Practical Guidelines for Evaluation of Loose Anagen Hair Syndrome

Julie L. Cantatore-Francis, MD; Seth J. Orlow, MD, PhD

Objectives: To better categorize the epidemiologic profile, clinical features, and disease associations of loose anagen hair syndrome (LAHS) compared with other forms of childhood alopecia.

Design: Retrospective survey.

Setting: Academic pediatric dermatology practice.


Main Outcome Measures: Epidemiologic data for all forms of alopecia were ascertained, such as sex, age at onset, age at the time of evaluation, and clinical diagnosis. Patients with LAHS were further studied by the recording of family history, disease associations, hair-pull test or biopsy results, hair color, laboratory test result abnormalities, initial treatment, and involvement of eyelashes, eyebrows, and nails.

Results: Approximately 10% of all children with alopecia had LAHS. The mean age (95% confidence interval) at onset differed between patients with LAHS (2.8 [1.2-4.3] years) vs patients without LAHS (7.1 [6.6-7.7] years) \((P < .001)\), with 3 years being the most common age at onset for patients with LAHS. All but 1 of 37 patients with LAHS were female. The most common symptom reported was thin, sparse hair. Family histories were significant for LAHS (n=1) and for alopecia areata (n=3). In 32 of 33 patients, trichograms showed typical loose anagen hairs. Two children had underlying genetic syndromes. No associated laboratory test result abnormalities were noted among patients who underwent testing.

Conclusions: Loose anagen hair syndrome is a common nonscarring alopecia in young girls with a history of sparse or fine hair. Before ordering extensive blood testing in young girls with diffusely thin hair, it is important to perform a hair-pull test, as a trichogram can be instrumental in the confirmation of a diagnosis of LAHS.

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The retrospective medical record review revealed that 37 patients were diagnosed as having LAHS among 374 patients with alopecia seen at the academic pediatric referral practice over a 10-year period. Table 1 summarizes the clinical and laboratory findings among patients with LAHS and, for certain variables, among patients without LAHS. The mean (95% confidence interval [CI]) age at onset in patients with LAHS (2.8 [1.2-4.3] years) was significantly younger than that in patients without LAHS (7.1 [6.6-7.7] years) (P < .001). As shown in Figure 1, the most common age at onset for patients with LAHS was 3 years, with description by most parents of a hair abnormality that began from birth to 3 years of age. The mean (95% CI) age at the time of evaluation among patients with LAHS (4.1 [2.4-5.9] years) was also significantly younger than that in patients without LAHS (8.3 [7.8-8.9] years) (P < .001) (Table 1). All except 1 patient among 37 patients with LAHS were female compared with 188 female patients among 337 patients without LAHS (P < .001).

Hair descriptions among patients with LAHS by patients and other family members were grouped into 4 categories (Table 2), with the most common report being thin, sparse, or fine hair. The most frequent comments shapen bulbs and ruffled cuticles, were further studied by the recording of family history, disease associations, hair-pull test or biopsy results, laboratory test results when available (including thyroid panel, antithyroid antibodies, and other values such as hormonal, antinuclear antibody, iron, or zinc levels), and initial treatment method. Hair color and the presence or absence of eyelash, eyebrow, and nail involvement were also recorded in these patients.

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made by parents with regard to the hair of their child were that the hair “has always been thin,” “has never been cut,” “was not growing,” “was unmanageable,” “was constantly shedding,” or “was easily pulled out.” The complete absence of hair, even in a localized area, was not noted. All patients for whom hair color was recorded had blond or light brown hair. Thinning of the eyebrows was noted in 1 patient, while eyelash and nail findings were normal in all 37 patients. Family histories were significant in 4 patients: 1 patient had a fraternal twin with LAHS, and 3 patients had family members with alopecia areata (2 of these had immediate family members [a sibling and a grandfather] with alopecia totalis).

Trichograms were recorded in 33 patients after a hair-pull test. Thirty-two of these patients had a predominance (>50%) of typical loose anagen hairs, anagen hairs with misshapen bulbs, ruffled cuticles, and an absent inner root sheath (Figure 2). Trichorrhexis nodosa was seen in 2 of these patients, while pseudotrichothiodystrophy (or alternating light and dark bands under polarized light with undulating shafts) was seen in 3 patients (Table 1). A fourth patient had a trichogram consistent with pseudotrichothiodystrophy and normal anagen hairs with tapered ends.

