Unusual Hypertrichosis Development on the Skin Involving Erythema Nodosum Migrans

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We describe a 32-year-old Korean woman who presented with a 4-month history of localized hair growth over tender, erythematous to yellowish, indurated large patches on both shins. In the beginning, a tender, coin-sized, violaceous nodule gradually expanded centrifugally and became a yellowish patch being overlaid with hair growth. Histopathological findings from the peripheral erythematous nodules showed a marked widening of the subcutaneous septa, in which lymphohistiocytic inflammatory cells, and multinucleated giant cells had been infiltrated. And there were many granulation tissue-like capillary proliferations which were strongly positive to CD34 immunostain. We diagnosed the case of localized hypertrichosis in association with erythema nodosum migrans. A possible mechanism of the overgrowth of hair is angiogenesis. (Ann Dermatol 16(3) 113~116, 2004)

Key Words: Localized hypertrichosis, Erythema nodosum migrans, Angiogenesis

Hypertrichosis is the overgrowth of hair on any part of the body beyond the normal variation for a patient's reference group, excluding androgen-dependent hair growth. It can be categorized as generalized or localized, a congenital or acquired form, and may either be an isolated finding or be associated with other abnormalities. An acquired and localized hypertrichosis has been described in variable skin lesions such as Becker's nevus, pretibial myxedema, local inflammation or irritation, orthopedic casts and splints, and topical applications of steroids. However, the localized hypertrichosis in association with erythema nodosum migrans (ENM) is rare. Herein, we describe a case of hypertrichosis associated with ENM and the possible mechanism which induces the overgrowth of hair.

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CASE REPORT

A 32-year-old Korean woman presented with a 4-month history of localized hair growth over tender, erythematous to yellowish, indurated large patches on both shins. A tender, coin-sized, violaceous, indurated nodule was first noticed on the left shin in January 2003, and then the lesion gradually expanded centrifugally and became a yellowish patch with mild tenderness and overlying hair growth. On the margin of the patch, erythematous nodules were persistent. Two months later, a similar lesion developed on the right shin, which followed a similar clinical course. Recently, a new lesion, a tender, erythematous pea-sized nodule, developed on the right ankle. On physical examination, hypertrichosis was observed in the center of the yellowish patches, but no hairs were observed on the normal skin or the ankle lesion (Fig. 1). From past history, there was no evidence of medication or upper respiratory tract infection. Laboratory findings, including total blood cell count, urinalysis by microscope, antinuclear antibodies, anti-streptolysin O (ASO) titer, ESR and a chest X-ray were all revealed as normal. On hormonal study, the levels of thyroid hormones, estrogen, LH, FSH, testosterone, and DHEA were

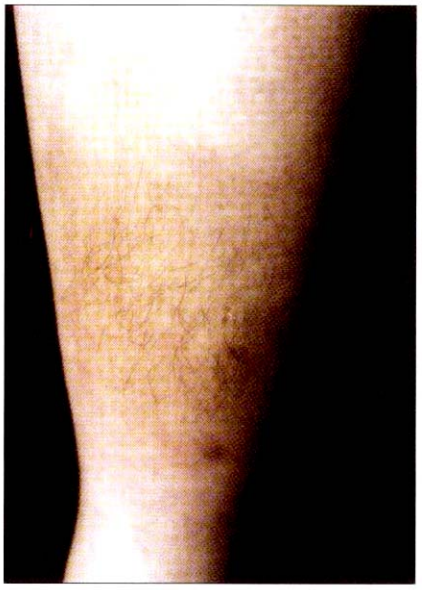

Fig. 1. Hypertrichosis on the leg: an overlying yellowish patch in the center with peripheral erythematous nodules.

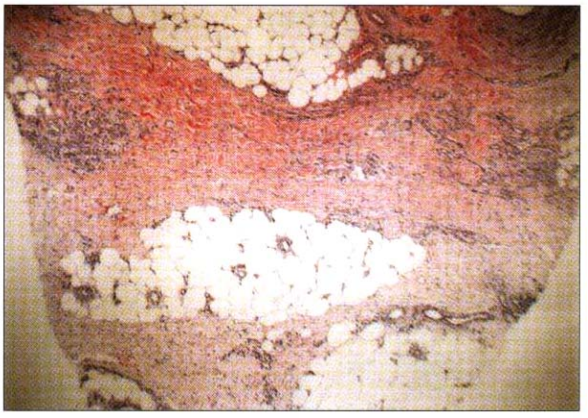

Fig. 2. Markedly widened subcutaneous septa with septal fibrosis, in which lymphohistiocytic inflammatory cells, and multinucleated giant cells were infiltrated (Haematoxylin and eosin; original magnification × 100).

all within normal limits. Histopathological examination of skin biopsy specimens from the peripheral erythematous nodules showed a marked widening of the subcutaneous septa with septal fibrosis, in which lymphohistiocytic inflammatory cells, and multinucleated giant cells were infiltrated (Fig. 2). Also, there were many granulation tissue-like capillary proliferations which were strongly positive to CD34 immunostain (Fig. 3A, 3B). But there was no definite evidence of vasculitis. ENM was diagnosed based on the clinical and histopathological features.

