WHAT IS YOUR DIAGNOSIS?

Figure 1. The 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 ("What is your diagnosis?") relates to the clinical image shown, while additional questions concern the findings reported in the JID article by McCarthy et al. (2021) (https://doi.org/10.1016/j.jid.2021.05.036).

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

QUIZ QUESTIONS

1. A female with obesity aged 30 years with a history of Crohn’s disease presents to the clinic with recurrent sores under her axilla for the last year. On examination, multiple erythematous subcutaneous nodules, sinus tracts, and scarring are present (Figure 1). Laboratory work is unremarkable. A review of social and family history reveals that the patient smokes cigarettes. What is your diagnosis?
   a. Furunculosis
   b. Cutaneous Crohn’s disease
   c. Intertrigo
   d. Hidradenitis suppurativa (HS)
   e. Candidiasis
2. In McCarthy et al. (2021), gut microbiomes differed between patients with HS and healthy controls. What bacteria was found to be increased in patients with HS that has been implicated in other inflammatory conditions, particularly in Crohn’s disease?
   a. *E. coli*
   b. *Ruminococcus gnavus*
   c. *Cutibacterium acnes*
   d. *Staphylococcus aureus*
   e. *Finegoldia magna*

3. Which pathogenic bacteria found to be increased in skin samples might contribute to the pathogenesis of HS and might be a potential therapeutic target for microbial-based therapies?
   a. *F. magna*
   b. *Clostridium ramosum*
   c. *C. acnes*
   d. *R. obeum*
   e. *Faecalibacterium prausnitzii*

See following pages for detailed answers
DETAILED ANSWERS

1. A female with obesity aged 30 years with a history of Crohn’s disease presents to the clinic with recurrent sores under her axilla for the last year. On examination, multiple erythematous subcutaneous nodules, sinus tracts, and scarring are present (Figure 1). Laboratory work is unremarkable. A review of social and family history reveals that the patient smokes cigarettes. What is your diagnosis?

CORRECT ANSWER: d. Hidradenitis suppurativa (HS)

Hidradenitis suppurativa (HS) typically presents with a combination of erythematous subcutaneous nodules, abscesses, sinus tract formation, and scarring similar to that presented in the picture shown. HS is a chronic, inflammatory skin disease affecting intertriginous zones, including the axillae, inframammary folds, groin, and perineum (Saunte and Jemec, 2017). Disease severity is often classified using the Hurley staging system, which includes three stages: mild, moderate, and severe. HS disease pathogenesis has not been fully elucidated, but follicular rupture and mechanical friction resulting in eventual follicular rupture and inflammation remain the most widely accepted theory (von Laffert et al., 2011). HS is a clinical diagnosis, and skin biopsy is not typically necessary. Comorbid conditions frequently present in patients with HS include metabolic syndrome, polycystic ovarian syndrome, type II diabetes, obesity, and Crohn’s disease (Pescitelli et al., 2018; Yadav et al., 2016). Disease prevalence estimates range from 0.5 to 4% (Ingram et al., 2018). The majority of patients with HS are female, and disease onset is typically after puberty. Most patients are diagnosed in the second or third decade of life. In the United States, African Americans are disproportionately affected. Genetics, obesity, hormones, smoking, and bacteria may also play a role in the development of HS. A recent study revealed that 41% of patients with HS have an affected first-degree family member (Liy-Wong et al., 2021). Hormones may also contribute, given that most cases develop after puberty, and hormonal contraceptives have been shown to be effective in some cases. Most patients with HS are smokers, and smoking has been strongly associated with HS, although smoking cessation does not typically lead to complete remission of the disease (König et al., 1999). Emerging research investigating the role of microbiome suggests that the imbalance of certain bacteria may contribute to disease pathogenesis in HS. Although acute, unruptured HS lesions are typically sterile, bacteria may contribute to the ongoing inflammatory response and promote the formation of biofilms, making some patients resistant to antibiotic treatment (Ring et al., 2017).

