Epidemiology and treatment of angiolymphoid hyperplasia with eosinophilia (ALHE): A systematic review

Brandon L. Adler, MD,[a] Aimee E. Krausz, MD,[a] Aurelia Minuti, MLS,[b] Jonathan I. Silverberg, MD, PhD, MPH,[c] and Hadar Lev-Tov, MD, MAS[a]
New York, New York, and Chicago, Illinois

Background: Current knowledge of angiolymphoid hyperplasia with eosinophilia (ALHE) derives from retrospective reports and case series, leading to a nonevidence-based treatment approach.

Objective: We sought to systematically review the literature relating to cutaneous ALHE to estimate its epidemiology and treatment outcomes.

Methods: A literature search of PubMed, EMBASE, Web of Science, and Google Scholar was conducted. Articles detailing cases of histologically confirmed cutaneous ALHE were included.

Results: In all, 416 studies were included in the review, representing 908 patients. There was no sex predominance among patients with ALHE. Mean age at presentation was 37.6 years. There was a significant association between presence of multiple lesions and pruritus, along with bleeding. Surgical excision was the most commonly reported treatment for ALHE. Treatment failure was lowest for excision and pulsed dye laser. Mean disease-free survival after excision was 4.2 years. There were higher rates of recurrence postexcision with earlier age of onset, longer duration of disease, multiple lesions, bilateral lesions, pruritus, pain, and bleeding.

Limitations: Potential for publication bias is a limitation.

Conclusions: Surgical excision appears to be the most effective treatment for ALHE, albeit suboptimal. Pulsed dye and other lasers may be effective treatment options. More studies are needed to improve the treatment of ALHE. (J Am Acad Dermatol 2016;74:506-12.)

Key words: angiolymphoid hyperplasia with eosinophilia; epidemiology; excision; histiocytoid hemangioma; pseudopyogenic granuloma; surgery.

Angiolymphoid hyperplasia with eosinophilia (ALHE) is an uncommon benign vasoproliferative disorder of unclear origin, first described in 1969 by Wells and Whimster.[1] ALHE typically presents with solitary or multiple pink to red-brown dome-shaped papules or nodules occurring most frequently on the head and neck.[2-4] More rarely, lesions may be observed on the trunk, extremities, and genitalia.[5] Extracutaneous cases have been reported, affecting the orbit, oral mucosa, parotid gland, colon, and bone.[3] It is unclear whether ALHE occurs more frequently in male or female individuals and reports in the medical literature are conflicting.[6-11] ALHE may be asymptomatic or may present with pruritus, pain, or spontaneous bleeding.[12] However, little is known about how often symptoms occur in ALHE or whether they have any prognostic value.

From the Division of Dermatology, Department of Medicine,[a] and D. Samuel Gottesman Library,[b] Albert Einstein College of Medicine, New York; and Department of Dermatology, Northwestern University Feinberg School of Medicine, Chicago.[c]
Drs Adler and Krausz contributed equally to this work.
Funding sources: None.
Conflicts of interest: None declared.
Accepted for publication October 12, 2015.

Reprint requests: Hadar Lev-Tov, MD, MAS, Division of Dermatology, Albert Einstein College of Medicine, 3411 Wayne Ave, 2nd Floor, New York, NY 10467. E-mail: lhadar1@gmail.com.
Published online December 11, 2015.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2015.10.011

Although ALHE is a benign condition, treatment is often pursued to provide symptomatic relief and address cosmetic concerns. Surgical excision is commonly used,[2,11] but other treatment modalities and spontaneous resolution have been reported.[11-13] The variety of treatment options attempted probably reflects a knowledge gap in the pathogenesis of ALHE. Its origin has been variously attributed to prior trauma, hyperestrogenemia (eg, pregnancy or oral contraceptive use), infectious agents, atopy, reactive hyperplasia, and benign neoplasia.[2,3,6] Kempf et al[14] postulated that ALHE (or a subset of cases) may represent a $CD4^+$ T-cell lymphoproliferative disorder, rather than a true vascular lesion. There appears to be a high rate of recurrence,[10,15] yet little is known about the predictors of disease recurrence. Given the low incidence of ALHE, there are no reports of large-scale prospective therapeutic trials. As a result, there is a knowledge gap in the therapeutic management of ALHE. Nevertheless, numerous case reports and multiple case series comment on the epidemiology and treatment of ALHE. Given the lack of evidence-based reviews regarding ALHE, we conducted a systematic review of the literature to better characterize the demographic and clinical features of patients with ALHE, approximate the global distribution of cases, determine frequencies and efficacies of treatment interventions, and uncover clinical factors associated with recurrence after treatment.

CAPSULE SUMMARY

- Understanding of the epidemiology and treatment outcomes of angiolymphoid hyperplasia with eosinophilia is limited to retrospective reports and case series.
- This data set suggests surgery, albeit suboptimal, is the most effective treatment for angiolymphoid hyperplasia with eosinophilia.
- Clinicians may consider surgery as first-line therapy for angiolymphoid hyperplasia with eosinophilia but should anticipate about 40% recurrence.

METHODS

Systematic review

We performed a systematic review of the literature following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[16] Systematic literature searches were conducted in PubMed/MEDLINE (1947—February 2014), EMBASE (1973-February 2014), and Web of Science (1985—February 2014) using both Medical Subject Headings terms and key words. For all databases, both controlled vocabulary and text word searches were performed, with no language restrictions. Full search strategy from PubMed is provided in Appendix I (available at http://www.jaad.org). Manual searches of references from retrieved articles and gray literature (eg, abstracts from scientific proceedings) as well as Google Scholar were also performed to identify any additional relevant articles.

Inclusion and exclusion criteria

To accurately characterize both epidemiology and treatment, we included original reports detailing cases of histologically confirmed cutaneous ALHE with or without descriptions of accompanying treatment. We excluded reports lacking unambiguous histologic confirmation of ALHE and reports of noncutaneous (eg, orbital, visceral) ALHE.

Study selection

Two reviewers (B. L. A. and A. E. K.) evaluated titles and abstracts of all identified articles to determine those meeting criteria for full-text review. The two reviewers subsequently applied protocol inclusion and exclusion criteria to full-text articles to identify articles for full-text review. We translated non-English-language articles for full-text review, using Google Translate (translate.google.com). Discrepancies between the reviewers' assessments were arbitrated by another researcher (H. L-T.). There were one English-language article[17] and five non-English-language articles[18-22] with full-text versions that could not be retrieved but had sufficient data in the abstracts and were included in the study.

Data extraction

Two reviewers (B. L. A. and A. E. K.) extracted data from included studies according to protocol-defined criteria. Data items collected were as follows: year of publication; latitude and longitude of location of corresponding author; patient age, sex, and race; disease location(s) and laterality; presence of single versus multiple lesions; maximum lesion dimension; duration of disease; associated symptoms (pruritus, pain, and/or bleeding); treatment(s) used; treatment outcome (complete vs incomplete disease resolution); recurrence after treatment; and time to recurrence. The primary outcome of interest was disease-free survival after treatment. All studies provided disease and outcome data for each patient individually, apart from 3 case series that presented aggregate data only.[6,10,23]