



REVIEW

Impact and Management of Loss of Eyebrows and Eyelashes

Michela Starace · Stephano Cedirian · Aurora M. Alessandrini ·

Francesca Bruni · Federico Quadrelli · Daniel F. Melo ·

Tatiana Silyuk · Andrei Doroshkevich · Bianca M. Piraccini ·

Matilde Iorizzo

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ABSTRACT

Eyelashes and eyebrows have different functions, ranging from practical purposes such as protecting the eye apparatus from external hazards to the definition of our facial expression. For this reason, their loss could have both functional and psychological impact on patients' quality of life. Complete or partial loss can occur any time during life, and identifying

the cause is mandatory to establish a correct and prompt treatment. The aim of this paper is to create a practical guide for the management of the most common causes of madarosis to the best of our knowledge.

Keywords: Eyebrow loss; Eyelash loss; Madarosis; Alopecia; Treatment; Management; Hair transplant; Quality of life

M. Starace · S. Cedirian (✉) · A. M. Alessandrini ·
F. Bruni · F. Quadrelli · B. M. Piraccini
Dermatology Unit, IRCCS Azienda Ospedaliero-
Universitaria di Bologna, Policlinico S. Orsola-
Malpighi, Via Massarenti 9, 40138 Bologna, Italy
e-mail: stephano.cedirian@studio.unibo.it

M. Starace · S. Cedirian · A. M. Alessandrini ·
F. Bruni · F. Quadrelli · B. M. Piraccini
Department of Medical and Surgical Sciences, Alma
Mater Studiorum, University of Bologna, Bologna,
Italy
e-mail: michela.starace2@unibo.it

A. M. Alessandrini
e-mail: aurora.alessandrini3@unibo.it

F. Bruni
e-mail: francesca.bruni3@studio.unibo.it

F. Quadrelli
e-mail: fedequadro@hotmail.it

B. M. Piraccini
e-mail: biancamaria.piraccini@unibo.it

D. F. Melo
Dermatology Department, Rio de Janeiro State
University (UERJ), Boulevard 28 de Setembro 77, Rio
de Janeiro, Brazil
e-mail: danielfernandesmelo@yahoo.com.br

T. Silyuk · A. Doroshkevich
Center of Hair Treatment and Transplantation,
Syeshinskaya 4, Saint Petersburg, Russia
e-mail: tatianasiliuk@gmail.com

A. Doroshkevich
e-mail: a.r.doroshkevich@gmail.com

M. Iorizzo
Private Dermatology Practice, Via Frasca 10, 6900
Lugano, Switzerland

M. Iorizzo
Private Dermatology Practice, Viale Stazione 16,
6500 Bellinzona, Switzerland
e-mail: matildeiorizzo@gmail.com

Key Summary Points

Reduction in the length, thickness, and pigmentation of eyelashes and eyebrows can be a physiological phenomenon due to aging.

Eyelashes and eyebrows serve as protection of the ocular area, definition of nonverbal communication, and self-expression.

Loss of eyelashes and eyebrows can be caused by genetic, autoimmune, endocrine, infectious, neoplastic, nutritional, traumatic, dermatological inflammatory, and drug-induced conditions.

Eyelash and eyebrow loss, especially loss of eyelashes, can have a severe impact on patients' quality of life.

No guidelines exist for the treatment of eyelash and eyebrow loss, and each condition needs to be addressed specifically.

INTRODUCTION

Madarosis is a condition that results in the loss of eyelashes and eyebrows. The term is derived from the ancient Greek *madaros*, meaning bald. It can be incomplete or complete, unilateral or bilateral, and non-scarring or scarring, but above all, it is the marker of many congenital conditions and acquired diseases as well as a physiologic phenomenon due to age [1, 2].

Eyelashes and eyebrows have specific functions in the human anatomy [3]. Eyelashes participate in protecting the ocular area from external disturbances, such as sweat, microorganisms, debris, and even light, water, and wind. Andersen et al. [4] reported that 44.3% of patients affected by madarosis secondary to alopecia areata had a variable degree of ophthalmological issues (e.g., ocular surface inflammation, dryness, and blepharitis).

Other than practical purposes, eyelashes and eyebrows are pivotal in the expression of

emotions and nonverbal communication; that is why they represent an important aspect of the facial esthetic, and people generally seek various beauty treatments able to enhance them [5–7]. For the above reasons madarosis may significantly impact the quality of life of affected patients, who feel as if their physical attractiveness is reduced [8].

