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Classifying discoid lupus erythematosus: background, gaps, and difficulties☆,☆☆,★

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ABSTRACT

To inform our ongoing efforts to develop defining features to be incorporated into a novel set of classification criteria for discoid lupus erythematosus (DLE), we conducted a literature review using the Ovid MEDLINE database. A search was performed to identify studies reporting criteria used to distinguish DLE from other cutaneous lupus erythematosus subtypes. We examined which clinical, histopathologic, and serologic features have data to support their use as effective features in distinguishing DLE from other potential disease mimickers and cutaneous lupus subsets. Through our search, we were also able to identify gaps that exist in the literature which can inform future directions for research endeavors. We found that localization of lesions, characteristic features of damage, and the absence of high titer Ro/SSA antibody seem most effective in differentiating DLE from other cutaneous lupus erythematosus subtypes. Histopathologic features and class of immunoreactant deposition appear to be less helpful.

Introduction

The grouping schema for the set of disorders known as cutaneous lupus erythematosus (CLE) has undergone various iterations throughout the years. Its complicated history has been described in detail elsewhere, but there is no agreement on how best to define and classify CLE (Sontheimer, 1997). Consensus on the current state of CLE definition and classification was expressed in 2013 at the 3rd International Conference on Cutaneous Lupus Erythematosus, where an international group of lupus experts mutually agreed upon the need for better definitions, grouping schema, and classification criteria for CLE variants (Merola et al., 2015).

The results of one study demonstrate the uncertainty that exists over the classification of CLE subtypes. 43% of patients with subacute cutaneous lupus erythematosus (SCLE) were classified with discoid rash, whereas 32% of generalized discoid lupus erythematosus (DLE) patients were classified with psoriasiform and/or polycyclic type lesions (Table 1) (Beutner et al., 1991). Either these patients have overlap between two CLE subtypes or there is some confusion over what a discoid rash really is.

Based upon the results of an initial Delphi questionnaire, a decision was made to begin by developing classification criteria for DLE for use in research endeavors. Since this subtype of chronic CLE is considered one of the most prevalent and readily recognizable forms of CLE because of its resultant scarring, chronic CLE was determined to be a good starting point for the classification of the larger disease state. To inform a consensus on the particular features that serve to best characterize DLE, it is useful to examine the literature for the features that have proven effective in differentiating DLE from other CLE subtypes in prior studies. Although there have been studies investigating the characteristics that distinguish DLE from other CLE subtypes, there is still much-needed research to be done.

This review highlights gaps that exist in the literature to describe future directions for research that might help physicians to better classify this disease. It is our hope that classification criteria will provide investigators with a foundation upon which to base observational and interventional clinical trials, and a common language with which to communicate effectively about this patient population.

Methods

An extensive literature search using the Ovid MEDLINE database was conducted from January 1, 1946, to April 14, 2015. Search terms

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included "discoid lupus erythematosus", "diagnosis", and "classification". Articles in English and pertaining to humans were included. A search of "discoid lupus erythematosus" and "classification" returned 39 articles, of which one was relevant. A search of "discoid lupus erythematosus" and "diagnosis" returned 436 articles, of which nine were relevant (Table 2). Studies included in the review were those that reported on the role of clinical, histologic, or serologic features in the diagnosis or classification of patients with DLE.

Table 2
Summary of literature search results

Terms used	Number of relevant results	Relevant articles
Discoid lupus erythematosus and diagnosis	9	Al-Refu and Goodfield (2010) Walling and Sontheimer (2009) Kontos et al. (2005) Fabbri et al. (2003) Lee et al. (1994) David-Bajar et al. (1992) Jerden et al. (1990) Bangert et al. (1984) Nieboer et al. (1987)
Discoid lupus erythematosus and classification	1	Beutner et al. (1993)

Historical context

Few authors have proposed criteria for the diagnosis of DLE. Fabbri et al. (2003) and Walling and Sontheimer (2009) authored the only two papers to describe characteristics that, if present, might allow physicians to make a diagnosis of DLE (Table 3). The criteria were created as diagnostic criteria derived from the authors' clinical expertise and were not validated. Neither set of authors comment on the number of criteria that must be fulfilled in order to reach a diagnosis of DLE. However, the criteria proposed by these authors serve as a good framework by which to examine the different clinical, histologic, and serologic features that might go into a classification criteria of DLE and to discuss the literature that supports or disproves the incorporation of these features. Although these authors proposed diagnostic criteria, the purpose of the Delphi initiative is to create classification criteria for research purposes. Although we use the diagnostic criteria by these two sets of authors as a framework for our discussion, it is important to recognize that their goals were targeted and may be useful for a different purpose.

