Eccrine Angiomatous Hamartoma: A Review of Ten Cases

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Background: Eccrine angiomatous hamartoma (EAH) is a rare benign nodular lesion characterized by the proliferation of eccrine and vascular structures, generally capillaries, in the middle and deep dermis. It may be congenital or appear later in childhood, but rarely arises in adulthood. Objective: To investigate the clinicopathologic features of EAH in Korean patients. Methods: Ten cases of EAH diagnosed at Ajou University Hospital and Gangnam Severance Hospital in Korea from 2007 to 2010 were retrospectively reviewed. Results: The age range of patients was between 5 and 66 years with an equal number of male and female patients. Apart from two congenital cases, the onset was late, ranging from 6 months to 65 years of age. All lesions were solitary and located on the distal extremities. Nine cases appeared as a yellow-brown nodule or plaque resembling a callus. Neither hyperhidrosis nor hypertrichosis was documented. Apart from the typical histological findings of EAH, prominent mucin deposition, fat component and nerve infiltration were observed. Conclusion: This is one of the largest single case series of EAH in the literature. Clinically, resemblance to callosities and the frequent occurrence in the adulthood were the unique features in our series. (Ann Dermatol 25(2) 208~212, 2013)

INTRODUCTION

Eccrine angiomatous hamartoma (EAH) is a benign nodular or plaque-like tumor of hamartomatous nature characterized by the proliferation of eccrine and vascular structures. It generally arises at birth or later in childhood, with a few reports of puberty- or adult-onset lesions, as solitary or multiple lesions affecting mainly the distal extremities. Hyperhidrosis and/or pain may be apparent and sometimes, hair follicles are associated with this lesion and hypertrichosis may be present. Histologically, it consists of proliferation of hyperplastic eccrine glands in association with foci of dilated capillaries at the dermosubcutaneous level. It is a rare entity and only 17 cases have been reported in Korea. We studied 10 cases of EAH diagnosed at Ajou University Hospital and Gangnam Severance Hospital in Korea from 2007 to 2010, one of the largest single case series in the literature.

MATERIALS AND METHODS

Ten cases of EAH diagnosed at Ajou University Hospital and Gangnam Severance Hospital in Korea from 2007 to 2010 were included in this study. From the retrospective review of medical records, the patients’ sex and age as well as the age of onset, location, and symptom, appearance of the lesion, and the mode of treatment were investigated. H&E stained slides from formalin fixed-paraffin embedded tissue blocks were reviewed for histopathological evaluation. Where mucin deposition was suspected, alcian blue staining at pH 2.5 was conducted.
Apart from two cases where the paraffin embedded blocks unavailable, immunohistochemical staining was performed with the following antibodies: D2-40 (1:50 dilution, Cell Marque, Rocklin, CA, USA) for visualization of lymphatics, S-100 protein (1:200 dilution, Thermo Scientific, Fremont, CA, USA) for eccrine structures and neural components and factor VIII-related antigen (1:100 dilution, Thermo Scientific) for delineation of vascular structures.

RESULTS

The clinical features of the patients are summarized in Table 1. The age range of patients was between 1 and 66 years (median age, 11 years) and there were an equal number of male and female patients. While two cases were congenital, others showed a late onset, ranging from 6 months to 65 years of age. Six cases developed before adolescence, and the remaining four cases had an adult onset. All of the lesions were solitary and located on the distal extremities. Nine cases appeared as a yellow-brown nodule or plaque (Fig. 1), and one case presented as a bluish nodule (Fig. 2). Three patients complained of pain and four complained of mild tenderness. In contrast to previous reports and the nature of the lesion, neither hyperhidrosis nor hypertrichosis was documented in our series. The histopathological findings were similar in all patients and were typical of EAH, exhibiting proliferation of mature eccrine and vascular structures (generally capillary) in the middle or deep dermis with normal appearing epidermis (Fig. 3, 4). There was one case showing a significant mucin deposition between eccrine coils beyond the normal extent, further confirmed by alcian

