

Hand eczema prevalence in this study is consistent with the findings of Lan et al,⁵ who reported a 74.5% prevalence of hand eczema among 526 HCWs during the COVID-19 pandemic.

Our findings showed no difference between HCWs and non-HCWs in terms of prevalence of hand eczema; however, there were some differences in the risk factors involved in eczema. According to previous studies conducted before the pandemic, it seems that hand eczema prevalence has increased during the COVID-19 pandemic (approximately 1.4) in HCWs. Proper identification of risk factors for hand eczema along with health education in this pandemic could aid in the prevention of eczema.

Mohammad Reza Pourani, MD
Mohammad Shahidi Dadras, MD
Hamideh Moravvej, MD
Skin Research Center
Shahid Beheshti University of Medical Sciences
Tehran, Iran

Atefeh Talebi, PhD
Colorectal Research Center
Rasool Akram Hospital
Iran University of Medical Sciences
Tehran, Iran

Hassan Vahidnezhad, PhD
Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College
Thomas Jefferson University
Philadelphia, PA
Jefferson Institute of Molecular Medicine
Thomas Jefferson University
Philadelphia, PA

Reza M. Robati, MD
Skin Research Center
Shahid Beheshti University of Medical Sciences
Tehran, Iran
Department of Dermatology
Loghman Hakim Hospital
Shahid Beheshti University of Medical Sciences
Tehran, Iran

Sahar Dadkhahfar, MD
Skin Research Center
Shahid Beheshti University of Medical Sciences
Tehran, Iran
sahar.dadkhahfar@gmail.com

Fahimeh Abdollahimajd, MD
Skin Research Center
Shahid Beheshti University of Medical Sciences
Tehran, Iran
fabdollahimajd@yahoo.com, fabdollahimajd@sbmu.ac.ir
Clinical Research Development Unit
Shohada-e Tajrish Hospital
Shahid Beheshti University of Medical Sciences
Tehran, Iran

REFERENCES

1. World Health Organization. Rational use of personal protective equipment (PPE) for coronavirus disease (COVID-19): interim guidance. World Health Organization. March 19, 2020. Available at: <https://apps.who.int/iris/handle/10665/331498>. Accessed June 1, 2020.
2. Cavanagh G, Wambier CG. Rational hand hygiene during the coronavirus 2019 (COVID-19) pandemic. *J Am Acad Dermatol* 2020;82(6):e211.
3. Flyvholm M-A, Susitaival P, Meding B, et al. Nordic Occupational Skin Questionnaire—NOSQ—2002. Nordic questionnaire for surveying work-related skin diseases on hands and forearms and relevant exposures. *TemaNord*. Copenhagen: Nordic Council of Ministers; 2002:518.
4. Sadeghian F, Delvarian Zadeh M, Kalalyan Moghadam H, et al. The prevalence of hand dermatitis, and some of the factors in the nursing and midwifery personnel. *Daneshvar Bimonthly* 2006;14(67):25–32.
5. Lan J, Song Z, Miao X, et al. Skin damage among health care workers managing coronavirus disease-2019. *J Am Acad Dermatol* 2020;82(5):1215–1216.

Acute Pancreatitis in 2 Adolescent Boys on Dupilumab Therapy for Atopic Dermatitis

To the Editor:

Dupilumab is an injectable, monoclonal interleukin 4 receptor antibody approved for the treatment of both moderate to severe atopic dermatitis (AD) and asthma in patients 12 years or older.¹ Adverse events related to dupilumab treatment are typically mild and include conjunctivitis and injection-site reactions.² Rare adverse effects of newer drugs such as dupilumab may arise during ongoing safety monitoring. Herein, we present 2 cases of acute pancreatitis in adolescent boys while on treatment with dupilumab.

