Primary Generalized and Localized Hypertrichosis in Children

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Objective: To review the causes, presentation, and therapy of primary generalized and localized symmetrical hypertrichosis in children.

Design: Retrospective medical record review.

Setting: Academic specialty referral clinic for pediatric dermatological disorders.

Patients: Case series of 11 prepubertal male and female patients who had idiopathic hypertrichosis between July 1, 1990, and November 30, 1999.

Interventions: None.

Main Outcome Measures: Clinical distribution of increased hair growth and types of hair removal methods used.

Results: Seven girls and 4 boys, ranging in age from 4 months to 11 years, were evaluated. Four patients showed generalized hypertrichosis. The other 7 patients had localized symmetrical hypertrichosis, representing the subsets of hypertrichosis cubiti, anterior cervical hypertrichosis, posterior cervical hypertrichosis, and faun tail deformity. All patients with generalized hypertrichosis manifested the condition at birth; the age of onset in children with localized symmetrical primary hypertrichosis ranged from birth to 4 years. One girl with generalized hypertrichosis had gingival hyperplasia and the girl with faun tail deformity had bony diastematomyelia with spina bifida occulta. The medical histories and physical examination findings of all of the children were otherwise unremarkable. All patients were referred for diagnostic and therapeutic considerations.

Conclusions: Primary hypertrichotic conditions, whether localized or generalized, are rare in pediatric patients and of unknown origin. Although otherwise benign, these disorders may result in cosmetic disfigurement and psychosocial trauma for patients and families. Patients and their families should be adequately advised of the available treatment methods for both temporary and permanent hair removal.

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HYPERTRICHOSIS IS a condition of excessive hair growth that must be distinguished from hirsutism, which is characterized by an androgen-dependent hair pattern with excessive body and facial terminal hair distributed in a male pattern. Hypertrichosis in prepubertal children, unlike hirsutism, is not associated with an underlying endocrine disorder and is most commonly an adverse effect of drug administration. Primary hypertrichosis has been classified based on the age of onset (congenital or acquired) and the extent of distribution (localized or generalized forms). In its generalized form, hypertrichosis may be an isolated finding, as in hypertrichosis lanuginosa congenita, or associated with gingival hypertrophy.

Primary localized symmetrical areas of hypertrichosis may occur as hypertrichosis cubiti (elbows), anterior cervical hypertrichosis, posterior cervical hypertrichosis, or faun tail deformity. We evaluated the presentation and course of pediatric patients with primary symmetrical hypertrichosis referred to a specialty dermatology clinic during a 9-year period and reviewed representative examples of these unusual hair disorders.

REPORT OF CASES

CASE 1

A 6-year-old girl was born with long, coarse, dark brown hair on her forehead, with the appearance within months of increased hair on the cheeks, sideburn areas, chin, chest, abdomen, back, arms, and
SUBJECTS, MATERIALS, AND METHODS

A retrospective medical record review was performed of children examined for excessive hair growth during a 9-year period from July 1, 1990, through November 30, 1999, at the Division of Dermatology, Children's Memorial Hospital, a tertiary care center serving the Chicago metropolitan area of approximately 3 million people. Eleven patients with primary generalized or symmetrical localized hypertrichosis were identified; all had medical records and photographs available for review. Through telephone and at least 1 clinic-based interview, the following data were collected: sex, age, race, medical history, drug history, distribution of increased hair growth, patient's age of onset of excess hair growth, change in pattern of hair growth, family history of increased hair growth, and treatments attempted. Patients with asymmetrical increased hair growth, with or without an underlying lesion (eg, nevoid hypertrichosis, congenital nevi, or smooth muscle hamartoma), and patients in whom hirsutism had been diagnosed based on clinical pattern and endocrine studies were excluded from this review.