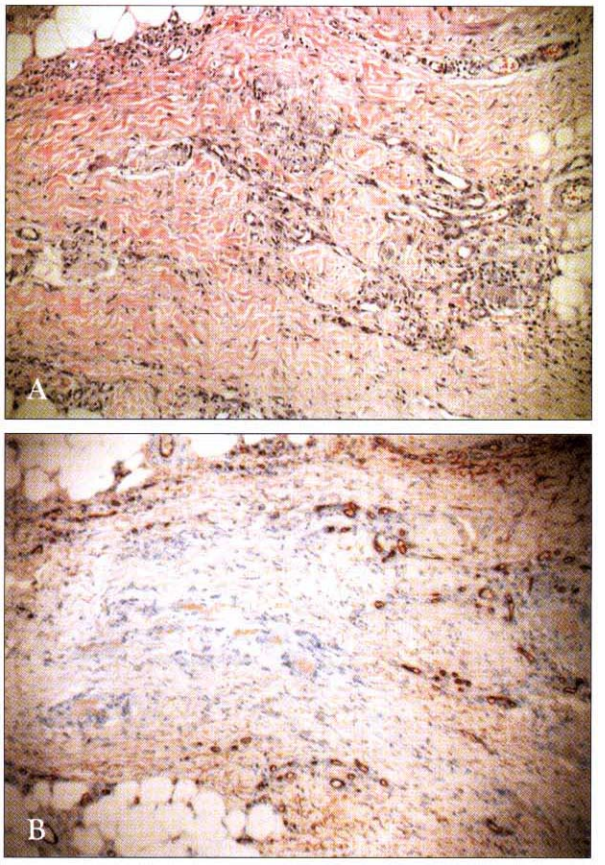

Fig. 3. (A) Many granulation tissue-like capillary proliferations in the septal area (Haematoxylin and eosin; original magnification × 200). (B) Many capillaries in the septal area are strongly positive to CD34 immunostain (Original magnification × 200).

The patient was treated with an oral prednisolone and an intralesional injection of triamcinolone acetonide to the nodular lesions. Two weeks later, hairs fell out on the injection sites, but old patches of hair were persistent.

DISCUSSION

Acquired, localized hypertrichosis may occur in a Becker nevus, or after chronic chemical or mechanical traumas to the skin[1]. Chemically induced dermatitis, such as repeated iodine application, or

psoralen application with UV irradiation, may cause localized hair growth. The excess hair in association with the removal of orthopedic casts is caused by the regional effect of a healing fracture, rather than the occlusive effect to the skin[2]. Localized hypertrichosis also develops in areas of skin subject to friction, patches of lichen simplex chronicus, the shoulders of sack bearers, sites of pruritic insect bites, sites of habitual biting in patients with mental retardation, and skin overlying areas of thrombophlebitis or chronic osteomyelitis. Localized inflammatory reactions after vaccinations, such as smallpox, diphtheria, tetanus, and measles, may also cause hair growth[3].

Erythema nodosum (EN), the most common type of panniculitis, is characterized by symmetric painful erythematous nodules, which become flat and undergo colour changes into a greenish-yellow hue with time[4]. The lesions heal without scar, atrophy or ulceration. EN is associated with many diseases, such as infections, drugs, malignancies, and sarcoidosis[5]. Histopathologically, EN is a mostly septal panniculitis w ith no vasculitis, therefore, the septa of subcutaneous fat is thickened and variously infiltrated with inflammatory cells. The histopathologic hallmark of EN is Miescher's radial granulomas, which consists of small, well-defined nodular aggregates of small histiocytes around a central stellate or banana-shaped clefts[6].

As clinical variants of EN, ENM, subacute nodular migratory panniculitis, and chronic EN have been reported. There is controversy over the nature of ENM, since Bavferstedt first described it[7]. Prestes et al[8]. reviewed 58 cases of septal granulomatous panniculitis; 14 cases of ENM and 36 cases of chronic EN. Histopathologically, ENM was characterized by markedly thickened and fibrotic septa, granulation tissue-like capillary proliferation, and a massive granulomatous reaction with giant cells. On the other hand, chronic EN showed mild septal change, little fibrosis, and lymphohistiocytic perivascular inflammation with only a focal granulomatous reaction. Clinically, ENM showed a limited number of nodules with a peripheral migratory tendency, which was not a feature of chronic EN. Recently, ENM, subacute nodular migratory panniculitis, and chronic EN are regarded as clinical variants of EN, and may be included within the spectrum of EN[9]. ENM differs from acute EN in clinical manifestations, such as persistent course, peripherally expanding lesions, a tendency to unilateral distribution, and a lesser degree of tenderness[10]. In this case, the patient had only 3 scattered lesions with migratory tendency, as their centers were flattened but the margins were still nodular. Histopathologically, there were numerous capillary proliferations and giant cells without Miescher's radial granulomas in the thickened septal area. This was compatible with ENM. With clinical and histpathological features, we confirm this case as ENM with localized hypertrichosis.

There are two major mechanisms of hypertrichosis[1]. One is the vellus-to-terminal switch, the conversion of vellus to terminal hairs[11]. The other is an alteration in the hair-growth cycle. Longer hair is caused by a prolonged anagen phase, while greater hair density is caused by a decrease in hair shedding due to the low percentage of telogen follicles. Therefore, when follicles spend longer in the anagen phase compared to other areas, localized hypertrichosis can be induced. An intrinsic growth pattern of hairs is also influenced by systemic hormones, such as androgens, thyroid, and growth hormones. Local irritation and inflammation induce abundant and localized arterial hyperemia, which can provide plenty of nutrition to stimulate the affected follicles[12]. Mecklenburg et al[13]. reported that angiogenesis, the growth of new capillaries from preexisting blood vessels, is a physiologic event in normal postnatal murine skin, and appears to be required for normal anagen development. In our case, there was no history of any medication, hormonal changes or scratching of the lesions to induce hypertrichosis. From the histopathological findings that numerous capillaries were developed as grouped and scattered patterns in widened subcutaneous septa, we assume that hypertrichosis is caused by increased angiogenesis, which prolongs the anagen phase of ENM lesions, and changes the hair-growth cycle.

This case shows that acquired, localized hypertrichosis can be induced by ENM, and maybe due to increased angiogenesis.

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