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Pain and Itch Are Dual Burdens in Hidradenitis Suppurativa

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Objective: Hidradenitis suppurativa (HS) patients experience varying degrees of pain and itch. This study aimed to characterize the burden of pain and itch based on anatomic location, lesion type, time of day, and interference of daily activities.

Methods: From 2017 to 2019, an anonymous survey was distributed to patients in-person at HS Specialty Clinics (University of Arizona—Tucson, University of California—Los Angeles, and University of California—Davis) and international HS support groups (Hope For HS, International Association of HS Network, and HS Warriors) through social media.

Results: 856 patients responded. 95.2% of respondents reported experiencing pain, 77.5% reported itch, and 74.9% reported both. Most respondents (70.7%) described pain as most bothersome, 5.6% reported itch, and 21.6% reported both equally bothersome. The most reported areas affected by pain and itch are the groin folds (61.0%, 63.5%), axillae (59.0%, 61.4%), and medial thighs (47.1%, 52.7%). Active boils (96.3%), sores/ulcerations (55.0%), and draining sinus tracts (53.2%) are the most painful lesion morphologies. Active boils (66.5%) are itchiest followed by draining sinus tracts (56.8%), scars (49.9%), and sores/ulcerations (42.0%). Most respondents reported that pain and itch occurred at "random times" (75.9%, 70.0%) or in the evening (29.3%, 24.0%). Pain and itch-related discomfort most frequently interfered with exercise/sports (65.4%), leisure activities (62.3%), and sleep (59.7%).

Conclusions: Pain and itch are strong contributors to the debilitating nature of HS. Future investigations are warranted to explore the symptomatology beyond pain and itch in HS patients. By incorporating unique symptoms into disease grading, more targeted treatments may be designed to address these burdens.

Commercial disclosure: None identified.

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Using clonality of T-cell repertoire to distinguish between drug hypersensitivity reaction and acute graft-versus-host disease

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Graft-versus-host disease (GVHD) is a serious complication of hematopoietic stem cell transplantation, which often leads to morbidity and mortality if not diagnosed and treated early. Acute GVHD is characterized by a clinical triad of cutaneous eruptions, gastrointestinal dysfunction, and liver abnormalities. Cutaneous manifestations of acute GVHD frequently appear before symptoms of other organ systems, but the clinical and histologic features are similar to those of acute morbilliform drug eruption, thus generating a major diagnostic pitfall. Previous studies attempted to define microscopic features of acute GVHD, but these features were later found to be non-specific. We hypothesize that GVHD is mediated by clonal amplification of T-cell repertoire, and therefore can be distinguished from drug hypersensitivity reaction (DHR) by the presence of dominant T-cell receptor clones. To test this hypothesis, we performed "immunosequencing" of T-cell receptors in ten patients with acute GVHD and seven patients with DHR. We calculated the clonality of T-cell repertoire by using normalized Shannon entropy, and found that GVHD patients had significantly higher clonality than DHR patients (P value = 0.05). When a numeric cutoff of clonality alone was used to distinguish GVHD from DHR, a receiver operating characteristic curve had an area under the curve of 0.77. Using a clonality cutoff of 0.042 resulted in sensitivity of 60% and specificity of 71%. Although further validation studies may be required, these results suggested that clonality of T-cell repertoire may be used to distinguish GVHD from DHR in combination of other clinical features.

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Determining accuracy of teledermatology diagnosis of cellulitis

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Background: Despite the established economic benefit and improved patient outcomes of dermatology consultation for presumed cellulitis, broad implementation of in-person consultation remains impractical for many hospitals. The usefulness of teledermatology diagnosis of cellulitis is unknown.

Design: Survey of dermatology attendings from four institutions.

Methods: A survey containing 10 randomly-ordered patient cases representing either cellulitis (gold standard in-person dermatology evaluation) or pseudocellulitis was distributed to dermatologists. Information for each case was presented sequentially in three steps: 1) history and photographs, 2) a cellulitis-specific questionnaire, and 3) thermal images. Each attending chose a most-likely diagnosis after each additional piece of information, and was unable to change previous responses after proceeding to the next.

Results: The average respondent rated 80% of combined (cellulitis and pseudocellulitis) cases correctly (range 60%-100%) when provided initial history and physical, 82.1% (range 60%-100%) combined accuracy with the subsequent addition of cellulitis questionnaire, and 86.3% (range 60%-100%) with the final addition of thermal imaging. Respondents' average accuracy of cellulitis images rose with additional information (70.2% for H&P, 76.3% cellulitis questionnaire, and 83.3% for thermal imaging), while average accuracy remained high with pseudocellulitis images (>90% accuracy for all questions). Conclusion Diagnostic accuracy via teledermatology consultation was high for both cellulitis and pseudocellulitis. Future higher-powered studies could potentially demonstrate the utility of these supplementary data points for remote diagnosis. Teledermatology is valuable for hospitals lacking resources for universal in-person dermatology consultation looking to reduce cellulitis misdiagnosis and associated treatment costs and patient harm.

Commercial disclosure: None identified.

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Recurrent driver mutations in basal cell carcinoma tumors from one individual

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Background: Basal cell carcinoma (BCC) is the most common human cancer. Driver mutations in Sonic Hedgehog pathway such as PTCH1, PTCH2, SUFU, and SMO are recurring events, but little is known about the mutational landscape in other pathways.

Methods: We have obtained exome sequencing data on matched tumor-normal skin pairs from 40 tumors, including 1 patient with 6 BCCs. Following GATK's best practices, we have identified somatic cancer variants from matched tumor-normal skin pairs. In this abstract we focus on the individual with six BCCs.

Results: As expected, the COSMIC mutational signature 7 (UV radiation; 28%-62%) is the dominant signature in all BCCs from the same patient. There is significant variation in the importance of secondary mutational signatures ($P < .01$), such as COSMIC signature 3 (failure of DNA double-stranded break repair; 0%-19%). Focusing on loss-of-function variants, recurrent driver mutations in six genes were found in ≥50% of BCC samples. Consistent with BCC tumorigenesis, PTCH1 is the single most mutated driver gene (5/6 samples), with TP53 a close second (4/6 samples). We uncovered novel driver mutations in TPTE/PTEN2 (3/6 samples), a cancer testis antigen signal transduction phosphatase, and DCC (3/6 samples), a well known netrin receptor whose loss-of-function is a key feature of metastasis. Interestingly, we observed mutually exclusive mutations either in CSMD1 (3/6 samples) or CSMD3 (the other 3 samples), two paralogs whose loss-of-function result in epithelial proliferation in many cancers.

Conclusions: We identified novel driver genes important for BCC tumorigenesis shared in most, but not all, tumors originating from one individual.

Commercial disclosure: None identified.