RESULTS

Seven girls and 4 boys with hypertrichosis were evaluated during the study period (Table 1). Four of the children had generalized hypertrichosis; the onset in all of these patients was at birth. Three of the 4 patients had no associated medical problems and were diagnosed as having hypertrichosis lanuginosa congenita (Medelian Inheritance of Man [MIM] classification: 145700, 135400). Of these 4 children, only the girl with hypertrichosis, but the family was unaware of associated abnormalities were found on physical examination, leading to the diagnosis of hypertrichosis lanuginosa congenita. The patient tried shaving and chemical depilatories, but was discouraged about the transient effect. Her parents agreed that electrolysis be considered but only when the patient was old enough to tolerate the potential discomfort of this procedure.

At follow-up, the patient was 17 years old. The hypertrichosis has persisted and remained the same in density and thickness. The patient was still battling with cosmetic and psychological issues related to the excessive hair growth. She had tried electrolysis, which decreased the excessive hair density but was both painful and expensive. The patient's family was unable to continue therapy after their insurance company denied payment, and they could not afford epilative laser therapy. The patient uses selective application of chemical depilatory agents that cause skin irritation and must be repeated weekly.

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CASE 2

A 7-year-old girl had excessive, fine, long vellus blonde hairs on the back, shoulders, arms, legs, and sacrum. The increased hair was first noted shortly after birth and had been progressively increasing in density. The patient was upset because her classmates teased her and called her "werewolf." There was no reported family history of excessive hair growth. No associated abnormalities were found on physical examination, leading to the diagnosis of hypertrichosis lanuginosa congenita. The patient tried shaving and chemical depilatories, but was discouraged about the transient effect. Her parents agreed that electrolysis be considered but only when the patient was old enough to tolerate the potential discomfort of this procedure.

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The patient suffered enormous emotional distress from the increased hair growth, especially on her face. She reported being teased at school and stared at in public. Bleaching agents caused minimal improvement in appearance. A trial of depilatory agents resulted in the return of long, thick, dark brown hairs within 1 week. A trial of epilative intense pulsed light laser therapy on the back at 5 years produced positive results with less hair growth, but was very painful, costly, and only limited areas could be treated at each session. The patient also had 8 dental restorations and 2 extractions to preserve her teeth and dental function. Tonsillectomy and adenoidectomy was performed at age 4 years for obstructive sleep apnea. The patient continues to be markedly distressed about her cosmetic problem and refuses to participate in activities that expose her, such as swimming.

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The other 7 children had localized hypertrichosis, distributed as follows: elbow and surrounding extensor arm (2 patients) (Figure 3), anterior cervical (3 patients) (Figure 4), posterior cervical (1 patient), and faun tail deformity (1 patient) (Figure 5). None of the children with localized hypertrichosis had an affected family member, although 2 of the girls were adopted (one of them having localized hypertrichosis of the arms and

<table>
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<th>Variable</th>
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<tr>
<td>Age at presentation</td>
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<td>Maternal great-uncle None None None Unknown None None None None Unknown</td>
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<td>Treatment</td>
<td>Chemical depilatory and intense pulsed light Electrolysis and chemical depilatory Trimming Chemical depilatory Trimming Chemical depilatory Trimming Chemical depilatory Trimming None</td>
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Table 1. Cases of Generalized and Localized Primary Hypertrichosis
the other the faun tail deformity). The parents of the 4-year-old girl with the faun tail deformity had never been counseled about the risk of associated underlying spinal cord and/or bony abnormality. Magnetic resonance imaging and computed tomographic scans were performed and showed diastematomyelia with spina bifida occulta affecting the lower lumbar spine from L2 through upper sacrum/S1. Neurosurgical intervention was undertaken.

The prenatal and perinatal histories of all patients were unremarkable; none of the children had been exposed to drugs known to cause hypertrichosis. All patients were counseled about the available methods of treating hypertrichosis and their risks. All patients except for 2 children with anterior cervical hypertrichosis attempted treatment. Five of the children chose to use chemical depilatories; application in the 3 patients with generalized involvement who used depilatories was limited to selected areas that caused the greatest cosmetic disturbance. One of the children with generalized hypertrichosis used electrolysis selectively to the face and distal arms. The patient with associated gingival fibromatosis tried epilative (EpiLight Hair Removal System; EpiLight, Ferndale, Mich) laser therapy but found it to be too painful and too costly. The parents considered the suggested treatment to be satisfactory for patients with localized involvement but unsatisfactory in all children with generalized hypertrichosis.