In the pediatric population, madarosis is as bothersome as in adults: Macey et al. [9, 10] described that some adolescents experience loss of eyebrows dramatically as they feel as though they look “weird.” Sometimes what is most feared for this age group is judgment by other people, and that is the reason why absenteeism and discontinued participation in social activities, such as sports, have been reported. Patients tend to cope with and become accepting of their disease, but the emotional impact remains forever. At this age, however, madarosis could be also a sign of an underlying disorder and should always be questioned during a dermatological consultation.

Unfortunately, no guidelines exist for the treatment of loss of eyelashes and eyebrows. Treatment is not always feasible due to the limited number of drugs available and areas being difficult to treat. Overall, most studies had small number of cases and lacked control groups and randomization. Identifying the underlying condition responsible for the loss is however the mainstay of the correct management.

In this paper we will review possible treatments for the most frequent causes of madarosis with the purpose of creating a practical guide for their management to the best of our knowledge. This article is based on previously conducted studies and does not contain new studies with human participants or animals performed by any of the authors. All the images collected for this paper were obtained after getting written informed consent from all of our patients, who are aware that their photos will be published in a journal.

ALOPECIA AREATA

Alopecia areata (AA) is an autoimmune disorder characterized by non-scarring alopecia that can involve any hair-bearing area, including eyebrows and eyelashes [11, 12]. Madarosis due to AA, presenting as an isolated finding, is uncommon and mostly underdiagnosed. It usually occurs in concert with scalp involvement and is seldom a huge complaint compared with the scalp hair loss. Most of the times, systemic treatments administered for scalp hair loss are useful also for lash and brow regrowth. When the loss is isolated instead, treatment is more challenging due to the limited drugs available.

Steroids

Intralesional injections of triamcinolone acetonide are the first choice for loss of eyebrows due to AA because the intralesional route of administration is considered an optimal targeted therapy, as the drug is delivered to the site of inflammation, namely the dermoepidermal junction and the upper portion of the subcutis, with numerous advantages and limited side effects [13]. Triamcinolone acetonide 2.5 mg/ml (10 or 40 mg/ml diluted with sodium chloride), brought down to room temperature, has to be slowly injected in the alopecic patches with an insulin syringe with a built-in needle and with no massage after the procedure. The maximum dosage per eyebrow should be 0.5 ml, and each injection site (five sites maximum) should be around 1 cm apart, but there is no consensus on this procedure: Data in the literature are scarce and mostly extrapolated from the same procedure performed on the scalp [14]. No local anesthesia is required before the procedure. Injections are usually performed every 6–8 weeks, but again, there is still no consensus on this. As for the scalp, at least 6 months should be waited before judging the treatment not effective. On achieving complete improvement, injections were tapered over the next few months. Tapering is best performed by extending the period between injections (Fig. 1a, b). This technique, besides being painful, might be

responsible for patchy hair regrowth in the case of total loss of eyebrows. Slowly retro-injecting triamcinolone with a 25G/50 ml blunt tip cannula (DermaSculpt) after local anesthesia with lidocaine 1:1 saline solution seems to be less painful and more promising for more wide and diffuse hair regrowth due to a more homogeneous steroid distribution [15].

Local side effects are rare with low concentrations of triamcinolone, but skin atrophy, hypopigmentation, hematoma, and residual telangiectasias at the injection site should always be considered (Fig. 2) [16].

Topical steroids (mometasone furoate or betamethasone dipropionate cream every other day) are also an option, but acneiform eruptions and periorcular rosacea can occur as midterm side effects, and such treatment should be refused by patients. Solutions, clobetasol dipropionate 0.05% in particular, could be better options, and in our experience, a few drops can be easily applied once a day with the aid of an eye shadow brush to avoid spreading on the upper eyelid. Abuse of topical steroids should be discouraged due to severe side effects such as glaucoma and cataract [17]—for this reason a strict follow up of the patient is mandatory. As far as we know, no topical or intralesional steroid treatment has been reported to be feasible and effective for loss of eyelashes, but the literature reports cases of patients treated for the



Fig. 1 Eyebrows affected by AA (a) and after 6 months of intralesional injections of triamcinolone acetonide (b)

eyebrows who also experienced lash regrowth [18]. It was unclear however how patients had achieved regrowth without direct application of treatment to the eyelids.