Discussion of incorrect answers:

a. Furunculosis: This is an abscess associated with hair follicles and is infectious in etiology, usually by Staphylococcus aureus (Nowicka and Grywalska, 2019). Similar to HS, furuncles may have purulent drainage and occur on the axillae, buttocks, thighs, and perineum. However, unlike HS, they also occur in areas unassociated with friction, including the face, and are most commonly found in males. Some predisposing conditions include immunosuppressive states such as human immunodeficiency virus/acquired immunodeficiency syndrome or Hyper IgE syndrome (Crum-Cianflone et al., 2007).

b. Cutaneous Crohn’s disease: This can present with a variety of skin findings and may occur before the development of gastrointestinal symptoms. Some skin findings in Crohn’s disease that are similar to HS include sinus tracts and abscesses. However, the pathogenesis behind these differs because the findings in Crohn’s disease are a result of a granulomatous inflammatory process similar to what takes place in the gut. Other skin findings include enterocutaneous fistula formation, skin tags, and oral ulcers (Marzano et al., 2014). Crohn’s disease is more common in Caucasian populations, namely those of Ashkenazi Jewish or Northern European descent, and similar to other autoimmune diseases, it has a predilection for females (Karlinger et al., 2000). Disease pathogenesis is likely multifactorial and involves a combination of genetic and environmental risk factors.

c. Intertrigo: This is typically found between sites subject to mechanical friction such as the inframammary folds, groin, axillae, and abdominal folds similar to HS. However, the characteristic lesions are erythematous patches with erosions and satellite vesicles, which are not present in HS (Kalra et al., 2014). Lesions may be secondarily infected with yeast (Candida) or other bacteria. Other symptoms include itching and burning. Intertrigo affects all races and sexes equally, unlike HS. However, patients with obesity are at greater risk given the propensity of skin-fold friction. Exacerbating factors may include heat, sweat, or urine.

e. Candidiasis: This encompasses many infections caused by C. albicans that may affect mucosal or skin surfaces, including oral candidiasis (thrush), vulvovaginal candidiasis, intertrigo, or generalized cutaneous candidiasis (Hani et al., 2015). Candidiasis also favors skin folds, similar to HS, but it presents with erythematous patches with vesicles and pustules, not abscesses or scarring. Chronic mucocutaneous candidiasis is an inherited cell-mediated
immunity deficiency that results in recurrent Candida infections starting in childhood (Kirkpatrick, 2001).

2. In McCarthy et al. (2021), gut microbiomes differed between patients with HS and healthy controls. What bacteria was found to be increased in patients with HS that has been implicated in other inflammatory conditions, particularly in Crohn’s disease?

CORRECT ANSWER: b. Ruminococcus gnavus

Microbial DNA was extracted from stool samples and profiled by 16S ribosomal RNA gene sequencing. McCarthy et al. (2021) then analyzed amplicon sequence variants (ASVs) unique to species of bacteria to compare the fecal microbiomes of patients with HS and those of healthy controls. They found statistically significant differences between healthy controls and patients with HS. The most proportionately abundant species included Streptococcus spp. (an average relative abundance of 0.19% in controls vs. 0.95% in the HS cohort) and Ruminococcus gnavus (average relative abundance values of 0.01% in healthy controls vs. 0.7% in the HS cohort). R. gnavus has been found to be overly abundant in patients with Crohn’s disease, and authors cite previous studies supporting its role in disease pathogenesis, including the production of a proinflammatory polysaccharide, which induces the production of TNF-α (Hall et al., 2017; Henke et al., 2019).

Discussion of incorrect answers:

a. E. coli: E. coli was not found to be significantly abundant in patients with HS by McCarthy et al. (2021). A previous study investigated the microbiomes of patients with psoriasis, inflammatory bowel disease (IBD), and HS. E. coli was increased in patients with psoriasis; however, it was not differentially abundant in HS (Eppinga et al., 2016).

c. Cutibacterium acnes: Cutibacterium acnes was found to be more abundant within healthy controls than in patients with HS by McCarthy et al. (2021), which supports previous studies that have found a similar abundance. Authors propose that the depletion of C. acnes in patients with HS may promote disease pathogenesis. C. acnes plays a role in the pathogenesis of acne vulgaris (Dréno et al., 2018).

d. Staphylococcus aureus: Staphylococcus aureus and Corynebacterium were the primary species shown to compose skin and nasal microbiomes by McCarthy et al. (2021). This is similar to previous reports. S. aureus is increased in patients with atopic dermatitis but not in patients with HS (Kong et al., 2012).

e. Finegoldia magna: Finegoldia magna was significantly more abundant in the groin and axilla skin samples from patients with HS than in those from controls, as found by McCarthy et al. (2021). An ASV called Seq 4 was assigned to F. Magna, and this ASV was found to be more abundant in these samples. However, F. magna was not found to be overly abundant in gut microbiome studies conducted by McCarthy et al. (2021).