Overall, all patients with LAHS were healthy. Two children had underlying genetic syndromes (Noonan syndrome and neurofibromatosis type 1), and 2 children had a history of atopic dermatitis. Eighteen children had laboratory testing performed, often before referral. No associated laboratory test result abnormalities were found in those children in whom laboratory testing had been performed. Treatment with topical minoxidil was started for 3 of 37 patients with LAHS. Two of these were lost to follow-up when they did not return for their later appointments, and the third had good improvement within 3 months. The remaining 34 patients were not treated.

**Comment**

Loose anagen hair syndrome is estimated to have an incidence of 2 to 2.25 cases per million per year.\(^4\) In our study of 374 children and teenagers referred to an academic faculty practice for hair loss, approximately 10% of the patients diagnosed as having alopecia had LAHS, which made it a common diagnosis in these children referred for evaluation. The syndrome has been reported to occur typically in young children and, in most cases, spontaneously improves clinically by adulthood or as early as adolescence.\(^1,7\) Most important, patients with LAHS vs patients without LAHS in our review were significantly younger at onset (2.8 vs 7.1 years) and at the time of evaluation (4.1 vs 8.3 years). Almost all children with LAHS were initially seen within the first 3 years of life. Therefore, practitioners should have a high index of suspicion for LAHS during the examination of an infant or toddler with diffuse nonscarring alopecia.

Overall, the clinical findings of children and teenagers with LAHS in this study were typical of patient reports in the medical literature: patients had light-colored hair, were almost exclusively female, and commonly reported thin, sparse, or fine hair that would easily shed and did not require frequent haircutting (Figure 3).\(^1,8\) In accordance with previous studies,\(^1,3,8,10-12\) a large subset of patients had hair with an odd texture or hair that was difficult to comb, frizzy, or unruly. This texture difference is usually described as “sticky”
or “matted” and is commonly located on the occipital scalp. True uncombable “spun glass” hair and even woolly hair have been associated with LAHS. Although many parents reported diffuse shedding of the hair or hair loss as their primary concern, none of our patients had clinically visible areas of complete hair loss, which can be a helpful sign in the narrowing of the differential diagnosis of nonscarring alopecia in children. Although LAHS is usually a condition limited to the scalp, the involvement of body hair and eyebrows has been reported in an adult patient with LAHS. A patient in our review had eyebrow thinning and a scalp trichogram consistent with LAHS; however, alopecia areata was also considered a strong possibility in this patient. Overlap between alopecia areata and LAHS has been reported. Nunez et al described a child having alopecia areata who was initially seen with clinical and microscopic features of LAHS. Nail findings, which are often present in alopecia areata, are not typically associated with LAHS, with only a single report of fragile nails described in a series by Chapalain et al. Nail involvement was not present in any of the patients with LAHS in our study.

Diagnosis of LAHS can be based on typical clinical features, as already described, and on results of light microscopic examination. The mere presence of some loose anagen hairs is not specific for LAHS, as they may also be found in unaffected individuals. Therefore, it has been proposed that LAHS should only be diagnosed microscopically when there is a predominance (>50%) of loose anagen hairs on a trichogram, as was the case in 32 of our patients. Trichorrhexis nodosa, a hair shaft disorder characterized by regularly spaced pale nodelike swellings, was found in 2 of our patients, and pseudotrichothiodystrophy (Figure 4) (hair shafts characterized by alternating dark and light bands with twisted shafts under polarized microscopy) was found in 3 patients in addition to typical loose anagen hairs (pseudotrichothiodystrophy was also found in 1 patient with normal anagen hairs and tapered ends on a trichogram). Although trichorrhexis nodosa, usually related to trauma and commonly found in patients with otherwise normal hair, was most likely an isolated or coincidental finding in our patients, light and dark horizontal banding in alternation with a twisted hair shaft under polarized light has been reported by Lee et al in a patient with LAHS and uncombable hair. We referred to this finding as pseudotrichothiodystrophy because in trichothiodystrophy, which is a specific term related to sparse hair with a low sulfur content and a “tiger-tail” banding pattern under polarized light, the banding is more regular than that in kinky hair and is a result of a continuous change in the orientation of keratin filaments within the hair shaft.