Prostaglandin Analogues

Latanoprost, bimatoprost, and travoprost ophthalmic solution are prostaglandin F2 alpha analogues, marketed for the treatment of ocular hypertension, that have the common side effect of eyelash hypertrichosis and trichomegaly. They have been evaluated as a potential therapeutic option for eyelash loss in adults and children because they are able to extend the anagen phase and to induce telogen follicles into anagen [19, 20].

Bimatoprost 0.03% is the only one approved for hypotrichosis of the eyelashes (2001 FDA approval); it promotes increased thickness, length, and darkening. In our experience, bimatoprost applied once daily, a few drops on the eyelid rim, has shown a moderate degree of efficacy after 1 year (unpublished data). The literature also reports acceptable cosmetic response with this treatment [21] (Fig. 3a, b).

The use of latanoprost 0.005% ophthalmic solution has shown less efficacy in clinical studies: If applied every night for 2 years in patients with eyelash AA, it has shown complete regrowth in 17.5% of the cases, moderate regrowth in 27.5%, slight regrowth in 30%, and no response in 25% of patients [22]. In other



Fig. 2 Skin atrophy after intralesional injections of triamcinolone acetonide

studies, it did not show statistically significant eyelash regrowth [23, 24].

Prostaglandin analogue solutions however are an affordable and easy-to-perform treatment, so they are worth a try. They can also be applied on the eyebrows once a day overnight. At present, this treatment should be prolonged over time since relapses are expected after stopping.

However, topical prostaglandins may cause unwanted side effects, such as darkening of the iris color, periocular pigmentation (very common side effect), uveitis, deepening of the superior sulcus and fat atrophy, enhancement of the eyelid crease, and a decrease in proptosis [25]—for this reason we encourage the discussion of this treatment with the ophthalmologist.

Immunotherapy

This is probably the best-documented treatment for AA. Before starting treatment, it is necessary to sensitize patients with a 2% solution of squaric acid dibutylester (SADBE) or diphenylcyclopropanone (DPCP) under closed patch test applied on the alopecic scalp for 48 h [26]. After 3 weeks treatment can start on the affected area, with a weekly application of the allergen diluted in acetone at a concentration chosen according

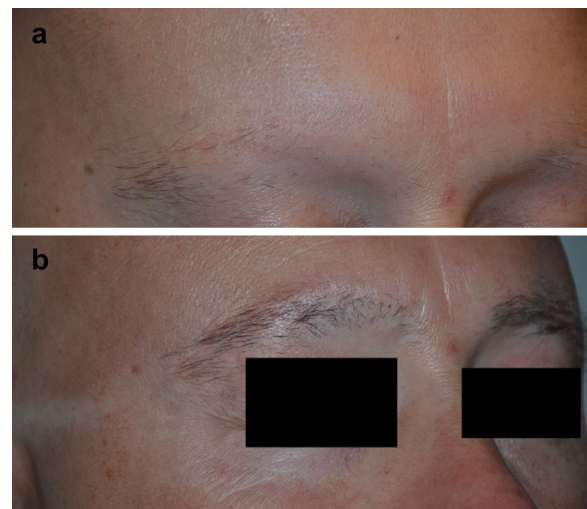


Fig. 3 Eyebrows affected by AA before (a) and after (b) 1 year of treatment with bimatoprost

to the severity of the dermatitis obtained with the patch test. These concentrations considerably vary among different patients and even in the same patient during the treatment period. For obvious reasons this treatment is suitable only for eyebrow loss and not for eyelash loss. The solution is applied with a cotton swab, wearing gloves and avoiding light exposure for the next 48 h (the bottle with the solution should also be protected from light). The objective of the application is to induce a mild contact dermatitis. The mechanism of action is unknown, possibly a modification in the cytokine profile and Th1 decrease. Topical immunotherapy is not effective in acute and rapidly expanding disease, but it is useful for longstanding AA and in children, as well [27, 28]. Side effects of immunotherapy are urticarial reactions, cervical lymphadenopathy, dyschromia, and possible development of lentigines. Tapering is necessary before stopping treatment once the hair has regrown (Fig. 4a, b).

Durdu et al. [29] assessed madarosis through immunotherapy, proving that treatment with DPCP was effective and even more so if combined with the previous application of anthralin, an irritating agent useful in increasing contact sensitization. Patients were treated with 0.5% anthralin ointment for 10 min daily (the contact time could reach up to 1 h, if no evidence of erythematous reaction was visible). If patients showed no response, they were moved to anthralin ointment 1% for 30 min (up to 1 h in the case of no response). Complete regrowth of the eyebrows and eyelashes was observed in 16.7% of the patients treated only with DPCP, while patients who had undergone the combination therapy showed complete regrowth of eyebrows and eyelashes in 66.7% and 68.7%, respectively.