COMMENTS

Primary and secondary hypertrichosis in children, particularly if extensive, may cause severe cosmetic alteration, resulting in a tremendous emotional burden. Treatment options are limited and the results of therapy disappointing. Although primary symmetric hypertrichosis is rare, it is often confused with hirsutism, leading to evaluation for adrenal gland disorders. We have examined the features and courses of children with excessive hair growth unrelated to systemic disorders or the use of medications. Four patients had primary generalized hypertrichosis and 7 had localized symmetric hypertrichosis (Table 1).

Acquired generalized hypertrichosis, especially that related to medication usage, is much more common and must be differentiated from primary causes of generalized hypertrichosis (for differential characteristics, Table 2). Several drugs are well known to cause significant generalized hypertrichosis, particularly oral minoxidil, diazoxide, phenytoin sodium, and cyclosporine. Each drug may show a unique distribution of increased hair growth, for example, minoxidil causes hypertrichosis primarily involving the face, shoulders, and extremities. In addition, medications such as oral contraceptives, systemic corticosteroids, and occasionally other drugs such as psoralens and streptomyacin sulfate, may increase hair growth, although not to the extent usually seen with minoxidil, diazoxide, phenytoin, and cyclosporine. Discontinuation of drug use leads to eventual resolution of this cosmetic adverse effect. Should drug regimen discontinuation not be an option, common methods of hair removal such as depilatory agents and shaving may be used.

Children with generalized hypertrichosis, known as hypertrichosis lanuginosa congenita (MIM: 145700, 307150), have a remarkable amount of long vellus hair on the entire body surface, sparing only nonhair-bearing areas, including the mucosae, palms, soles, prepuce, and glans penis. The blonde to black hair may be present at birth or develop during infancy. In some patients, hair will be spontaneously lost during childhood; in others, it will remain into adulthood. Associated abnormalities are rarely described but may include congenital glaucoma, skeletal abnormalities, and missing teeth. Most cases are autosomal dominant but there are also reports of X-linked dominant and autosomal recessive inheritance patterns.

Generalized hypertrichosis has also been associated with gingival hyperplasia as a distinct entity. Children with gingival fibromatosis with hypertrichosis (MIM: 135400) generally have excessive body and facial hair in an identical distribution to hypertrichosis lanuginosa. The hypertrichosis is often present at birth or develops during early infancy, but in up to half of the reported cases, the hypertrichosis begins during puberty. Some reports have described terminal hair, compared with the lanugo hair of classic congenital hypertrichosis lanuginosa, in this group of patients. Inheritance is autosomal dominant and the pathogenesis is unknown. Some cases have been associated with mental retardation and/or seizures. Gingival hyperplasia is usually noted when teeth fail to appear on schedule and, thus, usually following the observation of hypertrichosis. The gingivae are described as pink, firm, pebbly or nodular in appearance, and sometimes with "orange peel" stippling. There are no other associated dermatological features. Complications in these patients include interference with chewing, respiration, and speech. Failure of the teeth to erupt may be associated with periodontal abscesses. Patients may require surgical debulking of the gingivae to help preserve teeth and function, but recurrence is inevitable, requiring repeated procedures.