Loose anagen hair syndrome is thought to be an inherited condition in an autosomal dominant pattern with incomplete penetrance, although sporadic cases have been reported. It is thought that rare cases of LAHS in adults, usually characterized by increased hair shedding with a small percentage of typical loose anagen hairs on a trichogram, are diagnosed because they are family members of affected children. Chapalain et al discovered the K6HF mutation in hair keratin that may be responsible for premature keratinization of the inner root sheath, which impairs adhesion between the cuticle of the inner root sheath and the companion layer in some families with LAHS. In our case series, only 1 child had a fraternal twin with LAHS, although performance of an extensive family history was beyond the scope of this study. Notably, 3 patients with LAHS had family members with alopecia areata. In light of the overlap in clinical and trichogram features of LAHS and alopecia areata already discussed, perhaps there is a link between keratin hair mutations and immune response mutations responsible for familial forms of these initially clinically similar nonscarring alopecias.

In most cases, LAHS is isolated but can occur in association with developmental or ectodermal abnormalities, such as coloboma, Noonan syndrome, hypohidrotic ectodermal dysplasia, EEC (ectrodactyly-ectodermal dys-
plasia–clefting) syndrome, trichorhinophalangeal syndrome, nail-patella syndrome, and FG syndrome and has been described in patients with AIDS. In our review, 2 patients with clinically diagnosed LAHS had Noonan syndrome, and 1 patient had neurofibromatosis type 1, with the latter association not having been previously reported, to our knowledge. Although 2 patients with LAHS had coexisting atopic dermatitis, there is no clear association between the 2 conditions. Most important, no associated laboratory test result abnormalities were found in our patients with LAHS who underwent testing, which emphasizes the importance of the performance of a hair-pull test, as a trichogram is important to perform in the establishment of a diagnosis of LAHS; (3) before obtaining blood samples, which is stressful and invasive for young patients and their families, it is important to perform a hair-pull test, as a trichogram can be instrumental in the establishment of a diagnosis of LAHS; (4) parents can be reassured that LAHS will improve over time in most children; (5) in most cases of LAHS, observation is the treatment of choice; however, topical treatment with minoxidil may be considered in severe cases.

As mentioned previously, most cases of LAHS resolve spontaneously; however, the successful use of minoxidil therapy in infants is encouraging and may be a reasonable first-line therapy for patients with disease at the severe end of the LAHS spectrum. The patient who responded to minoxidil within 3 months of treatment in this study had many anagen hairs and tapered ends on her trichogram in addition to ruffled cuticles. Together, our conclusions about LAHS herein and the reported characteristics of other common nonscarring hair disorders in children, including alopecia areata, telogen effluvium, androgenetic alopecia, and trichotillomania (Table 3) should well equip the practitioner to make an appropriate diagnosis of alopecia.

In summary, our retrospective medical record review highlights LAHS as a common presentation in young patients with nonscarring noninfectious alopecia. Practical guidelines for the diagnosis of LAHS include the following: (1) the index of suspicion for LAHS used by a practitioner should be high in children younger than 4 years with a history of sparse, thin hair; (2) female sex or light-colored hair should strengthen the suspicion of LAHS; (3) before obtaining blood samples, which is stressful and invasive for young patients and their families, it is important to perform a hair-pull test, as a trichogram can be instrumental in the establishment of a diagnosis of LAHS; (4) parents can be reassured that LAHS will improve over time in most children; (5) in most cases of LAHS, observation is the treatment of choice; however, topical treatment with minoxidil may be considered in severe cases.

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Correspondence: Seth J. Orlow, MD, PhD, Department of Dermatology, New York University School of Medicine, New York University Medical Center, 560 First Ave, Suite H-100, New York, NY 10016 (seth.orlow@nyumc.org).

Author Contributions: Both authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Cantatore-Francis and Orlow. Acquisition of data: Cantatore-Francis. Analysis and interpretation of data: Cantatore-Francis and Orlow. Drafting of the manuscript: Cantatore-Francis and Orlow. Critical revision of the manuscript for important intellectual content: Cantatore-Francis and Orlow. Statistical analysis: Cantatore-Francis. Administrative, technical, and material support: Cantatore-Francis and Orlow. Study supervision: Orlow.

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