Angiolymphoid Hyperplasia With Eosinophilia Developing on an Antecedent Welding Burn: A Case Report

Hui-Wen Tseng,[1,5] Sou-Hsin Chien,[2] Chieh-Shan Wu,[1] Hui-Hwa Tseng,[3] and Chih-En Tseng[4]
Departments of [1]Dermatology and [3]Pathology and Laboratory Medicine, Kaohsiung Veterans General Hospital, [5]Department of Cosmetic Applications and Management, Yuh-Ing Junior College of Health Care and Management, Kaohsiung; and Departments of [2]Plastic Surgery and [4]Anatomic Pathology, Buddhist Dalin Tzu-Chi General Hospital, Chiayi, Taiwan.

Angiolymphoid hyperplasia with eosinophilia (ALHE) describes a group of benign anomalous vascular hyperplasias which consist of epithelioid-like endothelial cells attached to dilated blood vessels, and infiltration of inflammatory cells, predominantly lymphocytes and some eosinophils. Here, we describe a healthy 34-year-old man, who had 10 well-defined, non-tender, red-to-brownish papules and subcutaneous nodules of 0.3–1.0 cm in diameter on his left forearm. The lesions started to appear about 4 months after an earlier electric welding rod burn had healed. The histopathologic diagnosis of the lesions was ALHE. Because the new lesions developed progressively and malignancy could not be excluded, the patient underwent a wide elliptical excision and received a split-thickness skin graft from his left thigh. His postoperative recovery was successful and has showed no evidence of recurrence after 5 years of follow-up. The forearm is an unusual site for ALHE; the antecedent burn was the key trigger for ALHE onset in this case.

Key Words: angiolymphoid hyperplasia with eosinophilia, electric burn
(*Kaohsiung J Med Sci* 2010;26:266–70)

Angiolymphoid hyperplasia with eosinophilia (ALHE) is a term used to describe a group of benign anomalous vascular hyperplasias which consist of epithelioid-like endothelial cells attached to dilated blood vessels, and infiltration of inflammatory cells, predominantly lymphocytes and some eosinophils. Preceding injury-related ALHE is not common, particularly when the injury is a burn. We present a 34-year-old man with multiple ALHE lesions that developed on his left forearm in a area corresponding to a earlier welding rod burn.

Case Presentation

A 34-year-old man presented with 10 well-defined, non-tender, red-to-brownish papules and subcutaneous nodules of 0.3–1.0 cm in diameter on an unusual site, his left forearm. He was otherwise healthy. The lesions had developed on the skin of a wound that had previously healed and which was the result of an electric welding rod burn at work. The papules and nodules developed progressively over approximately 4 months after the burn wound had healed until he underwent an excisional biopsy. The first diagnosis by histopathology was ALHE with focal endothelial

Received: Jun 12, 2009 Accepted: Sep 4, 2009
Address correspondence and reprint requests to: Dr Chih-En Tseng, Department of Anatomic Pathology, Buddhist Dalin Tzu-Chi General Hospital, Chiayi, Taiwan, or 2 Minsheng Road, Dalin Township, Chiayi County, 622, Taiwan.
E-mail: p121521@gmail.com

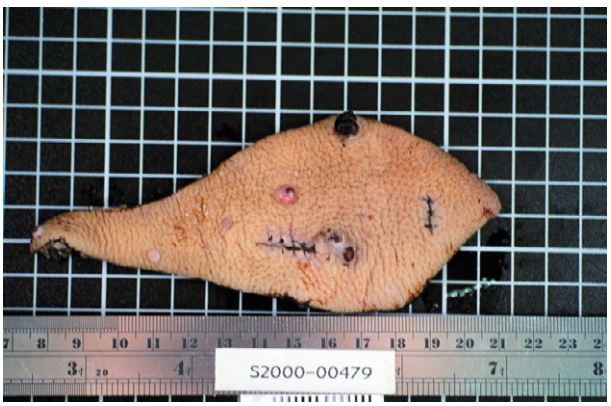

Figure 1. *Grossly, the wide elliptical excised specimen (14 × 6 cm) showed 10, separated, red-to-brownish papules, each measuring about 0.3–1.0 cm in diameter, located on the healed welding burn area.*