JAK Inhibitors

Topical ruxolitinib cream and topical tofacitinib ointment/gel/solution have been shown to help in the treatment of AA, especially in its facial localization, if used twice a day [30–32]. There is no need to prescribe an oral Janus kinase (JAK) inhibitor for AA limited to lashes or

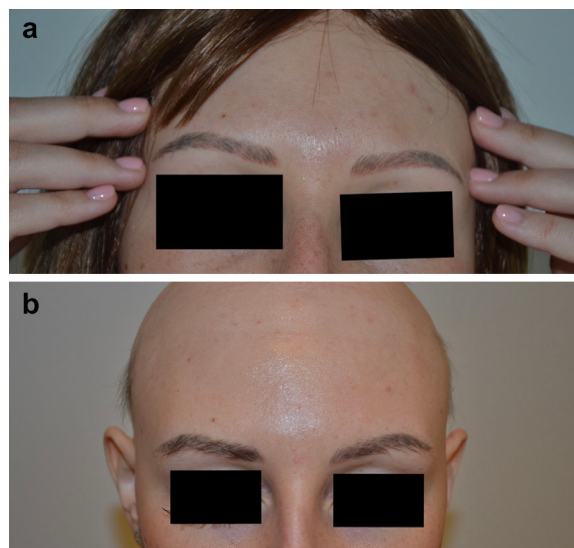


Fig. 4 Eyebrows affected by AA before (a) and after (b) 1 year of treatment with SADBE

brows unless the treatment is extensively discussed with the patient—topical administration could also reduce the risk of adverse events in such a limited disease and should be preferred. A randomized control trial compared topical tofacitinib, ruxolitinib, clobetasol dipropionate, and placebo applied twice daily to different areas of the scalp and eyebrows for a period of 12 weeks [33]. JAK inhibitors were successful (six patients demonstrated partial regrowth in the areas treated with 2% tofacitinib, and five patients in the areas treated with ruxolitinib 1%), but clobetasol dipropionate provided the most significant regrowth (10 out of 16). Topical JAK inhibitors can, however, be particularly valuable in children where topical or intralesional steroids may not be tolerated or wanted. At present only topical ruxolitinib is marketed for vitiligo (2022 FDA approval); others should be compounded. Their sustainability is however an area of concern since AA seems to relapse shortly after stopping [34].

TRICHOTILLOMANIA

Trichotillomania (TTM) is a condition characterized by repetitive hair pulling or plucking, which could lead to noticeable hair loss [35]

(Fig. 5a, b). The pulling or plucking can be automatic or focused. Patients are unable to properly regulate their emotional state, and the mania may offer temporary relief from a negative emotional state. TTM is an obsessive–compulsive disorder and in particular a body-focused repetitive behavior disorder. The word is derived from the Greek words *trix* (hair), *tillein* (to pull), and *mania* (madness).

The differential diagnosis with AA can be extremely challenging in some instances despite the aid of dermoscopy [36, 37], especially when only the eyelashes or eyebrows are affected [38]. TTM has an insidious onset, and hair loss of eyebrows and eyelashes is generally limited to the superior eyelid.

TTM has no standardized therapy, although multiple strategies have shown their efficacy [39–41]. In mild-to-moderate cases, patients may benefit from psychotherapy alone or in combination with drug treatment, whereas severe forms need a drug-based approach. A variety of drugs have been used, although there is no clear indication that one drug is preferable over others.

Psychoactive medications as selective serotonin reuptake inhibitors, tricyclic antidepressants, antipsychotics (olanzapine), and opioid

antagonists (naltrexone) have all be used in patients with TTM but should be always accompanied by psychiatric counseling. N-acetylcysteine (NAC), instead, can be easily and safely prescribed. In our experience it has shown its efficacy with a daily dosage of 1200–1800 mg/day, for at least 4 months. The safety profile is superior to that of antidepressants, and the mechanism of action may be related to its role in the reduction of oxidative stress through production of glutathione and reduction of glutamate, thus stopping the compulsive behaviors (Fig. 6a, b).

FRONTAL FIBROSING ALOPECIA

Frontal fibrosing Alopecia (FFA) is a primary lymphocytic cicatricial alopecia characterized mainly by selective involvement of the frontotemporal hairline and eyebrows [42]. Lateral or complete eyebrow loss, occasionally with perifollicular and intrafollicular erythema, may precede or follow the hairline involvement; however, madarosis could also be the sole presentation of the disease, leading to a misdiagnosis of AA or senile eyebrow loss (Fig. 7a, b) [43]. Eyebrow loss is observed in 75–94% of patients [44]. As for the eyelashes, a volume loss in patients with FFA has been reported to range from 3% to 26% [45].

