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## Early-onset effluvium secondary to COVID-19: Clinical and histologic characterization

*To the Editor*: As telogen effluvium (TE) is the most common manifestation of postacute COVID-19 syndrome, we read with keen interest the publication by Abrantes et al<sup>1</sup> reporting the clinical characteristics of 30 patients with post-COVID-19 acute TE. We would like to commend the authors and bring some other elements to this relevant discussion.

TE is a heterogeneous condition that can be elicited by multiple stimuli.<sup>2</sup> Headington<sup>3</sup> proposed 5 functional types of TE based on alternations in particular phases of the follicular cycle. Infections are thought to induce TE through the mechanism of immediate anagen release. According to this model, an acute inflammatory state converts the follicles from anagen to catagen, leading to the shedding of telogen hairs around 90 days after the infection. Interestingly, the median time for the onset of hair shedding observed by Abrantes et al<sup>1</sup> was 45 days after infection; in the most precocious case, it started 18 days after COVID-19.

This early onset was also observed in 2 multicentric studies. Moreno-Arrones et al<sup>4</sup> evaluated 214 cases of acute TE after COVID-19 and noted the onset of hair shedding, on average, 57.1 days after the infection. Starace et al<sup>5</sup> observed early onset especially when TE was associated with trichodynia. In these cases, the latency from the infection to hair shedding occurred at an average of 3 (range, 2-7.5) weeks.<sup>5</sup>

We recently assessed 203 hospitalized patients with confirmed COVID-19, of whom 11 (5.4%) reported hair loss with onset early during hospitalization, <30 days after the infection. Seven of them were assessed using trichoscopy, a trichogram, and a histologic evaluation. The detailed information of these cases is presented in Supplementary Table I (available via Mendeley at https://data.mendeley.com/datasets/p254jbh356/1).

Clinically, all the cases presented a positive pull test result. Trichoscopy did not reveal broken hairs, anisotrichosis, or yellow dots, but it did reveal some empty follicles. The trichogram obtained from the vertex revealed >10% dystrophic anagen hairs (Fig 1) and >20% telogen hairs in all the cases. Histologically, there was predominance of anagen terminal follicles, no relevant miniaturization (>10%), and no cases showing >25% telogen follicles. No inflammation was evident at the epidermis or throughout the hair follicle (Fig 2).



**Fig 1.** Early-onset effluvium secondary to COVID-19. A dystrophic hair (absence of root sheath and misshapen bulb) was observed using polarized microscopy.



Fig 2. Early-onset effluvium secondary to COVID-19. Histopathology showed predominance of anagen follicles and no inflammation (Haematoxylin & eosin -  $100 \times magnification$ ).

Postinfectious hair shedding has traditionally been classified as acute TE: however, the hair follicle may respond to an infection and inflammation in different ways. A more intense insult could also lead to dystrophic anagen effluvium, which presents as early onset, as we have demonstrated here. In patients with COVID-19, a cytokine storm during the inflammatory phase (especially interleukin 6 and tumor necrosis factor  $\alpha$ ), severe hypoxia, oxidative stress, microthrombotic events, and the toxicity of multiple drugs used for its treatment could play a role, especially in more severe cases. These issues can elicit TE by multiple mechanisms following COVID-19, which can justify the different patterns of presentation and the time to the onset of hair loss.

Further studies exploring the pathogenesis of early-onset effluvium elicited by COVID-19, as well as its prevalence and possible differences compared with other acute postinfectious TE, are needed.

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## **Conflicts of interest**

None disclosed.

## REFERENCES

- 1. Abrantes TF, Artounian KA, Falsey R, et al. Time of onset and duration of post-COVID-19 acute telogen effluvium. *J Am Acad Dermatol*. 2021;85(4):975-976.
- 2. Rebora A. Telogen effluvium: a comprehensive review. *Clin Cosmet Investig Dermatol.* 2019;12:583-590.
- 3. Headington JT. Telogen effluvium: new concepts and review. *Arch Dermatol.* 1993;129(3):356-363.
- Moreno-Arrones OM, Lobato-Berezo A, Gomez-Zubiaur A, et al. SARS-CoV-2-induced telogen effluvium: a multicentric study. J Eur Acad Dermatol Venereol. 2021;35(3): e181-e183.
- 5. Starace M, Iorizzo M, Sechi A, et al. Trichodynia and telogen effluvium in COVID-19 patients: results of an international expert opinion survey on diagnosis and management. *JAAD Int.* 2021;5:11-18.

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