SnapshotDx Quiz: April 2022
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WHAT IS YOUR DIAGNOSIS?

Figure 1. Images courtesy of Mariya Miteva, University of Miami

Editorial note: Welcome to the Journal of Investigative Dermatology (JID) Snapshot Dx Quiz. In this monthly online-only quiz, the first question (“What is your diagnosis?”) relates to the clinical image shown, while additional questions concern the findings reported in the JID article by Wang et al. (2021) (https://doi.org/10.1016/j.jid.2021.06.022).

Detailed answers and a list of relevant references are available following the Quiz Questions below.

QUIZ QUESTIONS

1. What is your diagnosis based on the clinical and dermatoscopic images?
   a. Psoriasis
   b. Seborrheic dermatitis
   c. Discoid lupus erythematosus (DLE)
   d. Tinea faciei
   e. Annular elastolytic giant cell granuloma

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2. Which of the following answers is TRUE?
   a. Serologic abnormalities are common in DLE.
   b. IFN-1s play a key role in driving cutaneous inflammation across all cutaneous lupus erythematosus (CLE) types.
   c. Jak/signal transducer and activator of transcription signaling pathway is significantly downregulated within inflamed lesions of CLE.
   d. The incidence of squamous cell carcinoma arising in DLE lesions is over 50%.
   e. Antimalarial drugs are not useful in the treatment of CLE.

3. Which of the following answers is FALSE about CLE according to the article by Wang et al. (2021)?
   a. Senescent cells secrete proinflammatory cytokines and chemokines thus potentially augmenting general inflammation, and p16 and p21 are commonly used as senescence markers.
   b. In unaffected skin, small numbers of scattered p16⁺ or p21⁺ cells were detected throughout the whole epidermis.
   c. In CLE lesions, significantly more p16⁺ and p21⁺ cells per mm² were detected in all three layers.
   d. Significantly more p16⁺ and p21⁺ cells per mm² were detected in the basal and suprabasal layers in dermatoses with dermal–epidermal junction (DEJ) infiltration than in those without DEJ infiltration and in unaffected skin.
   e. Chronic DLE lesions contain more p16⁺ and p21⁺ cells than subacute CLE lesions.

See following pages for detailed answers
DETAILED ANSWERS

1. What is your diagnosis based on the clinical and dermoscopic images?


The image corresponds to a patient with discoid lupus erythematosus (DLE). Clinical manifestations of DLE localized on the scalp are categorized by erythematos plaques that may evolve into depressed, white, alopecic patches as seen in the provided photo. The most common findings observed through dermoscopy in patients with scalp DLE include arborizing vessels, white scale, and white backgrounds with an absence of structure as seen in the photograph (Żychowska and Żychowska, 2021). Common nonscalp dermoscopic findings in patients with DLE include keratotic follicular plugs, perifollicular white halos, and telangiectasias (Lallas et al., 2013).

Discussion of incorrect answers:

a. Psoriasis: Psoriasis is a chronic, inflammatory skin disease characterized by well-demarcated erythematos plaques with silvery scale that are predominantly located on the extensor extremities but may also involve other body surfaces, including the scalp. Upto 80% of patients with psoriasis have scalp involvement (van der Vleuten and van de Kerkhof, 2001). Clinical features of scalp psoriasis may be confused with seborrheic dermatitis; however, trichoscopy is useful in distinguishing between the two. Trichoscopy findings of scalp psoriasis include tortuous, glomerular vessels, and red dots and globules.

b. Seborrheic dermatitis: Seborrheic dermatitis is a common, chronic, inflammatory condition that predominantly affects the scalp and face. Clinical features include erythema and yellow, greasy scale. Seborrheic dermatitis is clinically differentiated from DLE by the lack of atrophy, alopecia, and dilated follicles seen in DLE. Although exact pathogenesis is unknown, Malassezia spp. is known to play a pivotal role. Trichoscopic features include atypical, arborizing vessels and can be distinguished from scalp psoriasis by the absence of red dots and globules (Klosowicz et al., 2020).

d. Tinea faciei: Tinea faciei is a superficial dermatophyte infection affecting the glabrous skin of the face, mostly caused by Trichophyton tonsurans and Microsporum canis. Trichophyton spp. will not fluoresce under Wood’s light examination but Microsporum spp. will. When affecting the scalp, clinical features include characteristic black dot tinea resulting from the production of spores within the endothrix. Patients may also present with an inflammatory, deep, pustular plaque known as a kerion that can lead to scarring alopecia. Dermoscopic findings of tinea capitis include comma hairs (considered specific finding), corkscrew hairs, and Morse-code like hairs (Waskiel-Burnat et al., 2020). Early treatment with oral antifungal medication is essential, and adding a short course of systemic corticosteroids in kerion may aid in decreasing inflammation and preventing further scarring and hair loss.