The 7 other patients described in this article encompass the spectrum of localized symmetrical hypertrichosis (MIM: 139600, 239840), including hypertrichosis cubiti, anterior cervical hypertrichosis, posterior cervical hypertrichosis, and lumbosacral hypertricho-
sis. In patients with hypertrichosis cubiti or “hairy elbows syndrome,” lanugo hairs are present symmetrically at birth or develop during infancy on the extensor surfaces of the elbows, extending from midhumerus to midforearm. This uncommon form is usually not associated with other anomalies and most frequently only represents a cosmetic problem. There have been isolated case reports of hypertrichosis cubiti associated with short stature. In patients with anterior cervical hypertrichosis, the patch of hair is at the sternal notch and lower anterior aspect of the neck. The mode of inheritance is most likely autosomal recessive. Although usually an isolated finding, anterior cervical hypertrichosis may be associated with peripheral sensory and motor neuropathy (MIM: 239840) as an autosomal recessive trait.24 One case report describes a boy with anterior cervical hypertrichosis from early infancy, associated with developmental delay and peripheral neuropathy. In posterior cervical hypertrichosis, the excessive hair overlies the cervical vertebrae. It has been described as an X-linked or autosomal dominant trait. Posterior cervical hypertrichosis has been associated with underlying kyphoscoliosis (MIM: 117850) as an autosomal dominant disorder. Lumbar-sacral hypertrichosis or faun tail deformity is localized to the sacral midline. A variety of concurrent cutaneous malformations such as sacral dimple, lipoma, hyperpigmentation, port-wine stain, or dermoid cyst have been described in association. This developmental defect often overlies bone and spinal cord defects, most commonly spina bifida occulta and diastematomyelia. If undetected and uncorrected surgically, complications may ensue with advancing age. As the vertebral column grows disproportionately with respect to the spinal column, fibrous bands that connect the skin to the spinal theca pull on the spinal theca and may result in neurologic abnormalities. The most common defects are foot drop, nocturnal enuresis, and backache, sometimes developing as late as adolescence or adulthood. Computed tomographic and/or magnetic resonance imaging myelography are diagnostic. Early surgery is particularly critical with diastematomyelia associated with spina bifida.

**MANAGEMENT OF HYPERTRICHOSIS**

Long-term removal of unwanted hair is a challenge. The need for treatment depends on the degree of hypertrichosis and the psychosocial needs of the child. Even in exceedingly hairy newborns and young children, some hair removal may be necessary to alleviate problems the family and society may have in accepting the child. The current available treatment methods for removal of excessive hair include bleaching, trimming, waxing, physical and chemical depilatories, electrolysis, intense pulsed light therapy, and laser hair removal.
Bleaching is a quick, easy, and painless process that removes natural hair pigment partially or totally, lightening the hair to a yellowish hue.\textsuperscript{34} The active ingredient is hydrogen peroxide, which softens and oxidizes the hair. Bleaching can last up to 4 weeks. This method is best for use on light-skinned children because yellow bleached hair may emphasize the increased hair when viewed against the skin of more darkly pigmented children. Occasionally, bleeding results in skin irritation.

Trimming of the hair is a recommended option for young children with either localized or diffuse hypertrichosis. Trimming involved areas will make the hair less noticeable and will not result in acceleration of hair regrowth.

Physical depilation includes tweezing or plucking, shaving, and waxing.\textsuperscript{35} Tweezing is an effective temporary hair removal method, but it is a slow, tedious, and painful process. This temporary method only tears off anagen hair bulbs in varying break patterns allowing for regrowth of the hair follicles. Complete removal of the follicular bulb including both the matrix epithelium and papilla rarely occurs.\textsuperscript{36} For childhood hypertrichosis, plucking may be a feasible option for patients with very localized areas of increased hair growth but too demanding for diffuse hair growth. Adverse reactions include hyperpigmentation, folliculitis, scarring, ingrown hairs, and distorted follicles.\textsuperscript{37} The results of depilation can last up to 4 weeks, but in our experience have been particularly transient in these patients with hypertrichosis, leading to rapid hair regrowth within a week or two. Shaving does not affect the width or rate of regrowth of individual hairs,\textsuperscript{38} but the hairs as they grow out are thicker and more coarse, without the finer tapered end of unshaven hair. Shaving is not recommended because the diameter of the cut hair at the surface is greater than that of the uncut tapered hair. As a result, daily shaving must be undertaken or the cosmetic result is worsened. Certain areas of excessive hair, such as the legs, may be amenable to daily shaving. Males also have the option of shaving excess hair on the beard and mustache regions, but this may be unacceptable psychologically for women. Although dry or electric shaves are not as close as wet shaves, a dry electric razor has been effectively used to treat generalized hypertrichosis during the neonatal period.\textsuperscript{33}