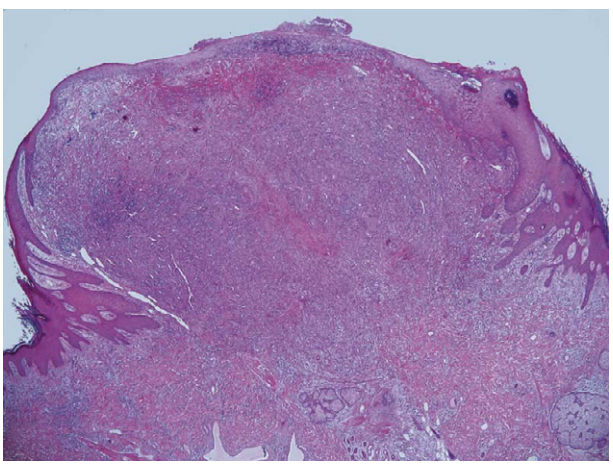

Figure 2. *The histopathologic specimen showed intradermal nodular proliferation of dilated blood vessels and mixed inflammatory infiltration (hematoxylin and eosin; original magnification, 20×).*

cell atypia. Because new lesions developed progressively and malignancy could not be excluded, the patient agreed to undergo a wide elliptical excision to simultaneously remove all of the cutaneous tumors (Figure 1). The resulting skin defect was covered with a split-thickness skin graft harvested from the patient's left thigh. The recipient and donor sites healed well after surgery. No lymphadenopathy was detected, including in the examination of the left axillary area, and the complete blood cell count was normal. The patient's postoperative recovery was successful and has been free of lesion recurrence after more than 5 years of follow-up.

The histopathologic features of the first and second specimens on hematoxylin and eosin stain were

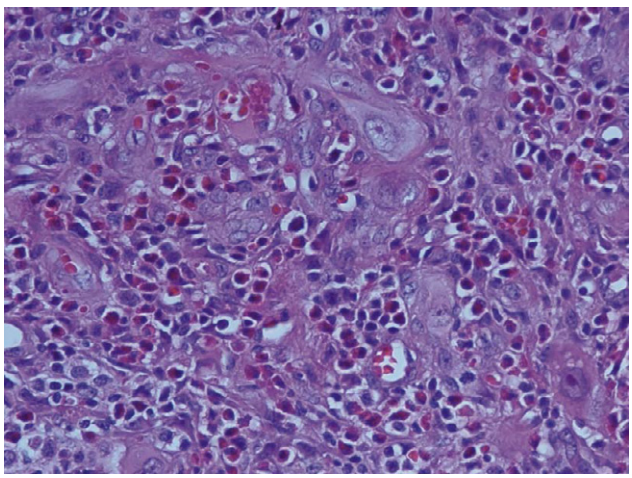

Figure 3. *Microscopic views of the biopsy specimen. The proliferated vessels had varying luminal diameters, prominent plump endothelial cells with copious eosinophilic vacuolated cytoplasm, and prominent nuclei displaying an epithelioid pattern. Many inflammatory cells, including lymphocytes and eosinophils, have infiltrated this nodular lesion (hematoxylin and eosin; original magnification, 400×).*

similar. Histopathology revealed a dome-shaped papule with a well-circumscribed intradermal nodular pattern of proliferative vascular channels (Figure 2). Similar nodular proliferative vascular channels were also located in different levels of the dermis or subcutaneous tissue in a different specimen. The epidermis had slight acanthosis, and the skin appendages were unaffected. The vessels had varying luminal diameters, and were mostly lined by large rounded or focal spindle endothelial cells. The plump endothelial cells, with copious eosinophilic cytoplasmic vacuoles and prominent nuclei, had an epithelioid pattern and a tombstone-like appearance. Many inflammatory cells, predominantly lymphocytes, histiocytes and eosinophils, had infiltrated to this nodular lesion (Figure 3). Immunohistochemical staining revealed that these epithelioid cells strongly expressed Factor VIII antibodies.

After careful examination of these two specimens, we found that the endothelial cells lining the proliferative vascular channels had protruded bizarre nuclei and prominent nucleoli. These global pathologic findings did not fully support the diagnosis of angiosarcoma or retiform hemangioendothelioma but rather supported ALHE.

We attempted further identification of histologic evidence supporting the relationship between the ALHE and the preceding injury. First, there were some

thick hyaline-like fibrotic collagen strands and circumscribed fibrous septa surrounding the lobular proliferative vessels and many dilated capillaries were surrounding them, but no vasculitis was found. Second, in some of the papules, the shape of endothelial cells did not have the typical epithelioid appearance as in ALHE, instead showing a granulation-like structure. One of the ALHE lesions was found just outside one mildly damaged median-sized muscular vein in the subcutaneous tissue. The infiltration of inflammatory cells, including lymphocytes, was found outside the vessel wall of this mildly injured muscular vein.

