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Case Report

# Management of folliculitis decalvans with ayurveda- A case report

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#### ABSTRACT

*Introduction:* The superficial infection that involves the hair follicle with bogginess or induration of involved parts of the scalp along with pustules, erosions, crusts, ulcers, and scales resulting in hair fall is known as folliculitis decalvans (FD). This condition accounts for approximately 11% of all cases with primary cicatricial alopecia. Based on clinical features like *Keshadhwansha* (hair fall) with *Harsha* (hypersensitivity), *Kandu* (itching), *Toda* (pain), FD can be correlated with *Raktaja Krimi Vikara* (RKV). *Observation and results:* A 24 years' male patient with the chief complaint of patchy hair loss in the scalp region associated with scale formation, itching, and pain for 2 months. He had a history of pustules-like eruption over the frontal and parietal regions. He tried various topical and oral medications for 8 days but didn't get any sign of improvement and came to NIA hospital for Ayurveda treatment. Due to the signs like pustules over the scalp, hair loss with honey-colored crusting, scarring, mild itching, and pain; he was diagnosed with RKV ~ FD. After treatment with Ayurveda medicine and leech therapy, complete remission of the scar, lesions, itching, pain, and hair loss was obtained, and there was new hair growth over the scalp with normal distribution. The patient was on follow-up for 33 months with no signs of itching, pain, and hair fall.

Conclusion: Complete remission of FD was achieved by Ayurveda medicine along with Jalaukavacharana and it seems highly effective on the basis of remission period compared to contemporary treatment modalities. It is suggested to have further clinical studies with large samples to analyze its effectiveness. © 2022 The Authors. Published by Elsevier B.V. on behalf of Institute of Transdisciplinary Health Sciences and Technology and World Ayurveda Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Any loss of hair from any body part is called alopecia; commonly occurs in the scalp region. There are two forms of alopecia: noncicatricial alopecia and cicatricial alopecia. Non-cicatricial alopecia is a condition where hair loss is not accompanied by any typical inflammation or scarring. While cicatricial alopecia (CA) occurs when hair loss is accompanied by scarring [1]. In CA, various factors and disorders destroy the hair follicles, replace them with scar tissue, and cause permanent hair loss. The superficial infection involving the hair follicle, with a central region of purulence surrounded by induration and erythema, is known as Folliculitis [2]. Among various types of CA, folliculitis decalvans (FD) is one, in which there is inflammation of the hair follicle leading to hair loss due to bogginess or induration of involved parts of the scalp along with pustules, erosions, crusts, ulcers, and scales [3]. It is most prevalent in males and starts after adolescence, while females tend to develop this condition after their thirties [4]. The actual etiology of folliculitis decalvans is unknown, however, it might be caused by an abnormal reaction to the bacteria *Staphylococcus aureus*. CA represents approximately about 7% of hair loss patients of which 11% of all primary CA cases are diagnosed with FD [5]. The clinical features of FD suggest it to be more similar to *Raktaja Krimi Vikara* (RKV) in Ayurveda. In Ayurveda, the word '*Krimi*' is used as a broad sense for worms and microorganisms perspective of modern science. Different texts of Ayurveda described the various types of Krimi viz. Different texts of Ayurveda described the various types of

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Krimi viz. Kaphaja, Purishaja, Raktaja, and Malaaja Krimi based on Sthana (location) and Prakruti (physical constitution) of Krimi [6]. Raktaja Krimi are Anu (minute), Adrishya (invisible), Vrita (round), Padarahita (without legs), and have Tamra Varna (copper color). Raktaja Krimi resides in Raktavahi Dhamani (channels carrying blood tissue) and causes Rakthadusti by different Doshas. They produce clinical features like hair fall, Harsha (hyperaesthesia), Kandu (itching), and Toda (piercing pain); treatment of this condition is similar to Kustha [6].

According to the British association of dermatologists, "There is no specific treatment licensed for folliculitis decalvans, and because the condition is so rare, no clinical trials exist that prove the benefit of any particular therapy over another." [7] Thus an attempt was done to treat FD through Ayurveda to assess the potentiality in this case. Despite the fact that there were several allopathic studies on FD, we were unable to find any Ayurveda studies in databases. Thus, this study may help the concerned patients and the scientific community.

