

Discoid lupus erythematosus and cutaneous squamous cell carcinoma

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ABSTRACT

Discoid lupus erythematosus (DLE) is a chronic autoimmune skin disorder characterized by inflammatory skin lesions. Patients with DLE often exhibit photosensitivity, scarring, and a higher susceptibility to skin cancers. This systematic review aims to comprehensively evaluate the existing literature to better understand the relationship between DLE and cutaneous squamous cell carcinoma (cSCC). A systematic search of major medical databases was conducted to identify relevant studies published between 1978 and 2023. Studies were included if they explored the association between DLE and cSCC and reported epidemiological data, clinical features and outcomes. Evidence shows a correlation between DLE and squamous cell carcinoma. The study aimed to find literature about DLE and squamous cell carcinoma (SCC) and analyse potential risk factors. Healthcare providers should be aware of the increased cancer risk in DLE patients, emphasizing the importance of regular skin examinations and sun protection.

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Keywords: discoid lupus erythematosus, squamous cell carcinoma, systematic review

INTRODUCTION

Discoid lupus erythematosus (DLE) is distinguished by well-defined, red, and scaly discoid plaques that undergo healing accompanied by atrophy, scarring, and alterations in pigmentation. Neoplastic transformation is a rare complication of this condition. The development of squamous cell carcinoma (SCC) within pre-existing DLE lesions has been regarded as the most severe consequence associated with DLE. The association between DLE lesions and SCC has not been fully investigated or integrated, despite the significant reporting of cases revealing SCC complicating DLE lesions. Early detection of SCC in a patient with DLE is crucial for effective treatment.

Aim

A literature study was conducted to identify and summarize the characteristics and meta-analysis of existing studies in this particular field.

MATERIAL AND METHODS

On September 26, 2023, a study was conducted to identify relevant literature. The PubMed and Medline databases were searched using different variations of two primary

keywords: “discoid lupus erythematosus” and “squamous cell carcinoma”. Additionally, additional variations of the aforementioned key terms, namely “DLE” and “SCC”, have been used in the following study. The selected publication dates encompassed the period from 1978 to 2023. A total of 153 papers, including abstracts, original texts, and case reports, were identified. A total of 93 publications were removed from the analysis. The literature review only comprised original publications written solely in the English language, focusing on a research population consisting of individuals with discoid lupus erythematosus (DLE) and squamous cell carcinoma (SCC). The review included case series, case reports, and experimental randomized controlled trials. The analysis focused on the general characteristics of the patient (age, sex, potential risk factors), on the side of characteristics of patients with DLE (age, duration of DLE, location of the lesions, treatment), and on the side of characteristics of patients with SCC (age at the time of diagnosis, location of SCC, stage of malignancy, metastasis, cancer treatment, mortality rate). A total of 84 patients diagnosed with DLE and SCC were included in the study. The study selection process is depicted in Table 1. The literature incorporated in this review consists of a total of 48 original papers [1–48].

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RESULTS

All the case reports and series fulfilled the minimum standards for quality assessment. The process of identifying the data proved to be challenging, primarily attributable to their scarcity. The majority of the papers consisted of case reports, with authors applying varying criteria in the evaluation of each case. Initially, the attention was directed towards patient demographics and overarching characteristics, followed by a comprehensive analysis of SCC data, specifically regarding SCC characteristics. Although some authors did not provide extensive information on histological details, patient details, and attempted treatments, the overall methodological quality of the selected articles was assessed as satisfactory.

DLE patients' general characteristics

A total of 84 cases were included in this analysis. General DLE patients' characteristics are detailed in Table 2. The majority were male patients — 57.14% (48 male cases vs. 36 female cases). The mean age of the patients was 51.93 years. Discoid lupus erythematosus duration time to SCC diagnosis (mean) was 14.83 years. Most patients had systemic treatment (71.74%), mainly antimalarial drugs. Only 5 patients were reported to be using only topical treatment for DLE.

Squamous cell carcinoma's general characteristics

The location of SCC on the DLE lesions was analysed. The majority was located in sun-exposed areas (91.67%). The most common locations were lips (35.71%; lower to upper lip ratio 1, 14:1), scalp (20.24%), and face and ears (19.04%). The authors also focused on metastatic status, where it was found that 65.9% of the included patients had no metastatic data. The majority of patients diagnosed with squamous cell carcinoma (75%) used surgical intervention as their primary treatment modality. A smaller proportion of patients (18.33%) received chemotherapy, while the remaining patients (6.67%) were treated with radiotherapy. General characteristics of SCC in DLE patients are shown in Table 3.