Discussion

ALHE was originally described by Wells and Whimster as a subcutaneous lesion in 1969 [1]. Histologically, ALHE is a term used to describe a group of benign anomalous vascular hyperplasias with dilated blood vessels and infiltration of inflammatory cells, particularly lymphocytes and eosinophils. Epithelioid hemangioma, describes the presence of endothelial cells with normal (epithelioid) appearance and abundant eosinophilic, sometimes vacuolated, cytoplasm.

The head and neck region is the major location of ALHE. Other, rarer, locations include the skin of the upper extremities, axillary area, inguinal area, mouth, tongue, parapharyngeal space, lung, breast, colon, lymph node, bone, nerve, arteries, ovaries, and testis. However, the forearm is an unusual location for ALHE and, before now, only five other published cases of ALHE located on the skin of the forearm have been reported [2–6].

The precise pathogenesis of ALHE is still unclear and it is unknown whether it is a true vascular neoplasm or a reactive process. The reactive process may be secondary to the damage of an artery or vein following injury, environmental factors, infection, hormonal imbalance [7] or immunologic dysregulatory mechanisms [8].

ALHE with preceding history of injury has been documented in numerous cases and two studies have attempted to clarify whether injury plays a role in the pathogenesis of ALHE [9,10]. In 1985, Olsen and Helwig reported that, of 116 cases, 10 patients had a previous history of injuries, including blunt trauma, frictional trauma, laceration, frostbite, incision and drainage, and otitis externa [9]. The period between the injury and the onset of the lesions ranged from 7 months to 20 years, with a median interval of 30 months. Mitotic figures were present in angiogenic foci with a frequency of 1 in 20 high-power fields, but anaplasia and atypical mitosis were not found [9].

In 1991, Fetsch and Weiss suggested that a significant percentage of ALHE lesions might arise on a reactive basis and they were probably secondary to a damaged and repaired artery or vein based on histopathologic evidence [10]. Damaged vessel walls, including fragmented elastic lamina, fibrointimal proliferation, and/or disruption of the muscular wall were also reported. The authors reviewed 96 cases and antecedent injury was documented in 12 cases, while the lesions in 60 cases arose from or were adjacent to a damaged medium-sized artery (37 cases) or vein (23 cases) [10].

ALHE lesions on the wrists and forearms, probably as a result of injury, have been recorded in one patient [2]. This patient was a man who sustained a crush injury on his left hand and wrist while cutting and forming plastic sheets at work. ALHE lesions developed just 2 months after the injury.

Busquets and Sanchez reported another case with a history of injury where ALHE lesions were found on the patient's scalp [11]. The first lesion developed at the same site that the patient had accidentally hit his head against a filing cabinet 2 years previously. Multiple new lesions developed slowly around the original nodule after excision of the first lesion and an arteriovenous malformation was detected on angiography. The patient was treated with embolization, which led to partial resolution.

In terms of the pathogenesis of ALHE, it has been proposed that elevated rennin and angiotensin II levels stimulate new vessel formation in ALHE [12]. The levels of eosinophilic cationic protein and interleukin-5 were also shown to be correlated with the clinical course of ALHE [13]. A study of the microcirculatory system suggested that the lack of periendothelial cells along the proliferative vessels might partially explain the angiogenesis seen in ALHE [14].

During the wound repair process after a burn, dysregulated reactive angiogenesis processes could play an important role in ALHE development. In a susceptible person, nonspecific injury might stimulate the proliferation of the vascular endothelium, particularly in an area with abundant blood supply. The proliferation of large endothelial cells may result from

the injury stimulus itself, or indirectly by the release of vasoactive metabolites, such as tumor angiogenic factor [7]. Nevertheless, further studies are needed to clarify the mechanism involved in injury-related ALHE.

In conclusion, our patient had 10 red-to-brownish ALHE papules on his left forearm, an unusual site, around the area of an earlier burn caused by an electric welding rod. These lesions developed progressively over approximately 4 months after the original wound had healed, prompting medical treatment. Thus the antecedent burn was the key trigger for ALHE onset in this case. We found histologic evidence to support the relationship between the preceding injury and ALHE. Those histologic findings included the presence of thick hyaline-like collagen strands, which might be the residual scar, fibrous septa surrounding the lobular ALHE, focal endothelial cell atypia, and granulation-like structures in some regions. However, the exact relationship between these histologic features and preceding injury is still unclear and warrants further studies.