## 2. Patient information

A 24 years male patient, a resident of Jaipur, India with no history of diabetes and hypertension visited (6th March 2019) the outpatient department (OPD) of the National Institute of Ayurveda (NIA), Jaipur, with the chief complaints of patchy hair loss over the head for 2 months associated with greying of hair.

#### 2.1. Primary concerns and symptoms of the patient

As reported by the patient, within the last four months, he gradually developed some pustular eruption over the scalp, associated with itching, pain, hair loss, and dandruff (may be scales) formation. The condition aggravated on rupturing the eruptions, resulting in the formation of a crusted ulcerated wound. Owing to worsening of the condition, the patient shaved his hair on December 1, 2018, for cosmetic reasons. Within one week, the pustules increased in number and became ulcerated crusty wounds ranging in size from 5 mm to a few centimeters (Fig. 1).

#### 2.2. Relevant past interventions with outcomes

The patient went to a nearby clinic for treatment in the first week of December 2018. On the first day of treatment, the doctor injected some medications (the name of which was not known to him) into the muscle of his left upper arm. He was also given the Povidone Iodine IP 5%, Fusidic Acid Cream IP 2%, Clotrimazole, Beclomethasone dipropionate, and Neomycin Sulphate Cream for local application. He took for eight days but didn't see any improvement, so he stopped these medications.



Fig. 1. Honey-colored wound (Dec 2018) and Patchy hair fall (Feb 2019).

#### 2.3. Relevant history

The patient reported to be on vegetarian diet and had normal sleep, but decreased appetite. He complained of incomplete evacuation of the bowel with frequency of once in 1-2 days. The patient admitted being under stress for about 2 months, because of his upcoming entrance exams. He reported neither history of substance abuse nor history of similar illness in his family or among his family members.

## 3. Clinical examination and findings

The general examination was normal and no significant finding was observed. The vitals recorded were 92/min pulse rate, 17/min respiration rate, blood pressure 120/70 mm of Hg, and weight 54 kg. On inspection of the site of the lesion, there were multiple numbers of irregular *Vrana* (wound) and *Vranavastu* (patches), varying in sizes over the frontal and parietal regions with *Kesha Dhwansha* (complete loss of hair) over there (Fig. 1). The color of the wounded scalp was *Tamra Varna* (honey-colored). The region with hair loss was tender while the rest of the scalp was normal. During the earlier days of treatment, two pustules erupted over the scalp which subsided on their own during the course of therapy.

## 4. Diagnostic assessment

The signs such as pustules followed by disruption and release of contents over the scalp, resulting in hair loss and scarring; associated with mild itching and pain assist to determine the cause of a CA [3]. As pustules are strongly suggestive of FD, they can also occur in lichen planopilaris (LP) and chronic cutaneous lupus (discoid lupus). But, the characteristics of itching were not as intense as in LP and the disease didn't aggravate on exposure to the sun or trauma (the Koebner phenomenon) as in discoid lupus. Along with these distinguishable clinical features, other signs like circumferentially expanding patches of complete hair loss, typically observed on the scalp; pustules (Fig. S4), and honey-colored crusting (Fig. 1) confirm it as FD.

#### 4.1. Ayurveda diagnostic assessment

According to Ayurveda, it can be differentially diagnosed with Arunshika, Indralupta, Kustha Raktaja Krimi Vikara. When there is the involvement of blood and Kapha, Kapha blocks the pore of the hair follicle, resulting in obstruction of new hair growth is known as Indralupta and if there is the involvement of Krimi along with Kapha and Rakta, small papulopustular eruption with multiple opening and excessive discharge occur in the scalp known as Arunshika. [8] Though the papulopustular eruption was a common feature with FD: the patchy hair loss, itching, and pain are not the clinical features of Arunshika. It was ruled out because the patient did not have Bahukleda (excessive mucopurulent discharge) [8]. It is difficult to elucidate Kustha with RKV, as the classics have stated the pathology and treatment of both diseases are the same and there are many clinical parallels. But, Keshdhwansh (hair loss) is not described as a Poorvaroopa (prodromal symptoms) or Lakshana (signs and symptoms) of Kustha. The RKV has clinical features like Keshadhwansha (hair fall) with Harsha (hypersensitivity), Kandu (itching), Toda (pain), Samsarpana (creeping sensation), and Twak-Sira-Snayu-Mamsa Bhakshana (involvement of skin, blood vessels, and muscles) (CS.VS.7/11) [6]. The patient had a history of Pitta Kapha Vardhaka Aharaj Viharaj Nidana Sevana, which ultimately causes vitiation of *Rakta Dhatu* like taking mustard oil, curd, sweets, 2–3 L milk intake daily, tea with Namkeen (Indian savory snacks mostly made up of wheat and gram flour) as diet; and day sleeping, regular