Clinical characteristics of DLE activity

Fabbri et al. (2003) and Walling and Sontheimer (2009) describe active DLE as being round, affecting sun-exposed areas, and involving follicular plugging. Walling and Sontheimer (2009) elaborate further on the appearance of the active lesion as being indurated with peripheral scale. David-Bajar et al. (1992) performed a study in 1992 to define features that could help distinguish patients with DLE from those with SCLE. They examined the features of 27 patients—11 with DLE and seven with SCLE—and found localization of lesions on the scalp/face was more prevalent in DLE than in SCLE (David-Bajar et al., 1992). However, a different study found a significantly higher incidence of malar rash in SCLE patients than in those with both localized and generalized DLE (Beutner et al., 1991) (Table 1). Precipitation by sun exposure was less helpful in distinguishing DLE and was more common in patients with SCLE (David-Bajar et al., 1992).

Beutner et al. (1991) presented their results utilizing new criteria developed by the European Academy of Dermatology and Venerology to classify CLE relative to other photodistributed skin eruptions. The new criteria comprised the 11 American College of Rheumatology criteria plus an additional 13 new criteria. Four out of these 24 new European Academy of Dermatology and Venerology criteria were dermatologic in nature: malar rash, discoid lesions, nonscarring diffuse alopecia, and psoriasiform and/or annular polycyclic type lesions. Alopecia, defined as nonscarring and diffuse, was more common in patients with SCLE than localized DLE (Table 1). As mentioned previously, 43% of patients with SCLE were classified with discoid rash, whereas 32% of generalized DLE patients were classified with psoriasiform and/or polycyclic type lesions, highlighting the uncertainty that exists when making a clinical diagnosis of CLE subtype.

Walling and Sontheimer (2009) described active DLE lesions as being indurated. David-Bajar et al. (1992) also investigated whether induration could distinguish between DLE and SCLE lesions. These authors found that 100% of DLE lesions (n = 11) had induration compared with 0% of SCLE lesions (n = 7). They concluded that induration is useful in differentiating early active DLE lesions from SCLE.

However, unpublished data from a study one of our authors (V.P.W.) is currently undertaking calls into question the utility of induration as a distinguishing feature of DLE lesions. In this study, two raters, one dermatologist (V.P.W.) and one pre- or postdoctoral autoimmune skin disease research fellow, independently assessed CLE lesions for different features including induration. Preliminary data include 20 lesions evaluated in eight subjects (seven DLE, one SCLE). Of the 20 lesions, 18 were DLE and two were SCLE, with a clinical diagnosis given by the dermatologist (V.P.W.). Of the lesions evaluated, 17% to 22% of DLE lesions had induration, compared with 0% of SCLE lesions, and all induration was classified as mild. Additionally, when raters were asked to report their level of confidence in assessing induration, both raters reported moderate levels of confidence with average confidence scores of 5.6 and 6.6 (out of 10) for rater 1 and rater 2, respectively.

The fact that neither rater had a high level of confidence in assessing induration calls into question the feasibility of determining the presence or absence of this feature. If it is difficult for dermatologists to determine whether a lesion has induration, it might be challenging for

Table 1
Comparison of 4 EADV criteria between CLE subtypes (Beutner et al., 1991)

Criteria	Localized DLE	Generalized DLE	SCLE
Malar rash	27%	20%	94%
Discoid rash	100%	100%	43%
Alopecia (nonscarring diffuse)	0%	0%*	49%
Psoriasiform and/or annular polycyclic type lesions	16%*	32%	100%

* $p < 0.0001$; no statistically significant difference between SCLE and other CLE subtypes.

Table 3
Potential diagnostic criteria proposed by two sets of authors (Walling and Sontheimer, 2009; Fabbri et al., 2003)

Walling and Sontheimer (2009)	Fabbri et al. (2003)
- Indurated coin-shaped plaque affecting the scalp, face, ears, anterior neck, extensor arm - Peripheral scale with central hypopigmentation - Adherent scale extending hair follicles leading to follicular plugging - Center of lesion hypopigmented and atrophic leading to a depressed scar - More than half of patients will develop destructive scarring - Histopathology qualitatively similar in each CLE subtype and not useful in determining clinical skin type	- Well-demarcated disk-shaped lesion associated with follicular plugging - Lesions most often located on exposed surfaces (face, ears, scalp) - Characteristic histologic alterations (ortho-hyperkeratosis of the epidermis, dilated follicular orifices filled with compact keratin, vacuolar degeneration of the basal keratinocytes, perivascular and perifollicular mononuclear cell infiltrate of the dermis) - Evolution of lesions with atrophy, scar formation, and pigmentary changes - Positive lupus band test on lesional sun exposed skin