Hidradenitis suppurativa in acute myeloid leukemia: Review of disease course and management

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INTRODUCTION
Hidradenitis suppurativa (HS) is a chronic inflammatory condition characterized by recurrent nodules and abscesses in apocrine gland-bearing regions. 1 Neutrophils are postulated to be pathogenic drivers in HS pathogenesis, since neutrophilia is often seen in patients with severe disease. 1-3 However, antineutrophil agents, such as dapsone, are generally ineffective in severe disease, suggesting that neutrophils may be a secondary contributor. 4 In order to further elucidate the role of neutrophils in HS pathogenesis, we performed a retrospective review of patients with HS and acute myeloid leukemia (AML) to observe the effect of neutrophil depletion during induction chemotherapy on HS. Our case series not only discusses the effect of neutrophil depletion on HS but also discusses the presentation, treatment, and impact of HS in patients with AML.

CASE SERIES
A retrospective review was performed by querying the patient databases of Mass General Brigham hospitals and Dana-Farber Cancer Institute for patients with International Classification of Diseases codes for HS and AML between January 1, 2010 and September 1, 2020. Patients with HS and AML treated with induction chemotherapy (7 days of cytarabine, 3 days of anthracycline, commonly referred to as “7+3”) were included. The primary outcome assessed was HS flare, which we defined as patient-reported new or enlarging nodules or sinus tracts with increased drainage and pain. Variables extracted included HS characteristics, vitals, lab results, and medications. Data were collected in REDCap.

Nine patients met the inclusion criteria; however, 1 was omitted because their HS diagnosis occurred after AML diagnosis. The remaining 8 patients included in the study are listed in Table 1. Five were women and 3 were men. Of those with Hurley staging described, 3 were stage II, and 1 was stage III. Average age of HS onset was 23 years old and average age of AML diagnosis was 42 years old. Seven of 8 patients experienced flares within one month of AML diagnosis. In 5 patients, HS flare was the main concern that led to AML diagnosis. These patients underwent multiple visits to their primary care provider or emergency department in the 4 weeks leading to AML diagnosis due to acute worsening of HS. Flares were recalcitrant to oral antibiotics and incision and drainage (I&D), which prompted blood work that revealed AML. One patient was diagnosed with AML after routine blood work, and his only abnormal symptom was increasing pain and drainage of HS lesions.

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| No. | Sex | PMH                                                                 | Age with first HS symptoms (years) | Age at AML diagnosis (years) | Hu St | Initial flare? | Description of initial flare                                                                 | Induction flare? | Count recovery flare? | HS treatments during chemotherapy |
|-----|-----|----------------------------------------------------------------------|-----------------------------------|-----------------------------|-------|---------------|------------------------------------------------------------------------------------------|-----------------|-----------------------|----------------------------------|
| 1   | F   | General anxiety disorder                                             | <20                               | 32                          | II    | Yes           | Presented to PCP for increasing size and drainage of axillary nodules. Cephalexin was started, and CBC was ordered, which revealed AML. | No              | No                    | Antibiotics, chlorhexidine wash    |
| 2   | M   | Hypertension, hyperlipidemia, Idiopathic thrombocytopenic purpura    | <20                               | 57                          | III   | Yes           | Routine blood work for a procedure revealed CBC concerning for AML. At the time, the patient's only symptom was increasing axillary pain and drainage for few weeks. | Yes             | Yes                   | Antibiotics                      |
| 3   | F   | Diverticulitis, hypertension                                         | <20                               | 42                          | II    | Yes           | Presented to PCP for constipation, severe fatigue, and 2 weeks of draining axillary and pannus nodules worse than usual. CBC revealed AML. Continued to develop axillary nodules and perineal abscess until induction chemotherapy was started. | Yes             | Yes                   | Antibiotics, chlorhexidine wash, I&D, intralesional triamcinolone |
| 4   | M   | Down syndrome, gout, hypothyroidism                                  | 24                                | 28                          | ND    | No            | N/A                                                                                       | N/A             | N/A                   | N/A                              |
| 5   | M   | Psoriasis, diabetes, coronary artery disease, heart failure, chronic obstructive pulmonary disease | <20                               | 64                          | ND    | Yes           | Developed recurrent “boils” in the perineum, which were treated with oral and intravenous antibiotics over the previous year. Presented to urgent care for evaluation of “boils” on the inner thighs associated with chills. CBC was ordered, which revealed AML. | ND              | ND                    | ND                               |
| 6   | F   | Migraines, PCOS                                                      | <20                               | 25                          | ND    | Yes           | Presented with “hidradenitis lesions” under the arm, bruising, and gum bleeding, which led to AML diagnosis.                                                                                      | ND              | ND                    | Antibiotics                      |
| 7   | F   | Asthma, migraines, PCOS                                              | 46                                | 47                          | II    | Yes           | Over 1 month, developed shortness of breath, fatigue, and worsening axillary nodules and drainage. Went to PCP and ED at least 3 times and received antibiotics and I&D. Ultimately, blood work revealed AML. Continued to develop axillary abscesses that required I&D until induction chemotherapy. | No              | No                    | Antibiotics, chlorhexidine wash, I&D, spironolactone |
| 8   | F   | Bipolar disorder, sweet syndrome                                      | 27                                | 27                          | ND    | Yes           | Diagnosed with HS due to multiple sinus tracks in the groin area and treated with antibiotics and marsupialization surgery. A few days later, discharge developed, prompting a CBC, which revealed AML. | ND              | ND                    | ND                               |