3. Which pathogenic bacteria found to be increased in skin samples might contribute to the pathogenesis of HS and might be a potential therapeutic target for microbial-based therapies?

CORRECT ANSWER: a. F. magna

F. magna is a gram-positive anaerobic commensal bacterium normally present on skin surfaces. However, when an injury occurs or the skin surface breaks, F. magna has the opportunity to become an opportunistic pathogen. F. magna has higher pathogenic potential given its ability to secrete collagenase; activate mast cells, basophils, histamine, and cytokines; and form capsules (Krepel et al., 1992; Genovese et al., 2000). In addition, F. magna has been shown to induce inflammation by activating neutrophils and promoting the formation of neutrophil extracellular traps (NETs) (Neumann et al., 2020). NETs are web-like structures that can create aberrant immune responses and have been implicated in a variety of different autoimmune diseases and HS. NETs are more abundant in HS lesions and are correlated with disease severity (Byrd et al., 2019). The authors discuss the lack of effective treatment options currently available in HS. Microbial-based therapies in the form of either supplementation to help increase alpha diversity of species in patients with HS or the selective depletion of pathogenic species found to be more abundant in patients with HS such as F. magna may be important therapeutic targets.

Discussion of incorrect answers:

b. Clostridium ramosum: Clostridium ramosum is an anaerobic gram-positive rod commonly found in the gastrointestinal tract of humans and is not usually associated with severe infections (Legaria et al., 2020). Although not typically pathogenic, it is capable of producing lgs A1 and A2 proteases allowing the bacterium to evade mucosal defense systems and contribute to the pathogenesis of IBD (Send et al., 1985). In McCarthy et al. (2021), C. ramosum was found to be increased in the gut microbiome of patients with HS compared with that in the controls.
C. acnes: C. acnes, previously known as Propionibacterium acnes, was recently reclassified to account for its specific ability to colonize the skin (Dréno et al., 2018). C. acnes is a gram-positive anaerobic bacterium that lives inside sebaceous follicles but may also be found in the intestine, stomach, lungs, and urinary tract. Some more specific strains of C. acnes have been implicated in the pathogenesis behind acne vulgaris; however, the majority of organisms are associated with healthy controls and normal skin as seen in McCarthy et al. (2021) (Lomholt and Kilian, 2010). McCarthy et al. (2021) further suggest that a decrease in C. acnes may alter the ecology of the skin and promote HS development.

R. obeum: R. obeum is a propionate-producing anaerobic bacterium commonly found in the gastrointestinal tract of humans. R. obeum has been implicated in metabolic syndrome and gestational diabetes (Mokkala et al., 2021). In McCarthy et al. (2021), R. obeum was found to be depleted in the gut microbiome of patients with HS.

Faecalibacterium prausnitzii: Faecalibacterium prausnitzii is a nonmotile, gram-positive bacterium that represents >5% of the total bacterial population in the human intestinal tract. It has since been identified as a potential biomarker of intestinal health in adults, and low levels have been associated with IBD (Miquel et al., 2013). Furthermore, decreased levels have also been shown to be associated with other disease states, including psoriasis (Eppinga et al., 2016). However, these same findings were not recapitulated in patients with HS. Possible mechanisms behind F. prausnitzii and its anti-inflammatory benefits include its ability to induce large amounts of IL-10 in mononuclear cells and inhibit the production of proinflammatory cytokines such as IFN-γ, TNF-α, IL-6, and IL-12 (Miquel et al., 2013). Eppinga H, Sperna Weiland CJ, Thio HB, van der Woude CJ, Niijsten TE, Peppelenbosch MP, et al. Similar depletion of protective Faecalibacterium prausnitzii in psoriasis and inflammatory bowel disease, but not in hidradenitis suppurativa. J Crohns Colitis 2016;10:1067–75.

REFERENCES


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