exposure to the sun, etc. as a lifestyle. The pathogenesis and clinical presentation of the patients like papulopustular eruption with pain and itching which after burst cause wound, hair fall with involvement of skin and blood vessels resulting in scarring over the scalp, and the given *Nidana* show the typical features of *Raktaja Krimi Vikara*.

## 5. Therapeutic intervention

Based on the clinical presentation, the patient was diagnosed with FD, which can be correlated to *Raktaja Krimi Vikara* in Ayurveda. The treatment for this is similar to *Kustha Chikitsa* (CS.VS. 7/ 11) [6]. Thus the treatment was focused mainly on *Krimighna Chikitsa, Kustha Chikitsa,* and hair growth. The treatment protocol (Table 1) was administered for one and a half months during which *Jalaukavacharana*/Leech Therapy (LT) was done weekly for 5 weeks. The patient was advised to follow *Nidanaparivarjana* (avoid the causative diet and lifestyle factors). Following the growth of new hair, medicines were prescribed (Table 1) to prevent, maintain, and promote hair growth.

#### 5.1. Pharmacological intervention

The powder form of *Triphala*, *Vidanga and Shuddha Gandhaka*, *Triphala Guggulu*, *Dhurdhurpatradi Taila*, and *Triphala lepa* was intervened (Table 1) [9–11,6]. The required amount of *Triphala* and water (eight times the powder) was kept in an iron vessel and

#### Table 1

Patient assessment and treatment timeline.

boiled in medium heat until it reduced to half. Then it was left as it is in an iron vessel for about 48 h. Within 48 h, the leftover water fraction was absorbed and/or evaporated properly, resulting in the formation of paste (consistency as like toothpaste). This technique usually resulted in a paste but sometimes it didn't (may be due to the low temperature of weather). In such a situation, the mixture was heated on low flame to form a paste. This paste was used over the scalp three times a week.

The powder and *Guggulu* were given from the outpatient dispensing section, NIA, Jaipur, prepared at GMP-certified NIA pharmacy whereas *Dhurdhurpatraadi Taila* (D.L.No. 33/25D/76, Batch No. ADK 089) of Arya Vaidya Sala, Kottakkal was purchased from a medical store. Follow-up was taken once in 7 or 15 days for 5 months.

## 5.2. Parasurgical intervention

*Raktamokshan* is recommended for *Pitta Pradhana Kustha* diseases and *Jalauka* is indicated for bloodletting of localized wounds (CS.CS.7/39) [6]. Bloodletting with *Jalauka* is also recommended for *Rakta* that has been vitiated by *Pitta* (SS.Soo.13/4) [8]. The procedure, mechanism, and its consequences were described to the patient before signing the consent form, and he was mentally prepared for the therapy. The LT was performed by applying two *Jalauka* over the affected site on a weekly basis for a total of five sittings. The patient was instructed to keep the LT site clean and ensure aeration.