DISCUSSION

Discoid lupus erythematosus (DLE) is a benign skin condition characterized clinically by red, scaly areas that heal with atrophy, scarring, and pigmentary changes, and histopathologically by vacuolar degeneration of the epidermis's basal cell layer and patchy dermal lymphocytic infiltrate. DLE can be classified into two distinct forms: a localized variant characterized by lesions limited to the face and neck, and a disseminated variant where lesions are present in other areas of the body as well. The areas of the body most frequently affected by this condition are

Table 1. Study selection

Identification of studies via databases	
Records identified from PubMed and Medline databases (n = 153)	Records removed before screening: duplicate records removed, records removed for other reasons (non-English papers, not SCC patients) (n = 93)
Record screened (n = 60)	
Full texts assessed (n = 48)	
Total number of detailed cases in all included papers (n = 84)	

SCC — squamous cell carcinoma

Table 2. Discoid lupus patients erythematosus patients profile

Characteristics of DLE patients	Number of patients	
Sex	Males	48
	Females	36
	Total	84
Age, mean [years] (range)	[51, 93] (35–78)	–
DLE duration time [years]	14.83	–
Mean DLE duration time to SCC diagnosis (range)	1–44	–
DLE treatment (n = 46)	Topical	5
	Systemic	33
	No treatment	8

DLE — discoid lupus erythematosus; SCC — squamous cell carcinoma

the sun-exposed regions of the head and neck, including the scalp, face, and ears [49, 50]. DLE typically does not involve the internal organs, as is the case with systemic lupus erythematosus (SLE). DLE can lead to the development of high-risk skin malignancies, which, although infrequent, pose significant health risks. DLE complicated by SCC was first mentioned in 1953 and has since been the focus of many case studies. The incidence of SCC in instances of long-standing chronic DLE ranges from 2.3% to 3.4%, with a higher prevalence observed in males [34, 37, 51]. There is a documented four-fold increase in the probability of cutaneous squamous cell carcinoma (cSCC) formation in patients with DLE [51]. Other neoplastic lesions in DLE, such as basal cell carcinoma, malignant fibrous histiocytoma, and atypical fibroxanthoma, have occasionally been reported [41]. Previous research has provided evidence of a latency period ranging from 7 to 30 years for the formation of SCC in DLE lesions. However, more recent investigations have indicated that this latency period can occur as early as 1–3 years [33]. Cutaneous squamous cell carcinoma (sSCC) exhibits a spectrum of clinical characteristics, varying from less aggressive forms to more aggressive forms that have

Table 3. General characteristics of squamous cell carcinoma in patients with discoid lupus erythematosus

Characteristics of SCC		Number of patients	Percentage of cases [%]
Location of SCC on DLE lesions (n = 84 patients)	Upper lip	14	16.67
	Lower lip	16	19.04
	Scalp	17	20.24
	Face and ears	16	19.04
	Limbs	14	16.67
	Sun protected areas	7	8.33
Metastatic status (n = 44 patients)	No metastases	29	65.91
	Metastases	15	34.09
SCC treatment (n = 60 patients)	Surgical excision	45	75
	Radiotherapy	4	6.67
	Chemotherapy	11	18.33

DLE — discoid lupus erythematosus; SCC — squamous cell carcinoma

a notable propensity for metastasis. Predisposing factors such as scarring and immunosuppression have been identified as related to high-risk subtypes [52]. Squamous cell carcinoma is often associated with prolonged sun exposure and can occur anywhere on the body. The potential variables contributing to the development of SCC include genetic predisposition, the severity of discoid lesions in DLE, and human papillomavirus (HPV) infection.

Squamous cell carcinoma typically appears as a firm, red bump or a scaly patch that can ulcerate and bleed. Cutaneous squamous cell carcinoma ranks as the second most prevalent form of non-melanoma skin cancer. It constitutes 20% of reported instances of skin cancer [53]. The occurrence of SCC as a complication of persistent DLE lesions has been well-documented in the literature, and SCC has been regarded as the most serious consequence associated with DLE.

Although there are a significant number of documented cases that describe the occurrence of SCC in individuals with DLE lesions, the precise pathophysiological mechanisms contributing to the development of cSCC in individuals with DLE have not yet been fully elucidated. However, various factors may confer a susceptibility to the development of skin cancer in individuals with DLE. There is a notable correlation between cutaneous malignancies and autoimmune connective tissue diseases (ACTDs) such as SLE, systemic sclerosis, dermatomyositis, and Sjögren syndrome. This association can be attributed to various potential pathogenetic mechanisms, including chronic scarring, exposure to ultraviolet (UV) radiation, inflammation, immunosuppressive therapies, viral infections, and smoking [54]. Various characteristics have been proposed as potential predisposing factors for

the development of malignancy in DLE lesions, such as the presence of chronic ulcers and inflammation associated with DLE. The prolonged scarring process could potentially contribute to the development of SCC originating from Marjolin's ulcers, as it may include a similar underlying pathomechanism [55].

