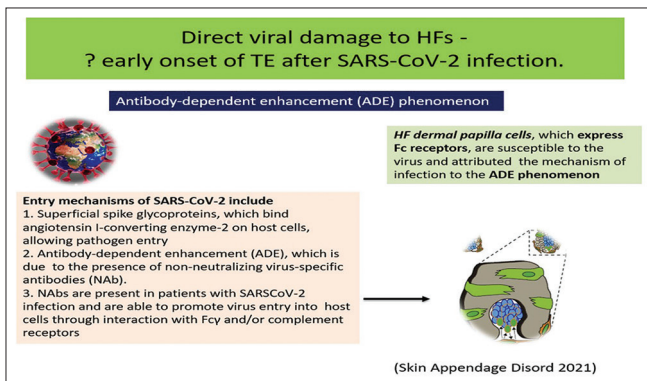


Figure 5: Direct viral damage to hair follicle and ADE phenomenon in causation of CITE

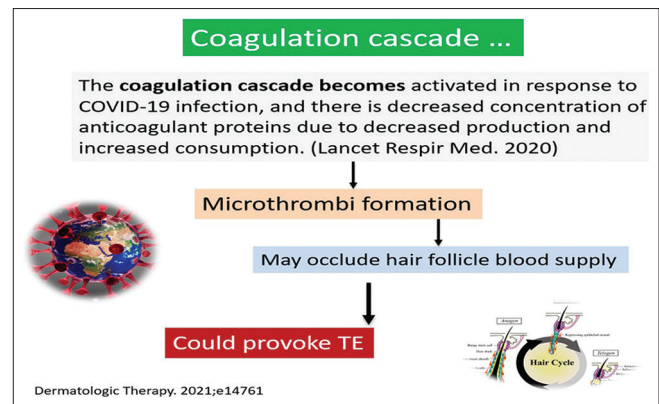


Figure 6: Depiction of coagulation cascade and microthrombi formation in post-covid TE

patients, there is no strong evidence to suggest that it is efficacious for TE.

- Educating the patient on the self-limiting natural course of the condition is a crucial component of management.
- The hair will eventually stop shedding and begin to grow back, but it may take up to 18 months for hair thickness to return to baseline.

Conclusion

Early onset of TE after SARS-CoV-2 infection hints at direct viral damage to hair follicles in COVID-19 TE. While trichoscopic features and trichogram showed no variations from classic TE, time to onset was shorter in COVID-19 TE. Further studies on a larger sample are needed to improve current understanding of this condition. It also should be pointed out that approximately one in ten patients suffered ATE with a subclinical SARS-CoV-2 infection, and therefore, in the context of the pandemic, past SARS-CoV-2 infection should be considered in every patient consulting for ATE. In the current era of pandemic, SARS-CoV-2 infection should be suspected and investigated in a patient who presents with acute TE.

It is reversible and is expected to improve without any treatment, and it can be addressed by explaining the patients the conditions, sharing medical information, and eliminating psychophysical stress by managing systemic complications.

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Conflicts of interest

There are no conflicts of interest.

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