Wax epilation is a painful process for the removal of fine vellus hair. Waxing methods are used with cold, warm, or hot wax. A soft regrowth occurs within 4 to 6 weeks. All areas of the body, excluding genital regions, can be treated with waxing methods. Waxing causes greater discomfort and is more expensive than shaving. Other possible adverse effects include skin irritation and folliculitis.\textsuperscript{39} Another drawback of this epilating technique includes the requirement for the hair to be a minimum length of 2 to 3 mm to be grasped by the wax. Therefore, no other hair removal methods may be used for several days prior to waxing.\textsuperscript{40} This physical depilatory method is too painful and traumatic for use on children but may be an option for older adolescents.

Chemical depilatories contain sulfides, thioglycolates, and enzymatic depilatory agents. They break down hair by cleaving its cysteine linkages\textsuperscript{37} and cause minimal damage to the underlying skin. Sulfides are quick, easy, and effective, but the generated hydrogen sulfide releases an unpleasant odor and can often irritate the skin. Most commercially available chemical depilatories, as a result, consist of thioglycolates. Thioglycolates are less odorous and less irritating, but take a longer time to act than the sulfides. They can be used in less sensitive areas, such as the face and work best on fine vellus hair. Enzymatic depilatory agents do not have the offensive odor and are nonirritating, but they are not effective.

The use of chemical depilatories is limited because of several disadvantages: (1) they are only suitable for small areas, (2) they are associated with a risk of allergic contact dermatitis, (3) their application is messy, (4) they have an unpleasant odor, and (5) they are relatively expensive, especially if treating larger areas. The localized irritation is a well-known potential adverse reaction to chemical depilatories. Additional adverse effects from use of thioglycolates, as in permanent wave products and straighteners, include allergic contact dermatitis and, with inadvertent eye contact, corneal alkali burns.\textsuperscript{41-44} To minimize the risk of local irritation, it is prudent to apply the chemical depilatory to a test site first, adhere to the recommended time limitations, wash the treated area thoroughly, and follow application with use of a moisturizer.\textsuperscript{45,46}

Children with more extensive hypertrichosis must limit treatment with chemical depilatories to localized sites because of the additional (theoretical) risk of systemic thioglycolate absorption and toxic reactions. Data are lacking on the potential adverse reactions from accidental ingestion of thioglycolates or on systemic toxic reactions from local application; however, parenteral administration of large amounts of thioglycolates in rats leads to increased lacrimation, increased intestinal peristalsis, convulsions, and respiratory failure with death.\textsuperscript{47-49}

Permanent hair removal methods, such as electrolysis and laser therapy, have not been studied in prepubertal children, and their use has been limited in older children and adolescents. Both are costly alternatives. Electrolysis, a permanent hair removal technique, can be accomplished by 1 of the 3 following methods: galvanic, thermolysis, and blend.\textsuperscript{37} In galvanic electrolysis, a direct electric current is delivered to the hair follicle through an inserted needle. The current produces sodium hydroxide, which acts as a caustic agent to destroy the hair bulb and dermal papilla. This modality is the most effective, but the slowest. In thermolysis, a high-frequency alternating current produces heat in the follicular tissue causing destruction of the hair bulb. This method is quick, requiring only a few seconds per hair, but not as effective in thick hairs or in highly curved hair follicles. The blend method combines galvanic electrolysis and thermolysis; it is the most efficient electrolysis technique. The best result occurs if the area is shaved several days before epilation so that only anagen hairs are epilated. Permanent hair removal can occur only if the needle is inserted deep into the follicle, enabling the current to travel to the germinative bulb. Hair is not an electrical conductor and cannot transmit an electrical current to the hair bulb. Therefore, the commercially promoted electric tweezer method does not produce permanent hair removal.\textsuperscript{50}
The main disadvantage of electrolysis is the associated pain. Although preapplication of ice packs or topical anesthetics, such as a eutectic mixture of 2.5% lidocaine and 2.5% prilocaine hydrochloride (Emla Cream; Astra USA Inc, South San Francisco, Calif) or 4% lidocaine (ELA-Max; Ferndale Laboratories Inc, Ferndale, Mich) may decrease discomfort, electrolysis is poorly tolerated in children. Other adverse effects include transient postinflammatory erythema and whealing, bruising, swelling, and, in darker-skinned patients, postinflammatory hyperpigmentation.