Ultraviolet radiation is widely recognized as a significant risk factor for cSCC and DLE lesions, which tend to occur mostly in sun-exposed regions of the body. Possible pathogenetic processes include immune system dysfunction related to disease and cutaneous inflammation. The potential impact of UV light exposure is likely to be substantial in the context of DLE, particularly when combined with the reduced presence of protective melanin in individuals with hypopigmentation and those with fair skin [56]. The role of immunosuppressives in encouraging the development of cSCC has been under consideration. However, a study revealed an identical prevalence of cSCC in individuals with DLE, regardless of their history of immunosuppressive medication use [51]. Additionally, it has been noted that early anti-inflammatory medication can reduce the chance of cSCC developing in DLE, despite the clinical presentation's potential for difficulty [57, 58]. In their study, Ju et al. [59] presented a clinical case involving an individual of African American descent who exhibited the development of squamous cell carcinoma on a pre-existing discoid plaque of extended duration. The examination of the lesion indicated a pattern of p53 protein expression characterized as null type, along with a significant presence of CD123+ plasmacytoid dendritic cells. These findings suggest that the p53 protein may play a role in driving oncogenesis, while the abundance of CD123+

plasmacytoid dendritic cells may contribute to inflammation [59]. Gao et al. [60] conducted a study to investigate the immunoexpression of podoplanin in samples obtained from patients diagnosed with DLE and to examine its potential link with the risk of developing lip squamous cell carcinoma (LSCC). The findings of the study indicate a substantial correlation between the expression of podoplanin and the malignant transformation of DLE into LSCC. Hence, the expression of podoplanin has the potential to identify a specific subgroup that carries a heightened risk of malignant development in DLE [60]. Long-standing discoid lesions appear to be a crucial determinant of cSCC emerging in DLE, as previously published patients often presented with a long-term DLE history [19]. The clinical progression of cSCC as a consequence of DLE might exhibit an aggressive nature, characterized by the occurrence of early metastases and an elevated risk of mortality, compared to spontaneous cSCC cases [5, 9, 19].

The long-term prognosis of such instances exhibits considerable variability. Squamous cell carcinoma that arises in DLE is commonly recognized as a carcinoma of low grade with a locally aggressive nature, characterized by recurrences and infiltration into the underlying tissue. A study conducted by researchers found that approximately 20% of individuals experienced local recurrences, whereas 30% of cases exhibited metastasis [17]. Multiple metastases have also been documented as a cause of mortality [39].

The prompt and adequate management of DLE has the potential to reduce the probability of occurrence of this uncommon complication. Furthermore, alongside the implementation of UV protection and the use of anti-inflammatory topical treatments such as corticosteroids or calcineurin inhibitors, antimalarial medications have been widely recognized as the prevailing therapeutic approach [61]. It is recommended that smokers abstain from smoking, as the efficacy of the latter is diminished in this population. If a patient experiences mild intolerance reactions or if the antimalarial medicine is not sufficiently effective, it may be advisable to consider transitioning to another antimalarial agent [62].

The precipitating variables associated with SCC include individuals aged 40 years or older, male gender, exposure to sunlight or UV radiation, skin pigmentation, and chronic inflammatory processes. The development of SCC is inversely related to skin pigmentation due to the preventive properties of melanin [63]. To minimize the risk of SCC and maintain overall skin health, individuals with DLE should take measures to protect their skin from UV radiation, such as wearing sunscreen and protective clothing and avoiding excessive sun exposure.

Regular follow-up of patients with DLE is strongly advised, especially for those who exhibit the following traits: (1) male; (2) early onset of DLE; (3) involvement of lips; (4) resistance to treatment; and (5) cigarette usage.

Although SCC remains a rare complication of DLE, healthcare providers and individuals with DLE should remain vigilant, recognizing the importance of ongoing monitoring and preventive measures to minimize the risk of SCC development and ensure timely intervention if needed. This multifaceted approach contributes to improved outcomes and a better quality of life for individuals living with DLE. Once SCC has been established, it is imperative to allocate adequate focus towards monitoring potential recurrences and/or metastasis due to their heightened aggressive nature.

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