e. Annular elastolytic giant cell granuloma: Annular elastolytic giant cell granuloma (AEGCG) is a chronic, palisaded granulomatous dermatis characterized by atrophic, thin, asymptomatic, yellow plaques with central clearing that may first appear on the forehead, also known as Miescher granuloma. Some lesions may appear on sun-exposed areas of the upper extremities. Under dermoscopy, yellow-orange areas with the absence of structural components overlying pink background with occasional hyperpigmentation and white lines may be appreciated in patients with AEGCG (Errichetti et al., 2019). Although most patients are healthy, there are reported cases of association with temporal arteritis and acute myelogenous leukemia. Treatment of AEGCG includes aggressive sun protection, topical corticosteroids, and topical calcineurin inhibitors.

2. Which of the following answers is TRUE?

CORRECT ANSWER: b. IFN-1s play a key role in driving cutaneous inflammation across all cutaneous lupus erythematosus (CLE) types.

The aforementioned answer is true. Although the pathogenesis of cutaneous lupus erythematosus (CLE) is multifaceted and complex, studies have shown the pivotal role that IFN-1s, particularly IFN-1e and IFN-3, play in driving cutaneous inflammation across CLE subtypes (Wenzel, 2019). Studies have shown that in lesional biopsies of patients with CLE, there is a dominant B-cell signature in patients with CLE, regardless of the presence or absence of systemic involvement. This suggests that B-cells and their production of IFN-1s play significant roles in driving autoreactive cutaneous manifestations of lupus (Abernathy-Close et al., 2021).

Discussion of incorrect answers:

a. Serologic abnormalities are common in DLE: The aforementioned statement is false. Serologic abnormalities may or may not be present in patients with
The incidence of squamous cell carcinoma arising in DLE. In Callen et al. (1985)’s evaluation of serologic abnormalities in patients with DLE, 45% of patients showed positive antinuclear antibody (ANA) findings, 10% showed positive anti-Ro antibodies, 5% showed positive anti-La antibodies, and 5% showed antinuclear ribonucleoprotein antibodies; the remainder of the evaluated sera were found to be negative for abnormalities. Some studies suggest that the presence of single-stranded DNA antibodies may positively correlate with active, progressive disease and increased risk of progression to systemic lupus erythematosus (SLE) (Callen et al., 1985). Callen et al. (1985) also showed that of the 20 patients with DLE, serologic evaluation of ANA was not a statistically significant marker for progression of the disease because 10 of 16 patients with negative ANA findings continued to experience symptoms at the 2-year follow-up.

c. Jak/signal transducer and activator of transcription signaling pathway is significantly downregulated within inflamed lesions of CLE: The aforementioned statement is false. Jak/signal transducer and activator of transcription (STAT) pathway is a major contributor to many inflammatory dermatologic and rheumatologic disease processes by way of enhancing the transduction of intracellular cytokine signaling. Studies have shown that the Jak/STAT signaling pathway is upregulated in active DLE lesions of affected patients (Fetter et al., 2020). With this logic, Jak inhibitors may be a promising avenue of treatment for patients with CLE to decrease the expression of proinflammatory cytokines promoted by activated Jak. Currently, there are a few clinical trials exploring the safety and efficacy of topical Jak inhibitors ruxolitinib and delgocitinib for patients with DLE (NCT04908280 and NCT03958955).

d. The incidence of squamous cell carcinoma arising in DLE lesions is over 50%: The aforementioned statement is false. The incidence of squamous cell carcinoma (SCC) in patients with DLE is low with approximately 2–3% patients developing SCC. Although neoplastic change in patients with DLE is rare, it is important for physicians to be aware of a small chance of malignant transformation of these lesions. Factors associated with increased risk of SCC in patients with DLE include increased age, lighter skin pigmentation, increased sun exposure, and a medical history significant for chronic inflammatory disease (Mufti et al., 2021).

e. Antimalarial drugs are not useful in the treatment of CLE: The aforementioned statement is false. Although the mechanism is unknown, antimalarial drugs hydroxychloroquine and chloroquine phosphate may be useful in the treatment of CLE. A recent Cochrane database review supported the use of chloroquine and hydroxychloroquine in the treatment of CLE (Hannon et al., 2021). In addition, antimalarials help treat the symptoms of SLE. They may provide a cardiovascular benefit, have been shown to reduce the overall risk of all thromboembolic events in patients with SLE, and may prevent systemic development of SLE in patients with CLE (Jung et al., 2010). Studies suggest that smoking may interfere with the efficacy of antimalarial treatment. Therefore, it is important for physicians to counsel patients with DLE about smoking cessation when initiating antimalarial therapy (Jewell and McCauliffe, 2000).