References

1. Wells GC, Whimster IW. Subcutaneous angiolymphoid hyperplasia with eosinophilia. *Br J Dermatol* 1969;81:1–14.
2. Morton K, Robertson AJ, Hadden W. Angiolymphoid hyperplasia with eosinophilia: report of a case arising from the radial artery. *Histopathology* 1987;11:963–9.
3. Dannaker C, Piacquadio C, Willoughby C, et al. Histiocytoid hemangioma: a disease spectrum. *J Am Acad Dermatol* 1989;21:404–9.
4. Arnold M, Geilen CC, Coupland SE, et al. Unilateral angiolymphoid hyperplasia with eosinophilia involving the left arm and hand. *J Cutan Pathol* 1999;26:436–40.
5. Conill C, Toscas I, Mascaro JM, Jr., et al. Angiolymphoid hyperplasia with eosinophilia of the nail bed and bone: successful treatment with radiation therapy. *J Euro Acad Dermatol Venereol* 2004;18:584–5.
6. Macarenco RS, do Canto AL, Gonzalez S. Angiolymphoid hyperplasia with eosinophilia showing prominent granulomatous and fibrotic reaction: a morphological and immunohistochemical study. *Am J Dermatopathol* 2006;28:514–7.
7. Zarrin-Khameh N, Spoden JE, Tran RM. Angiolymphoid hyperplasia with eosinophilia associated with pregnancy: a case report and review of the literature. *Arch Pathol Lab Med* 2005;129:1168–71.
8. Hallam LA, Mackinlay GA, Wright AM. Angiolymphoid hyperplasia with eosinophilia: possible aetiological role for immunisation. *J Clin Pathol* 1989;42:944–9.
9. Olsen TG, Helwig EB. Angiolymphoid hyperplasia with eosinophilia. A clinicopathologic study of 116 patients. *J Am Acad Dermatol* 1985;12:781–96.
10. Fetsch JF, Weiss SW. Observations concerning the pathogenesis of epithelioid hemangioma (angiolymphoid hyperplasia). *Mod Pathol* 1991;4:449–55.
11. Busquets AC, Sanchez JL. Angiolymphoid hyperplasia with eosinophilia induced by trauma. *Int J Dermatol* 2006;45:1211–4.
12. Fernandez LA, Olsen TG, Barwick KW, et al. Renin in angiolymphoid hyperplasia with eosinophilia. Its possible effect on vascular proliferation. *Arch Pathol Lab Med* 1986;110:1131–5.
13. Onishi Y, Ohara K. Angiolymphoid hyperplasia with eosinophilia associated with arteriovenous malformation: a clinicopathological correlation with angiography and serial estimation of serum levels of renin, eosinophil cationic protein and interleukin 5. *Br J Dermatol* 1999; 140:1153–6.
14. Katoh N, Hirano S, Kishimoto S, et al. Microcirculatory segments identified with monoclonal antibody against alpha-smooth muscle actin: comparison between Kimura's disease and angiolymphoid hyperplasia with eosinophilia. *Acta Derm Venereol* 1995;75:15–8.

血管淋巴增生併嗜伊紅球增多症發生於前電焊燙傷癒合處 — 病例報告

曾慧文[1,5] 簡守信[2] 吳介山[1] 曾暉華[3] 曾志恩[4]

高雄榮民總醫院 [1]皮膚科 [3]病理檢驗部

佛教大林慈濟醫院 [2]整形外科 [4]解剖病理科

[5]育英醫護管理專科學校 化妝品應用與管理科

血管淋巴增生併嗜伊紅球增多症是一種良性腫瘤，為不正常的血管增生及擴張，血管內皮細胞呈現類似上皮樣變化，病灶內有許多發炎細胞浸潤，包括淋巴球及相當多的嗜伊紅性球。此報告是有關一位 34 歲健康男性的病例，他的左手前臂有 10 顆直徑約 0.3–1.0 cm 的紅色至褐色丘疹，其位置剛好發生於電焊棒燙傷癒合處，自燙傷癒合、發病、至門診求診，其間約有 4 個月的時間，切除後之病理組織表現為血管淋巴增生併嗜伊紅球增多症。由於持續有新的病灶發生，且因其病理組織表現出局部有細胞核不正常的變化，於是選擇將全部病灶切除，在切除處用取自左大腿的半層皮膚移植片覆蓋，手術後情況相當好，追蹤 5 年之後並無復發跡象。前臂處皮膚並不是血管淋巴增生併嗜伊紅球增多症的典型常見好發處，尤其臨床上發病前有電焊棒燙傷病史是極為罕見的。

關鍵詞：血管淋巴增生併嗜伊紅球增多症，電燒傷病史

（高雄醫誌 2010;26:266–70）

收文日期：98 年 6 月 12 日

接受刊載：98 年 9 月 4 日

通訊作者：曾志恩醫師

佛教大林慈濟醫院解剖病理科

嘉義縣大林鎮民生路二號