SnapshotDx Quiz: February 2020

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WHAT IS YOUR DIAGNOSIS?

Figure 1. Image is published with permission from the patient.

Editorial note: Welcome to the Journal of Investigative Dermatology (JID) SnapshotDx Quiz. In this monthly online-only quiz, the first question relates to the clinical image shown, while additional questions concern the findings reported in the JID article by Callewaert et al. (2019) (https://doi.org/10.1016/j.jid.2019.05.024).

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

QUIZ QUESTIONS

1. A 55-year-old female presents with erythematous scaly plaques on her right antecubital fossa (as shown in Figure 1), abdomen, back, and bilateral popliteal fossae.
   a. Seborrheic dermatitis
   b. Allergic contact dermatitis
   c. Psoriasis
   d. Atopic dermatitis
   e. Scabies

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2. According to the paper by Callewaert et al. (2019), the skin microbiome of atopic dermatitis lesions is characterized by which of the following?
   a. High microbial diversity
   b. High absolute abundance of *Staphylococcus aureus*
   c. High relative abundance of *Streptococcus*
   d. Low quantities of total bacteria

3. In the group of atopic dermatitis patients treated with dupilumab, which of the following occurred?
   a. Decrease in serum TARC (thymus and activation-regulated chemokine) and PARC/CCL18 (pulmonary and activation-regulated chemokine) levels
   b. Increase in absolute and relative *S. aureus* abundance in lesional skin
   c. Decrease in Shannon microbial diversity
   d. Increase in Eczema Area and Severity Index (EASI) scores

See following pages for detailed answers.
DETAILED ANSWERS

1. A 55-year-old female presents with erythematous scaly plaques on her right antecubital fossa (as shown in Figure 1), abdomen, back, and bilateral popliteal fossae.

CORRECT ANSWER: d. Atopic dermatitis

This picture demonstrates an erythematous scaly plaque on the antecubital fossa of an adult, consistent with atopic dermatitis.

Atopic dermatitis is a common, chronic inflammatory skin condition that can have significant morbidity, if left untreated. While it classically develops in childhood and infancy, it can also develop de novo in adults, affecting approximately 17.8 million people in the United States (Hanifi et al., 2007). Atopic dermatitis is characterized by pruritic, erythematous, scaly plaques often localized to the flexural surfaces of the body. Diagnosis is based on history and careful physical examination. A widely accepted diagnostic criteria for atopic dermatitis includes at least three of the following: history of asthma or allergic rhinitis, history of family history of atopic dermatitis, exudative involvement, history of generalized dry skin, onset of rash before two years of age, and visible flexural dermatitis (Gu et al., 2001; Williams et al., 1994).

Early diagnosis and treatment can significantly alleviate the disease burden in patients. Emollients remain the mainstay of therapy for atopic dermatitis. Patients should be advised to liberally apply emollients to their body regardless of disease activity (Hanifi et al., 2004; National Collaborating Centre for Women’s and Children’s Health, 2007). For flare-ups, topical corticosteroids and topical calcineurin inhibitors can be used. However, for moderate to severe atopic dermatitis, UV phototherapy and/or systemic immunomodulatory agents, including cyclosporine and mycophenolate mofetil, can be added. In recent years, more targeted therapies have been developed, including dupilumab, a human monoclonal antibody that blocks the shared receptor subunit for IL-4 and IL-13 (Beck et al., 2014; Wenzel et al., 2013).

Discussion of incorrect answers:

a. Seborrheic dermatitis: Seborrheic dermatitis is a common inflammatory condition of the skin characterized by scaly plaques with “greasy-like” yellow scale distributed along sebaceous areas of the skin. It is common in adolescents and in adults over the age of 50, affecting 1–3% of immunocompetent adults (Gupta and Bluhm, 2004). Although the involvement of flexural areas can be seen occasionally, patients more commonly have involvement of the scalp, eyebrows, nasolabial folds, ears, and chest (Gupta and Bluhm, 2004). On histology, lesions of seborrheic dermatitis have a spongiform appearance with increased epidermal proliferation and focal parakeratosis, distinguishing it from other diagnoses (Pinkus and Mehregan, 1966). The first-line treatment of seborrheic dermatitis includes topical anti-fungals, such as ketoconazole, topical keratolytic agents like selenium sulfide, and topical steroids for symptomatic relief.

b. Allergic contact dermatitis: Allergic contact dermatitis is a T-cell-mediated skin condition that is thought to develop after exposure to an environmental agent. After the allergen first makes contact with the skin, antigen-specific T cells are generated, which initiate inflammatory responses upon subsequent exposure to the allergen. In sensitized individuals, pruritic lesions develop 24–96 hours after contact with the allergen. Lesions are initially characterized by erythema and edema and evolve into erythematous papules and vesicles (Saint-Mezard et al., 2004). Histologic features of allergic contact dermatitis include spongiosis of the lower epidermis, dilated vessels in the papillary dermis, and perivascular lymphocytic infiltrates (Saint-Mezard et al., 2004). A careful history and physical exam can provide indications of what the culprit antigen may be. Patch testing can often identify the offending antigen. Treatment involves the elimination of exposure to the culprit allergen and application of topical steroids.