Date	Health Event	Clinical Features	Medication	Rationale
06th March 2019	First visit Provisionally diagnosed as Khalitya D/D- Arunshika, Indralupta, Raktaja Krimija Vikara (RKV)	Patchy hair loss over the scalp Hair fall Itching sensation Dandruff Greyish of hair	1. Triphala Churna [9] 3 g Vidanga Churna 3 g Shuddha Gandhaka 500 mg 1 dose bd before food with lukewarm water 2. Triphala Guggulu [10] 3 tab tds before	
	Medication started		food with water 3. Dhurdhurpatradi Tailam [11]- LA on an alternate day 4. Jalaukavacharana (LT)	
13th, 20th March 2019	Final diagnosis as RKV ~ FD	Patient-reported control on itching	CST	
	h 2019 and continues for 5	sitting once per week with regular healt		
01 <sup>st</sup> April 2019	2nd LT done	Reduction in hair fall with gradual progress in the development of hair.	CST + 5. Triphala Churna Lepa [6]	Lepa should be applied after Shodhana for quick action (CS.CS. 7/53).
09th, 16th April 2019	3rd and 4th LT done	Remission of complaints with small light brownish new hair growth over the patchy region.	CST	
23rd April 2019	The last LT done	A significant improvement was achieved in the growth of hair all over the scalp.		
05th May 2019		Hair development continued. No other complaints.	LT Stopped. CST 1, 2, 3 and 5.	Due to the inability of leeches to get attached over the scalp for sucking the blood due to hair growth.
13th May 2019		Complete remission of disease, no other complaints.	Dhurdhurpatradi Tailam stopped. Continue 1, 2, and 5.	As there was hair growth over the previous patchy region.
28th May 2019		Complete remission of the disease. Burning sensation in the abdomen (maybe due to dietetic factors).	Continue 1, 2 and 5 + 6. Avipattikar Churna 5 g Pittantaka Yoga 1 g 1 dose bd before the meal	For the sustenance of improvement by balancing the vitiated <i>Pitta</i> and to prevent the vitiation of <i>Rakta</i> .
11th June and 02 <sup>nd</sup> July 2019		No fresh complaint	CST	
7th August 2019		No fresh complaint. Complete remission of the disease continued.	Medicine stopped. The patient was advised to be under supervision for 1 month.	

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#### 5.2.1. Identification and collection of Nirvisha Jalauka

The local people/collector used to collect *Jalauka* from the bank of Yamuna river and from ponds, tanks of Agra region and the species were of *Hirudinaria granulosa*. The species was identified jointly by Indian Biological Team and the staff of NIA on the basis of both Ayurveda and conventional science system i.e. scientific name of leech and the *Nirvisha* characteristics mentioned by *Sushruta*. The *Nirvisha Jalauka* (NJ) can be collected from "*Pautan*" region, the area at around Mathura and Agra. Also, the leeches from clean and fresh water are considered as NJ. The smoothness and green gramlike color on the back along with the *Manashila* (realgar) like light colored lines on the side resembled with *Kapila* type of NJ (SS.Soo.13/13). Those collected leeches used to keep in an aerated transparent glass container filled with fresh water.

## 5.2.2. Purvakarma (preceding procedure)

The leeches were collected from a container and purified by applying turmeric powder over their bodies and immersing them in turmeric-infused water (SS.Soo.13/19) for around 1 *Muhurta* (around 48 min) [8]. During this process, the leech did *Vamana* (emesis) resulting in its purification and became active. They were then washed with water and placed in an aerated transparent container filled with fresh water. A silent atmosphere was established inside the *Jalaukavacharana* room, and the patient was advised to remain calm so that the leech can suck comfortably.

## 5.2.3. Pradhana Karma (main procedure)

The necessary materials, such as leeches, medications, and instruments, were prepared following aseptic methods. The site of the lesion was cleaned. The leech's head was positioned over the infected area and covered with wet cotton to prevent the leech from moving to the other side. If the leech was unable to suck, a sterile syringe needle was used to prick the scalp, allowing a drop of blood to exit. The peristalsis-like movement from the head to the posterior end of the leech was observed during sucking (Fig. S1). In case the leech did not remove itself after filling up with blood, *Saindhava Lavana* (rock salt) was spread over the leech's mouth (SS.Soo.13/21) [8].

## 5.2.4. Paschata Karma (post-procedure)

Immediately after detachment of leech, the *Shubhra Bhasma* (BR.3/94) was spread over the wound to control bleeding (Fig. 2) [10]. The detached leech was kept in hand (sometimes in the tray) and powder of rock salt was spread over its frontal end for *Vamana*. Residual blood after *Vamana* was then again regurgitated by pressing the body from posterior to the frontal end of the leech. This resulted in its purification so that the same leech can be used



Fig. 2. Anterior view- After 4 month (July 07, 2019) and Posterior view- After 4 month (July-07, 2019).

for the same patient again in the next sitting. After proper *Vamana*, it was placed in an aerated jar half filled with fresh air. If the leeches swam freely with an elongation of the body, then the condition was evaluated as normal. The water in the container was replaced every 2-3 days. (SS.Soo.13/17) [8].

