Proposing a Simpler Classification of Telogen Effluvium

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Key Words

Telogen effluvium · Hair loss · Alopecia · Teloptosis

Abstract

Telogen effluvium (TE) is a pathogenically heterogeneous condition which so far has been classified into acute and chronic forms – or, according to Headington, into 5 different pathogenetic forms. Regrettably, Headington's classification is difficult to apply in the office, and most papers dealing with TE ignore it. The present review intends to propose a novel classification of TE and to introduce, tentatively, a new variety of TE. Three pathogenetic types of TE can be identified, whose common clinical element is the profuse shedding of hairs: (1) premature teloptosis, (2) collective teloptosis, and (3) premature entry into the telogen phase. In particular conditions, they may also be associated, as occurs in seasonal shedding and postpartum TE.

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Introduction

Telogen effluvium (TE) is one of the commonest occurrences in a trichology clinic, but it is also one of the most misunderstood and neglected entities. From a pathogenetic standpoint, TE is a heterogeneous condi-

tion, but a review of the literature reveals that only two attempts have been made to classify it. One divides TE into an acute form and a chronic form [1] when TE lasts more than 6 months. The second, accredited to Headington [2], divides TE according to 5 different pathogenetic mechanisms, namely (1) immediate anagen release, (2) delayed anagen release, (3) shortened anagen, (4) immediate telogen release, and (5) delayed telogen release.

Regrettably, and probably because of the relative obscurity of its labels, Headington's classification is very difficult to apply in clinical practice. In the literature, therefore, most papers dealing with TE refer to TE generically as if TE were a single entity; thus, they are, from a practical point of view, of limited value.

The heterogeneity of TE was stressed by Kligman [3] in his description of the condition. Kligman defined TE as a 'nonspecific reaction pattern' in which the main symptom is the increased shedding of telogen hairs developing 3–4 months after the causing event. Alopecia would occur only when about 40% of hairs have been shed. While suggesting febrile and chronic systemic illnesses, childbirth, major surgery, and emotional strain as possible causes, Kligman failed to find any histological inflammatory signs or other abnormalities apart from the increased number of telogen follicles.

Actually, the first description of TE dates back to 1960, when Sulzberger et al. [4] drew the attention of dermatolo-

gists to an unexplained apparent increase in the incidence of diffuse alopecia in women and described the main accompanying symptom, trichodynia. In the same year, Guy and Edmundson [5] reported on diffuse cyclic hair loss in women, stressing its characteristic intermittency.

Due to the heterogeneity of TE, Kligman's description of its clinical presentation is only generic. In addition, important information is lacking. In fact, we still do not know whether the shed hairs have telogen or exogen roots [6], whether the intensity of shedding is identical in the various varieties, whether trichodynia is present in all or only in some of them, whether trichodynia is directly related to the severity of shedding, and many other issues.

The present review intends to propose a novel classification of TE and to introduce, tentatively, a new variety of TE, which, in fact, is the one most commonly encountered by dermatologists in their everyday practice.

TE Classification

Three pathogenetic types of TE can be identified, whose common clinical element is the profuse shedding of hairs: (1) premature teloptosis, (2) collective teloptosis, and (3) premature entry into the telogen phase. In particular conditions, different mechanisms may overlap. For example, seasonal shedding may be a combination of types 1 and 2, and postpartum TE may be a combination of types 2 and 3.

Type 1: Premature Teloptosis

Premature teloptosis may correspond to Headington's immediate telogen release. The mechanism of shedding is unclear, but proteolysis can play a pathogenetic role. In particular, any factor, exogenous or endogenous, capable of breaking down cadherins may induce premature hair dislodgment [7].

Exogenous causes, for example, may be all-*trans* retinoic acid and salicylic acid contained in hair medications, which have been proven to damage cadherins including desmoglein [8, 9]. In the first weeks after starting minoxidil medication, TE may occur [10], which disturbs the unaware patient and may lead to interruption of the treatment. It may be that some component of the vehicle damages cadherins. Exceeding UV exposure in summer may have the same effect [11], being one of the possible causes of seasonal hair shedding. Conversely, cytokines released by local inflammatory processes such as seborrheic dermatitis – which patients so often accuse for their hair loss – may be endogenous causes.

Type 2: Collective Teloptosis

Collective teloptosis may correspond to Headington's delayed anagen and telogen releases. In adult humans, hairs follow an individual cycle, but there may be physiological or drug-induced conditions in which the hair cycles are synchronized as in newborns. As a consequence, molt-like shedding may occur.

Neonatal Hair Loss

In newborns, the occipital hairs enter telogen only near term and shed 8–12 weeks later, causing transient neonatal hair loss [12].

Postpartum TE

During the 2nd and 3rd trimesters of pregnancy, more scalp follicles are in anagen and enter telogen simultaneously after delivery. Two to 3 months later, this process results in molt-like shedding.

Collective Teloptosis Induced by Noncytostatic Drugs

Estrogens synchronize the cycles, and long-lasting medication with contraceptives may induce collective teloptosis. Minoxidil and finasteride tend to synchronize the cycles as well, inducing collective teloptosis 3–4 months after interrupting the medication.