c. Psoriasis: This condition is a chronic inflammatory skin disease histologically characterized by epidermal hyperproliferation due to the aberrant differentiation of keratinocytes and mixed inflammatory infiltrates containing lymphocytes and neutrophils in dermis and epidermis. As a result, patients develop pruritic, scaly plaques. However, in contrast to the flexural distribution of lesions seen in atopic dermatitis, the lesions are typically distributed along the extensor surfaces. Given the flexural distribution of this patient’s lesions, psoriasis is less likely. In addition to cutaneous manifestations, nails and joints can also be affected in psoriatic patients. The treatment of psoriasis includes topical corticosteroids, narrow band UVB phototherapy, and systemic treatments such as methotrexate (Boehncke, 2003). For patients refractory to first-line therapies, biologics are employed (e.g., tumor necrosis factor-alpha inhibitors, IL-12/IL-23 inhibitors, IL-17 inhibitors) (Sterry et al., 2004).

e. Scabies: This condition is a parasitic dermatitis caused by the mite, Sarcoptes scabiei var hominis, that burrows into the epidermis of human skin.
Patients develop severe pruritus in the affected areas. Burrows, which are small linear plaques in the skin formed from the digestive secretions of the mite, can serve as diagnostic clues. Lesions have a predilection for interdigital web spaces, flexor surfaces of the wrists, extensor surfaces of elbows, axillae, nipples, and genitalia, making it unlikely that the patient shown in Figure 1 has a diagnosis of scabies. Treatment options include 5% permethrin cream and oral ivermectin (Golant and Levitt 2012).

2. According to the paper by Callewaert et al. (2019), the skin microbiome of atopic dermatitis lesions is characterized by which of the following?

CORRECT ANSWER: b. High absolute abundance of S. aureus

In this cohort of atopic dermatitis patients, quantitative PCR (qPCR) was used to quantify the absolute amount of S. aureus in lesional and non-lesional skin at screening and baseline. The authors performed statistical analyses comparing lesional and non-lesional skin and found that there was a significantly higher absolute abundance of S. aureus in lesional skin compared with non-lesional skin at both screening ($P = 0.0079$) and baseline ($P = 0.026$).

Discussion of incorrect answers:

a. High microbial diversity: The Shannon diversity index was employed to assess microbial diversity of the skin of atopic dermatitis patients. The authors performed statistical analyses comparing lesional and non-lesional skin and found that lesional skin had significantly lower Shannon diversity scores than did non-lesional skin at both screening ($P = 0.0057$) and baseline ($P = 0.0063$).

b. High relative abundance of Streptococcus: The authors investigated the relative abundance of the most dominant phyla and genera in both lesional skin and non-lesional skin in order to better characterize the microbiome of lesional skin in atopic dermatitis lesions. They observed that S. aureus comprised a majority of the microbiome population, whereas other bacteria such as Streptococcus and Anaerococcus had substantially lower relative abundances.

c. Low quantities of total bacteria: Total bacteria from samples were determined by the absolute quantification of 16S ribosomal RNA (rRNA) using qPCR. When comparing lesional and non-lesional skin at baseline, the authors observed that the lesional skin had significantly higher amounts of total bacteria than the non-lesional skin at both screening ($P = 0.0068$) and baseline ($P = 0.048$). As such, it was determined that the atopic dermatitis lesions were characterized by higher total amounts of bacteria.

3. In the group of atopic dermatitis patients treated with dupilumab, which of the following occurred?

CORRECT ANSWER: a. Decrease in serum TARC and PARC/CCL18 (pulmonary and activation-regulated chemokine) levels

The type 2 inflammation pathway is thought to drive the pathogenesis of atopic dermatitis. Previous studies have demonstrated that TARC and PARC/CCL18, two markers of type 2 inflammation, are associated with atopic dermatitis (Thijs et al., 2015; Pivarcsi et al., 2004). It has been hypothesized that treatment with dupilumab can reduce inflammatory cell infiltrates in atopic dermatitis lesions by inhibiting T helper type 2 polarizing chemokines, including PARC and TARC. In order to further investigate this hypothesis, the authors measured serum TARC and PARC levels using Quantikine ELISA kits before and after treatment. They observed a reduction in both TARC and PARC scores after week 16 compared with baseline levels in the dupilumab group, whereas this trend was not observed in the placebo group.

Discussion of incorrect answers:

b. Increase in absolute and relative S. aureus abundance in lesional skin: The authors measured the absolute and relative abundance of S. aureus longitudinally over the 32-week treatment duration. They observed that after up to 16 weeks of treatment with dupilumab, the relative abundance of bacterial S. aureus had decreased significantly in lesional skin ($P < 0.001$). Additionally, by week 4, patients treated with dupilumab had a significantly lower absolute abundance of S. aureus as measured by qPCR compared with the placebo-treated patients ($P = 0.00042$).

c. Decrease in Shannon microbial diversity: Shannon microbial diversity was measured over the 32-week treatment duration. The authors found that after up to 16 weeks of treatment with dupilumab, the Shannon alpha microbial diversity of lesional skin had significantly increased from baseline ($P < 0.001$), whereas there was not a statistically significant difference in the placebo-treated group.

d. Increase in EASI scores: The EASI is widely used to assess the extent and severity (redness, thickness, scratching, and lichenification) of atopic dermatitis (Tofte et al. 1998, Leshem et al. 2015). The authors
found that EASI scores in patients correlated with relative ($P < 2.2\times10^{-16}$) and absolute ($P < 2.2\times10^{-16}$) abundance of \textit{S. aureus}. In the dupilumab-treated group of patients, a reduction of both EASI scores and relative \textit{S. aureus} abundance was observed, whereas this trend was not observed in placebo-treated patients. Additionally, EASI scores decreased over time in the lesional skin treated with dupilumab in both male and female patient subgroups.

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**REFERENCES**