After the stoppage of bleeding from the wound, the paste made by mixing *Yastimadhu* and turmeric powder with honey was pasted over the wounded area (SS.Soo.13/23) (Fig. S2) [8]. Honey, turmeric and *Yastimadhu* have *Vranaropaka* properties which help to heal the wound. Beside these turmeric has also *Raktastambhana* (hemostyptic) and *Krimighna* (anti-microbial) activity that controls the bleeding and combats the infection [12]. After five sittings, the LT was terminated as the hair grew significantly.

#### 6. Follow-up and outcomes

The follow-up and outcomes have been mentioned in Table 1, Figs. 1 and 2; S1-S6. Even after the growth of hair, he was kept under the same medicine. The follow-up was conducted on a regular basis for 5 months up to 7th August 2019. The treatment was then terminated and monitored for a month for any pathological changes. During that withdrawal phase, no clinical signs or symptoms of FD were found. No adverse or unanticipated effects were observed during the treatment period. The patient was pleased to get the same hair growth all over his scalp as it was before (Figs. S5 and S6). The patient is in complete remission for the next 37 months, till October 2022.

## 7. Discussion

FD is characterized by painful follicular pustules at a central point that subsequently crusts and spreads outward to develop a patch of hair loss in an increasing folliculitis zone that results in scarring of a central area. The scar, in the early stages, is indurated and boggy rather than atrophic. In advanced cases, there is generally one, but occasionally more, rounded patches of hair loss over the vertex of the scalp surrounded by crusting and a few follicular pustules [4].

*Krimi Chikitsa* is based on three principles-(i) Apakarshana (removal of the *Dosha* or other harmful substances) (ii) *Prakrutivighata* (counteracting the cause of disease i.e. *Krimi*) and (iii) *Nidana Parivarjan* (avoidance of etiological factors). The classics also instruct to perform treatment of *Raktaja Krimi* as like *Kustha Chikitsa*. In *Kustha* and *Raktaja Krimi*, *Rakta* is the main vitiated *Dhatu*. So, for *Apakarshana*, *Raktamokshana* with *Jalauka;* for *Prakrutivighata*, medicines having *Katu*, *Tikta*, *Kashaya* rasa with *Krimighna* property; and for *Nidanaparivarjana*, avoidance of the *Nidana* (mentioned in 4.1) was planned.

The mechanism of action (MoA) of leech therapy for this disease is not well defined. However probable MoA can be determined based on the Dosha, Dhatu involved, and the clinical features. Its main action is the purification of Dushit Rakta (impure blood), pacification of aggravated Pitta Dosha. It also has antimicrobial properties which combat the Krimi (infection), and Vranaghna properties recover wounds. It also improves blood circulation, allowing the lesion area to be well-nourished. Since Jalauka is found in water, it has a *Madhura* effect, making bloodletting beneficial for Pitta-aggravated diseases. (SS.Soo.13/6) [8]. Ayurveda text mentioning Jalauka states that it has the capacity of removing Dushita Rakta Dhatu. Susruta states that the Raktamokshan done properly results in Prasada Mana (normalization of the physiology of the Mana or the whole body with senses) and it prevents the development of Raktaja Roga like Twaka Dosha (skin disorders), *Granthi* (abnormal outgrowth), and *Shopha* (inflammation) (SS.SS.14/33-34) [8].

Leech saliva (LS) contains anticoagulant substances like hirudin, calin, and destabilase, which in the course of therapy increase bleeding time and clotting time. It also contains carboxypeptidase inhibitor, acetylcholine, and histamine-like substances that cause vasodilatation, endothelial muscle relaxation, and increase local vascular permeability resulting in increased blood flow at the feeding site [13]. Though the antimicrobial action is not a completely established phenomenon but the presence of compounds like destabilase, chloromycetin, theromacin, theromyzin in saliva signifies these properties [14]. Destabilase has  $\beta$  -glycosidase activity, which disrupts  $\beta$ 1–4 bonds in the peptidoglycan layer of bacterial cell walls directly. Even the denaturated type destabilase has a dose-dependent bacteriostatic impact on S. aureus, Pseudomonas aeruginosa, and Escherichia coli. Chloromycetin is a potent antibiotic present in the secretions of leeches. Antimicrobial peptides theromacin, theromyzin, and peptide B have also been isolated [15]. LS contains enzymes that reduce adhesions and scar tissue. Fibrinases and collagenase in saliva reduce the density of scar tissue and it helps to decrease the development of fibroblasts in keloids and hypertrophic scars [16].