Type 3: Premature Entry into the Telogen Phase

In this type of TE, which may correspond to Headington's immediate anagen release, the anagen phase is interrupted prematurely and the hairs accelerate their process to telogen, in which they remain for 3 months before eventually being dislodged. The premature interruption of the anagen phase is caused by an interruption of keratinocyte mitoses in the hair matrix. In contrast with other epitheliocytes, however, in which the response depends only on the intensity of the insult (i.e. the dosage of a drug) and/or its duration, hair keratinocytes, which undertake periodic and regular phases of mitotic activity and rest, respond according to 2 more conditions: the phase of the hair cycle in which the hair follicle is when affected by the insult and the existence of factors which can alter the normal duration of the cycle phases [most often the coexistence of androgenetic alopecia (AGA)].

As for the first condition, the insult is expected to cause dystrophic shedding if a follicle is in a subphase with the highest mitotic activity (anagen I–V). Conversely, if a follicle is approaching the end of the anagen phase (anagen VI), when the mitotic rate is already abating, the result is

simple acceleration of the normal conversion to telogen. Telogen, being a mitotically inactive phase, represents a sanctuary in which the insulted hair remains for 3 months before being shed [13, 14].

As for the role of coexistent AGA, the anagen/telogen duration ratio is a crucial factor for determining the hair's response to the insult. In fact, when this ratio is low – as in AGA, in which the anagen duration is reduced – the insult is unlikely to find keratinocytes with a high mitotic rate. Because of the high prevalence of AGA in the general Caucasian population, most human scalps do not have a 'normal' anagen/telogen duration ratio, but one in which the telogen duration prevails. The usual modality of shedding would therefore be TE. In other words, the response to the same mitosis-blocking insult may be anagen effluvium in some cases and TE in others, or a combination of both.

Untimely interruption of mitosis may occur on account of drugs provided with cytostatic activity, dietary deficiencies, and, possibly, lymphocytotoxic activity.

Drug-Induced TE

Since they have a toxic effect on the hair's matrix, most of the 90 chemotherapeutic drugs currently in use cause hair shedding. Heparin sodium and heparinoids cause it as well in at least 50% of patients. Whether hair loss presents as dystrophic or telogen shedding does not depend on the quality of the drug but rather on the 4 factors mentioned above, namely the intensity and duration of the insult, the phase of the hair cycle in which the hair follicle is when affected by the insult, and the coexistence with AGA.

TE due to Dietary Deficiencies

Dietary deficiencies may induce hair shedding, especially when chronic anorexia is the possible cause. This kind of hair shedding has been reported to be dystrophic [15], or hair shafts are described as being dry and brittle [16], but, again, the shedding modality depends on the 4 factors mentioned above.

TE due to Lymphocytotoxicity ('Autoimmune' TE)

This form represents the commonest occurrence in any trichology office. Its presentation is standard. Typically, the patient is a woman who claims having had a 'full head of hair' but noticed that it 'began suddenly' to 'come out by the handful'. Usually, and in contrast to AGA, the patient is precise in specifying the date of onset of hair shedding and often complains of a 'pain in the hair' (trichodynia) [4, 17]. She is in good health and without

signs of anorexia or nutrient deficiencies. Often, the course is chronic/intermittent, featuring sparseness of hair in areas normally spared by AGA (especially the supra-auricular area). Tentatively, I labelled this condition 'autoimmune' because of its common association with other autoimmune diseases. In fact, circulating antithyroperoxidase antibodies and Hashimoto's thyroiditis are present in up to 60% of cases [18, 19]. More rarely I observed other thyroid autoimmune diseases, Sjögren syndrome, inflammatory bowel disease, or autoimmune atrophic gastritis.

This variety shares some features with alopecia areata (AA). Trichodynia is also present in 14% of AA cases [20]. Emotional stress plays a crucial role in both disorders, and has been related, at least in mice, to perifollicular inflammation (neurogenic?) via substance P-dependent pathways [21, 22]. Some relationship to trichodynia exists in this respect, since trichodynia sites are those locations hairs are coming out from [23]. Also, corticotropin-releasing factor receptor antagonists proved to reverse alopecia in corticotropin-releasing factor-overexpressing mice that display phenotypes of chronic stress including alopecia [24]. Lastly, antithyroperoxidase antibodies with possible Hashimoto's thyroiditis are present also in AA [25].

Interacting Mechanisms

Postpartum TE is an example of the interactions of two TE mechanisms. It occurs between 2 and 4 months after delivery, usually lasts 2 months (rarely more, and only exceptionally becoming chronic), and is commonly followed by complete recovery [3]. Most probably it is related to the synchronization of hair cycles during pregnancy (possibly due to scalp-wide shortening of the anagen phase), but it cannot be regarded as a physiological phenomenon, since it does not occur in all women and in all pregnancies of the same women. Synchronization of the cycles plays a definite role, but I suggest that the mechanism of mitotic arrest is possibly related to the stress of delivery. In fact, it occurs mostly at the first delivery, when the emotional stress is stronger, and only rarely in ensuing pregnancies. The possible coexistence with postpartum thyroiditis that occurs in about 5% of new mothers [26] should be studied.

Another example of interaction is the so-called seasonal hair loss. A negative influence of UV irradiation causing premature teloptosis seems probable, but the coexistence of a synchronization factor (AGA?) should be taken into consideration as well.

Conclusions

TE is a heterogeneous condition that needs a rational and simple classification. The pathogenetic mechanisms are likely to be numerous, and the present review suggests at least 3 of them. Of course the distinction between acute and chronic TE remains, but it should be clarified whether chronicity is a prerogative of only some of the new types. For example, it is unlikely that type 1 TE can be-

come chronic. Many other clinical items should be elucidated, but they cannot be clarified efficaciously without a user-friendly classification. I hope that the present effort of mine is fruitful in this respect.

Disclosure Statement

The author has no conflicts of interest to disclose.

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