Table 1. Clinicopathological features of the patients

| Number | Sex | Age (yr) | Location | Age at onset | Symptom | Morphology    | Color     | Size (mm) | Treatment | Other features    | D2-40 | Factor VIII |
|--------|-----|----------|----------|--------------|---------|---------------|-----------|-----------|-----------|------------------|-------|-------------|
| 1      | M   | 1        | Rt. palm | 6 mo        | X       | Nodule        | Yellowish | 8 × 6     | Excision  | −                 | +     |             |
| 2      | M   | 4        | Rt. 2nd finger | 3  yr     | Tenderness | Nodule    | Brown     | 7 × 5     | Excision  | −                 | +     |             |
| 3      | F   | 5        | Lt. heel | Birth       | Tenderness | Nodule    | Yellowish | 10 × 8    | Excision  | −                 | +     |             |
| 4      | M   | 8        | Lt. foot | 6 yr        | Pain     | Nodule      | Yellowish | 10 × 8    | Excision  | −                 | +     |             |
| 5      | F   | 10       | Rt. sole | Birth       | Tenderness | Plaque    | Brown     | 15 × 10   | Excision  | Mucinous stroma  | −     | +           |
| 6      | M   | 11       | Lt. 2nd finger | 9  yr     | Pain     | Nodule      | Bluish    | 3 × 3     | Excision  | −                 | +     |             |
| 7      | F   | 29       | Rt. 4th finger | 29 yr    | Tenderness | Nodule    | Bluish    | 3 × 3     | Excision  | Fat component of nerve infiltration | −     | +           |
| 8      | F   | 38       | Lt. 4th finger | 38 yr    | Pain     | Nodule      | Yellowish | 3 × 3     | Excision  | −                 | +     |             |
| 9      | M   | 44       | Lt. 5th finger | 43 yr   | X         | Nodule      | Yellowish | 3 × 3     | X         | NA                 | NA    | NA          |
| 10     | F   | 66       | Rt. dorsum of hand | 65 yr    | X         | Nodule      | Brownish  | 8 × 6     | X         | NA                 | NA    | NA          |

M: male, F: female, Rt.: right, Lt.: left, X: not mentioned, NA: not available.

Fig. 1. A yellow-brown plaque on the right sole, resembling a callus (patient 5).

Fig. 2. A bluish nodule on the left second finger (patient 6).
blue staining. Other interesting features among the cases included the presence of fat component (patient 7) and nerve infiltration (patient 8).

Proliferated blood vessels were present in all specimens by factor VIII-related antigen immunohistochemical staining, while the absence of lymphatic proliferation was confirmed by negative staining against D2-40 antigen. The eccrine apparatus in the specimens were all positive for S-100 protein at a variable intensity. Eight of the patients were referred to the plastic surgery for excision.

**DISCUSSION**

EAH was first described by Lotzbeck in 1859, from an angioma-like tumor on the face of a child. It is a rare cutaneous lesion characterized by the proliferation of multiple eccrine structures and vascular elements. The lesions generally present on an extremity at birth, or appear in early childhood, and commensurably enlarge as the patient grows. However, there is no clear explanation for the predilection for the extremities. They typically present as a solitary brownish or bluish tumor accompanied by pain and/or tenderness, but multiple lesions can occur. The lesion in patient 8 had focal neural infiltration in the dermis, which Challa and Jona suggested as a potential source of the discomfort and pain that accompanies EAH.

A previous article reviewed the characteristics of 15 Korean cases of EAH. The lesions were mostly congenital (9/14, 64.2%), and although hyperhidrosis was frequent (10/15, 66.7%), they could be asymptomatic (5/15, 33.3%) or painful (6/15, 40.0%). A solitary lesion was most common (12/15, 80.0%) and the majority was a nodule (11/15, 73.3%); only three cases presented as a patch.

EAH is known to rarely arise after puberty, although there have been a few case reports of adult-onset disease (Table 2). Interestingly, two fifths of our cases noticed the lesion in the adulthood. One possible explanation could be the absence of symptoms in those particular patients, leading to late discovery of the lesion and obscuring the actual age of onset.

EAH usually lies in the deep dermis and contains increased numbers of eccrine structures and numerous capillary channels surrounding or intermingled with the eccrine structures. The histologic criteria for EAH may include hyperplasia of normal or dilated eccrine glands; close association of the eccrine structures with capillary angiomatous foci; and the variable presence of pilar, lipomatous, mucinous, and/or lymphatic structures. In our series, pilar structures were not seen, whereas single cases...
showing lipomatous, mucinous and neural components were present. These hamartomatous components contribute to the external features of EAH, such as hyperhidrosis and hypertrichosis. However, neither of the symptoms was observed in our patients. Since the largest lesion in our series barely reached 15 mm in diameter, the effect of increased eccrine glands, i.e. hyperhidrosis, would not have been noticeable to the patient.

In previous immunohistochemical studies of EAH, the vascular elements stained positively for *Ulex europaeus*-1 and factor VIII-related antigens. The vessels were negative for glucose transporter-1 protein, supporting the hamartomatous nature of the lesion over hemangioma. In our study, the vascular nature, rather than lymphatic, of the proliferated luminal structures in the dermis was confirmed by positive staining of the endothelial cells against factor VIII-related antigens and absence of D2-40 stained cells. The secretory portions of the eccrine glands were positive for S-100 protein, carcinoembryonic antigen, epithelial membrane antigen, and Cam5.2. The ductal components stained positively for carcinoembryonic antigen and cytokeratin 1 and weakly positive for epithelial membrane antigen. These antigenic expressions were qualitatively diminished in some cases but remained comparable to normal structures. Mitotic figures and cytologic atypia have not been observed. In summary, our cases were typical of EAH in histopathology, demonstrating proliferation of eccrine and vascular structures. However, the frequent occurrence in the adulthood and absence of symptoms may distinguish our series from previous reports. Also, the close resemblance to callus in our series warrants skin biopsy whenever the diagnosis is doubtful.

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