Early recognition of this disease allows early treatment and eventually prevents its progression. FFA is however a chronic condition, and this means that patients need long-term treatments, even if at present there is no validated or approved treatment for this disease. The lack of randomized clinical trials does not allow, in fact, definitive conclusions regarding the most effective among available treatments. Moreover, the variable course of this disease and the possibility of a spontaneous stabilization present a risk of overestimating the effects of the prescribed treatments [46].

Regarding eyebrow hair loss, most of the times it requires an additional treatment besides the systemic one, and intralesional triamcinolone acetonide 10 mg/ml, 0.125 ml per eyebrow, has shown to be effective [47]. In our experience, intralesional administration of

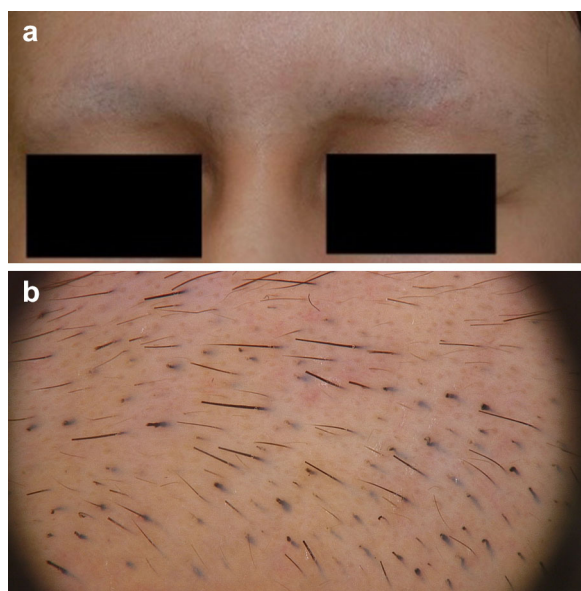


Fig. 5 Clinical picture of eyebrows affected by trichotillomania (a) and (b) trichoscopy

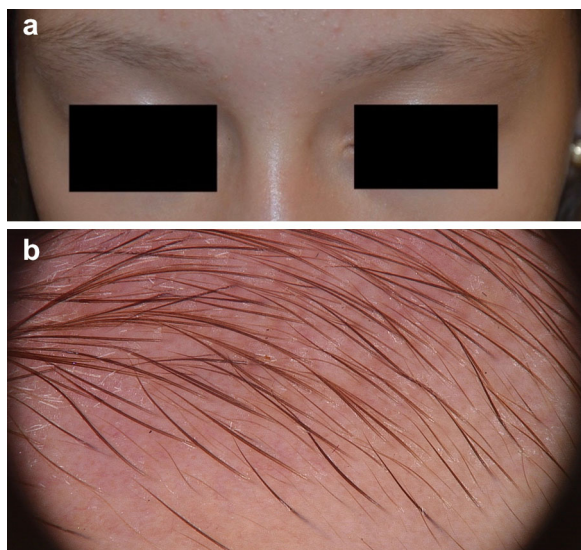


Fig. 6 Clinical picture of patient from Fig. 5 (a) and trichoscopy (b) after 8 months of treatment with NAC;

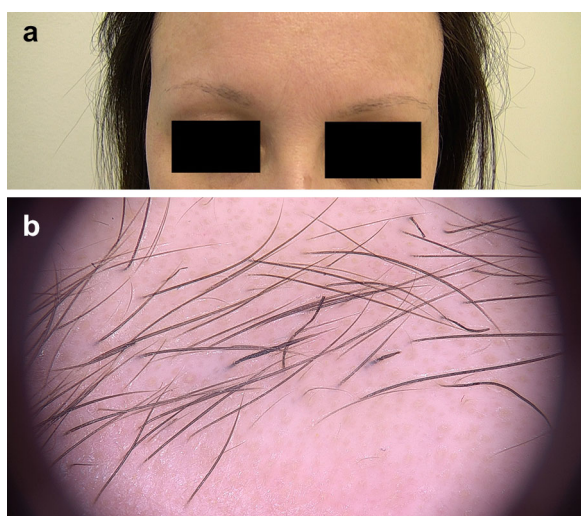


Fig. 7 Clinical picture of eyebrows affected by FFA (a) and trichoscopy (b)

triamcinolone acetonide done in the same way as for AA madarosis is a better option. Continuous treatment is often required to maintain response, and side effects such as skin atrophy are always a possibility, even with low dosages (Fig. 8a, b).