Laser therapy and intense pulsed light therapy are the newest available permanent hair removal systems.53-58 These techniques remove unwanted hair through the selective photothermal destruction of melanin-rich structures, thus, entailing light energy absorption in hair follicles and minimal absorption by surrounding tissues. This method achieves photothermal destruction of hair follicles while maintaining a low temperature of the surrounding tissue to avoid skin damage. This hair removal system seems to be more effective for darker hair. Treatments result in significant clearance of excess hair, with the neck, chin, and lip as the most common areas of treatment. Occasionally, posttreatment erythema, edema, blisters, and hyperpigmentation occur. Lasers capable of hair removal include ruby, diode, Nd:YAG, and Alexandrite.57,58 As with traditional electrolysis, laser electrolysis is uncomfortable for children, which limits its usefulness.

A promising novel treatment for retarding excessive hair growth (not removing hair) is efomithine cream, which irreversibly inhibits ornithine decarboxylase, an enzyme present in hair follicles that is important in hair growth.59,60 Twice daily application of 15% efomithine hydrochloride cream reduced excessive, unwanted facial hair compared with vehicle treatment. Local irritation, characterized by burning, stinging, and/or tingling, occurred more frequently in efomithine-treated patients.61 Studies to date have involved limited application in adult women; the safety and effectiveness in children have not been established.

**PATHOGENESIS OF HYPERTRICHOSIS: POSSIBLE CANDIDATE GENES**

The regulation of hair cycling is not completely understood. The hair growth cycle is defined as having 3 phases: anagen, the stage of follicular regeneration and growth; catagen, the stage in which cell proliferation ceases and the hair follicle shortens; and telogen, the stage during which the hair is shed. The abnormal hair growth patterns found in patients with hypertrichosis are not caused by abnormal hair shaft formation, but are probably due to delayed anagen termination. While the underlying mechanism of hypertrichosis is unclear, the cloning of several genes that affect hair growth, and the availability of mouse models provide a variety of candidate genes for study.

The angora (go) gene has been shown to have a regulatory function in hair growth. The go/go recessive mutation62 produces abnormally long hair in mice by delaying the transition between anagen and catagen hair. In these mutant homozygotes, anagen VI, the last stage of anagen in which the hair elongates and protrudes through the skin, is approximately 50% longer than in heterozygotes or wild-type mice. This mutation does not affect other stages of the hair cycle or produce any structural abnormalities. The angora gene has been shown to be a mutant allele of fibroblast growth factor 5, a signaling molecule that is localized to the outer root sheath of the lower one third of the hair follicle,63 only during mid to late anagen VI. No human homologue for the angora mouse has yet been found. Keratinocyte growth factor, also known as FGF7, has also been shown to stimulate proliferation and differentiation of early progenitor cells within hair follicles and sebaceous glands.64 The absence of FGF7 in a knockout mouse model led to a greasy or matted rough hair coat.65 The phenotypic result of excessive expression of or mutations in keratinocyte growth factor in humans is unknown. Understanding the molecular nature of the signals of the hair growth cycle will be critical to understanding the mechanisms for increased hair growth in generalized or localized hypertrichosis and may lead to novel therapies.

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