Triphala is Kusthaghna, Vranaropaka, Raktavikara Shamaka which acts as a Rasayana which according to modern science prevents the formation of any free radicals in the human body and has powerful antioxidant effects and thus can prevent signs of premature aging, such as greying of hair [9]. Amalaki, the main source of vitamin C, boosts immunity, maintains proper absorption of minerals and circulation of blood which in turn maintains healthy hair. Bibhitaki helps to strengthen the hair's root, minimizes hair loss, and prevents premature greying of hair [17]. Haritaki acts as Vranaropaka (wound healing agent) and Twaka Prasadana (skin nourishing agent).

Vidanga is Jantughna, Kusthaghna, Varnya and Krimihara (BR.11/ 3) [10,17]. Various modern research verified it as an antibacterial, analgesic, anti-inflammatory, and antioxidant. *Gandhaka* is *Rasayana*, *Kandu* and *Kustha Nashaka*, *Krimihara* and its antimicrobial activity had been proved by various research (BR.3/82) [10]. *Triphala Guggulu* is best for *Puyasrava* (pus discharge), *Pidayukta* (painful) *Vrana* (BR.47/49) [10].

Dhurdhurpatradi Tailam eliminates itching and reduces hair fall [11]. Dhatura has the capacity of eliminating Twak Dosha, Kandu, and Krimi and heals Vrana. Vagbhata has mentioned its indication in Indralupta and for Kriminashanam [18]. Astangahridaya mentioned the use of Dhaturapatra Rasa Lepa in Indralupta after bloodletting through Siravedhana [19]. Dhatura has the characteristics of antimicrobial, wound healing, analgesic, immune-modulatory, and antifungal activity [20].

Currently, there is a scarcity of information on the effectiveness of FD-specific therapies. An evidence-based review study of current treatment effectiveness for FD states that there was no high-quality research evidence in the treatment efficacy of FD and Grade 3 was the highest level of evidence found as per the American College of Physicians Treatment Grading Guidelines [21]. This study states that the shortest remission period was 3-6 months and the longest disease remission at an average of 7.2 months for the contemporary allopathic treatment with doxycycline or azithromycin or clindamycin and rifampicin or tetracycline, clobetasol lotion and intralesional triamcinolone, etc. medicines. The disease remission varies from 2 months to 4 years. There was a need for continuation of treatment or maintenance dose for about half of the patients to maintain remission [21,22]. In our case, the remission period was about 1.5 months, and no recurrence to date (almost 3 years). Though this study shows the potentiality of Ayurveda treatment as compared to contemporary allopathic treatment, it cannot be claimed with a single case study. But, it has paved the way for further research.

Also, further joint studies can be conducted in order to evaluate the efficacy in larger samples and for a longer duration.

Laboratory investigations for hematological status, pus swabs from intact pustules for culture, and scalp biopsies must be done for proper diagnosis and prognosis before treatment, and LT which had been missed in this study which can be considered as limitations of this study. The strength is the complete remission of itching, pain, pustular formation, and patchy hair fall, by the Ayurvedic medicine with leech therapy (no other allopathic medicine) within one and half months without any recurrence and adverse effects for 33 months until our observation.

# 8. Conclusion

Folliculitis decalvans though being considered as permanent destruction of the hair follicle and irreversible hair loss, complete remission was achieved by Ayurveda medicine along with *Jalaukavacharana* and it is highly effective compared to contemporary allopathic treatment. Further research studies need to be done to validate this finding before incorporating it into the treatment protocol.

## **Patient perspectives**

"I was very worried about my hair fall problem as English medicine was not giving me any relief. Hair fall and wounds were increasing day by day. After that I went to NIA Madhovilas Hospital for treatment and took Ayurvedic medicines along with getting *Jalauka*. This made me feel in control of hair fall and itching. Later, after taking about one and a half months of treatment, all my complaints got cured and hair also started growing. Now, I am very happy that my hair has grown on my head like before and for this I am thankful to the doctors."

#### Informed consent

The patient had signed an informed consent form for the treatment procedure, study, and publication.

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## **Conflicts of interest**

None.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jaim.2022.100673.

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