3. Which of the following answers is FALSE about CLE according to the article by Wang et al. (2021)?

CORRECT ANSWER: c. In CLE lesions, significantly more p16$^+$ and p21$^+$ cells per mm$^2$ were detected in all three layers.

The aforementioned answer is false. Although p16$^+$ cells per mm$^2$ were significantly detected in the basal, suprabasal, and further differentiated (FD) areas of the epidermis, this was true for p21$^+$ cells per mm$^2$ only in the basal and suprabasal areas (Wang et al., 2021). As explained in the article, cellular senescence is defined by the abruption of proliferating cells in conjunction with apoptotic resistance. The upregulation of key cyclin-dependent kinase inhibitors p16$^+$ and p21$^+$ have been shown to initiate growth arrest and thus serve as markers of senescence. The significant levels of p16$^+$ and p21$^+$ cells highlighted at the evaluated epidermal areas suggest that dysfunctional cells at the basal, suprabasal, and FD sites may be senescent owing to nearby inflammatory infiltration at the dermal–epidermal junction (DEJ) (Wang et al., 2021). Further quantification of p16$^+$ and p21$^+$ cells revealed significantly greater accumulation in skin lesions of chronic DLE (CDLE) than in skin lesions of subacute CLE (SCLE) (Wang et al., 2021).

Discussion of incorrect answers:

a. Senescent cells secrete proinflammatory cytokines and chemokines thus potentially augmenting general inflammation, and p16 and p21 are commonly used as senescence markers: The aforementioned statement is true. Cellular senescence is defined by a permanent abruption of proliferating cells in conjunction with apoptotic resistance (Gorgoulis et al., 2019). Senescent cells have been shown to produce proinflammatory cytokines and chemokines such as IL-1a, IL-6, IL-8, and CCL-2. In addition,
cycillin-dependent kinase inhibitors such as p16\(^{\text{+}}\) and p21\(^{\text{+}}\) have been shown to be key promoters of senescence and are often used as markers of senescence (Hernandez-Segura et al., 2018).

b. In unaffected skin, small numbers of scattered p16\(^{\text{+}}\) or p21\(^{\text{+}}\) cells were detected throughout the whole epidermis: According to the findings in the referenced article (Wang et al., 2021), the aforementioned statement is true. Figure 1b, d, e, and g show that although p16\(^{\text{+}}\) and p21\(^{\text{+}}\) cells are upregulated in senescent cells, they can be found in small amounts in unaffected skin. The small number of p16\(^{\text{+}}\) and p21\(^{\text{+}}\) cells may be a sign of normal aging.

d. Significantly more p16\(^{\text{+}}\) and p21\(^{\text{+}}\) cells per mm\(^2\) were detected in the basal and suprabasal layers in dermatoses with dermal–epidermal junction (DEJ) infiltration than in those without DEJ infiltration and in unaffected skin: According to the findings in the referenced article (Wang et al., 2021), the aforementioned statement is true. When diseases with and without DEJ infiltration were compared, significantly higher numbers of p16\(^{\text{+}}\) and p21\(^{\text{+}}\) cells per mm\(^2\) were found in the basal and suprabasal layers of dermatoses with DEJ infiltration than in those without DEJ infiltration and in unaffected skin (Figure 2k and l). A similar trend was seen in the FD area for p16\(^{\text{+}}\) cells; however, this trend was not present for p21\(^{\text{+}}\) cells where dermatoses with and without DEJ infiltration had similar levels; the levels were higher than those in unaffected skin (Figure 2k and l). These findings seem to indicate that inflammation and senescence are associated and may even augment one another (Wang et al., 2021).

e. Chronic DLE lesions contain more p16\(^{\text{+}}\) and p21\(^{\text{+}}\) cells than SCLE lesions: According to the findings in the referenced article (Wang et al., 2021), the aforementioned statement is true. There were more p16\(^{\text{+}}\) cells in all three layers of the epidermis in CDLE than in SCLE; however, this same trend was only seen in the basal and suprabasal layers for p21\(^{\text{+}}\) cells (Wang et al., 2021).

Overall, quantification of p16\(^{\text{+}}\) and p21\(^{\text{+}}\) cells revealed significantly greater accumulation in skin lesions of CDLE than that in skin lesions of SCLE (Wang et al., 2021). These findings are consistent with those described in answer 3d that dermatoses with DEJ infiltration show higher levels of p16\(^{\text{+}}\) and p21\(^{\text{+}}\) cells in the epidermis because CDLE lesions show a denser DEJ infiltrate than SCLE lesions (Wang et al., 2021).

REFERENCES