AML, Acute myeloid leukemia; CBC, complete blood cell count; ED, emergency department; F, female; HS, hidradenitis suppurativa; Hu St, Hurley stage; I&D, incision and drainage; M, male; N/A, not applicable; ND, not described; PCOS, polycystic ovarian syndrome; PCP, primary care provider; PMH, past medical history.

*Initial flare: Did HS flare <4 weeks before AML diagnosis?

Induction flare: Did HS flare with induction chemotherapy?

Count recovery flare: Did HS flare with count recovery?
Description of HS severity during induction chemotherapy was available for 4 patients (Table I). Two patients experienced improvement in HS flares after induction chemotherapy (despite remaining recalcitrant to oral antibiotics and I&D prior), and HS remained quiescent even when cell counts recovered. Conversely, 2 patients flared throughout induction chemotherapy and cell count recovery. Thus, patients may experience HS flares when neutrophils are depleted, but may also remain in remission when cell counts recover. This suggests that neutrophils (and white blood cell counts in general) do not correlate with HS symptoms, and may not be the primary driver in HS pathogenesis.

HS complicated these patients’ cancer treatment. Chemotherapy was often delayed due to concern for infection, fevers, or abscesses. Dermatology was frequently consulted for permission to proceed with chemotherapy and HS management. All patients survived induction chemotherapy with cell count recovery. However, 1 patient later passed away after his bone marrow transplant was heavily delayed due to severe perirectal HS requiring extensive surgical management. Finally, what is not represented in our data is the significant pain that patients experienced during their chemotherapy as a result of HS flares.

Treatment for HS during induction chemotherapy included chlorhexidine wash, systemic antibiotics, intraleional triamcinolone, I&D, and spironolactone (Table II). Antibiotics included vancomycin and cefepime for broad-spectrum coverage. Future clinicians may also consider ertapenem, clindamycin, rifampin, linezolid, and ceftriaxone, which have all been shown to improve HS. Ertapenem, in particular, is an effective rescue therapy for severe HS with fast onset. These antibiotics may also be considered for HS flares following bone marrow transplant.

**DISCUSSION**

This is the first retrospective study of HS and AML. Our data show that HS patients still exhibit active disease despite low-to-absent neutrophils in the peripheral blood, suggesting that neutrophils are not the primary pathogenic drivers. In 7 of 8 cases, acute and recalcitrant HS flare was a presenting sign of AML. Clinicians should have a low threshold to obtain complete blood count in such patients. In addition, clinicians should be prepared to treat flares in HS patients with AML. Uncontrolled disease may lead to neutropenic fever with or without sepsis or infection. Imaging studies can be performed to identify large abscesses, which should preferably be drained prior to chemotherapy induction, when immune cell counts drop. Treatments include topical and systemic antibiotics, intraleional triamcinolone for small lesions, and I&D of large abscesses (though only with stable blood counts). Antibiotics such as ertapenem, clindamycin, rifampin, linezolid, and ceftriaxone can provide both improvement in HS and broad antimicrobial coverage. Study limitations include the retrospective nature of the study, its small sample size, and lack of standardized lesion counts and physician global assessments. Further investigation on the role of other cells involved in HS pathogenesis is warranted.

**CONFLICTS OF INTEREST**

None disclosed.

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