Bimatoprost ophthalmic solution 0.03% applied to eyebrows twice a day for 1 year resulted in positive regrowth in some patients after at least 9 months of treatment [48]. The

number of cases was however too low to draw definitive conclusions.

In our experience, eyebrow transplantation has proven to be another solution for loss of eyebrows due to FFA despite the fact that this is a cicatricial alopecia. Primary scarring alopecias have been labeled as unstable by Unger et al. [49] because of their unpredictable course and their tendency to relapse. The authors advised contemplating surgical correction only after having confirmed at least 1–2 years of quiescence; that is because, if the disease is active, the transplanted follicles could be the target of the ongoing inflammatory reaction as well [49].

Once the possibility of a transplant has been established, the first step is to determine the shape of the eyebrow. It is recommended that the patient get the help of a professional makeup artist to choose the best eyebrow shape. Once the shape is outlined, it is important to properly select the donor follicles based on which part of the eyebrow we intend to rebuild. For instance, for making the contour, only single hair unit grafts must be chosen, whereas double hair units are selected for filling the body with a herringbone pattern (it gives more density). The donor hair should match the

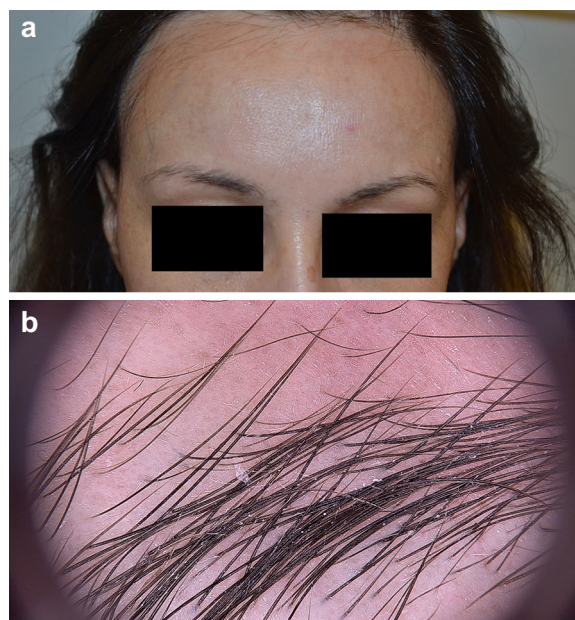


Fig. 8 Clinical picture of patient from Fig. 7 (a) and trichoscopy (b) after 8 months of intralesional injections



Fig. 9 Patient affected by FFA of eyebrows before (a) and after (b) the transplantation of 432 grafts

existing eyebrow in terms of caliber, curl, and texture. The most appropriate zone for harvesting is the postauricular area. Motorized punches are used for harvesting, while blades and forceps place the grafts. The number of transplanted grafts depends on the size of the eyebrow, ranging from 100–400 grafts per eyebrow. Respecting the principle of donor dominance, we explain to the patient the need to trim the eyebrows. Also, it is essential to consider the hair angularity and direction, as well. It is recommended to use eyebrow styling products to give harmony in the future (Fig. 9a, b). Complications are rare. Swelling of the upper lid is common, lasts for 3–4 days, and is not considered an actual complication. Moisture facial spray is prescribed for 10 days to relieve possible itching and soften scab formation. Hair regrowth begins 2–3 months after the transplantation, and the final result is observed after 6–7 months.

A progressive loss of transplanted hairs is however expected, and this should be discussed previously with FFA patients.

CONCLUSION

The conditions examined above are the most common causes of eyebrow and eyelash hair loss encountered in clinical practice, although

in dermatology, many other diseases can cause them.

Eye-brow and eyelash loss are a significant cosmetic defect, and their restoration can have a positive impact on patients' happiness.

The importance of an early diagnosis is necessary not only to reduce the impact of the disease on a patient's quality of life but also to halt disease progression. This article aims then to recap the main causes of eyebrow and eyelash alopecia, as well as their related treatments.

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Disclosures. All authors declare that they have no competing interests.

Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain new studies with human participants or animals performed by any of the authors. All the images collected for this paper were obtained after getting written informed consent from all of our patients. Patients are aware that their photos will be published in a journal.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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