Patient 1 was a 17-year-old adolescent boy with no significant medical history when he presented for treatment of severe AD. Prior therapy included methotrexate 20 mg weekly (stopped in 2016). The patient continued to flare, despite treatment with cyclosporine 250 mg daily. In April 2017, he started dupilumab 300 mg every 2 weeks. In June 2017, dupilumab was increased to 300 mg weekly because of lack of improvement. After 2 weeks, he had an AD flare and secondary bacterial infection and was treated with a 1-week prednisone taper and doxycycline 100 mg twice daily for 10 days. Cyclosporine 300 mg daily was also restarted at this time. (Patient 1 had been taking this medication intermittently for severe flares since 2014). Twenty days after increased frequency of dupilumab was commenced, he presented to the emergency department with acute onset of severe abdominal pain, nausea, vomiting, and diarrhea. Workup was notable for elevated triglyceride (253 mg/dL) and elevated lipase (2879 U/L) levels. Abdominal ultrasound revealed inflammatory changes along the pancreas but no cholelithiasis or bile duct

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dilation. Abdominal computed tomography showed peripancreatic fluid. Findings were consistent with acute pancreatitis. He had no history of smoking, alcohol abuse, drug use, abdominal trauma, or autoimmune disorder. Dupilumab was restarted at 300 mg every 2 weeks with a prednisone taper at discharge. He did not experience further pancreatitis upon rechallenge of dupilumab. Because of lack of AD control, prednisone was required intermittently, and after 6 months of ineffective therapy, dupilumab was discontinued.

Patient 2 was a 15-year-old adolescent boy with AD and no significant medical history. In December 2018, he started a 10-day course of clindamycin 300 mg twice daily for a severe flare of AD with secondary bacterial infection. Given lack of improvement, a 3-week prednisone taper was started 3 days later. Two days after the initiation of prednisone (December 19, 2018), the patient began dupilumab 300 mg every 2 weeks. Previous treatments included topical corticosteroids (ongoing) and methotrexate (stopped in November 2018). Patient 2 received a total of 3 injections of dupilumab 300 mg, before presenting to the emergency department with severe left lower quadrant pain on January 25, 2019. Workup was notable for elevated lipase (1502 U/L) and mildly elevated total bilirubin (2.2 mg/dL) levels. Abdominal ultrasound showed mild amounts of free fluid in the upper perisplenic area but no evidence of cholelithiasis, pancreatic parenchymal abnormalities, or bile duct dilation. He had no history of smoking, alcohol abuse, drug use, abdominal trauma, or autoimmune disorder. He was admitted for symptomatic treatment of acute pancreatitis (ie, intravenous fluids, liquid diet, and pain control) and then discharged to our dermatology clinic. Because his AD had not improved after receiving 3 doses of dupilumab, and a drug-induced etiology for the pancreatitis could not be ruled out, the drug was discontinued, and AD was treated with topical steroids. The patient denied further symptoms of pancreatitis over the subsequent 3 months.

Acute pancreatitis presents with sudden-onset severe abdominal pain, resulting from pancreatic inflammation. Common causes include gallstones, alcohol, hypertriglyceridemia, and pancreatic duct injury.³ Acute pancreatitis due to medications is rare and is estimated to represent fewer than 5% of cases.³ Various mechanisms are implicated in drug-induced pancreatitis, including immunologic reactions, accumulation of toxic metabolites, direct toxic effects, increased viscosity of pancreatic fluid, and intravascular thrombosis.⁴ The comprehensive workup for the underlying cause of acute pancreatitis in both patients failed to demonstrate evidence of common etiologies. We therefore considered possible rare causes of acute pancreatitis, including medications.

Two different classification systems for estimating causality of medication-associated adverse events have been proposed. Naranjo et al⁵ in 1981 developed a probability scale for drug-associated

events. When applying the Naranjo scale to our cases, patient 1 scored 2/10, and patient 2 scored 5/10, which classify as possible and probable adverse drug reactions, respectively. Badalov et al⁴ in 2007 published a 3-tier classification system for medications implicated in drug-induced pancreatitis. In this system, class I drugs are considered likely causes of pancreatitis (having at least 1 case report with positive rechallenge), and class III are possible culprit medications (having at least 2 cases in the literature, with no consistent latency and no reports of rechallenge). Doxycycline is a class I medication, and prednisone and cyclosporine are both class III.

Both patients were taking medications that have been associated with drug-induced pancreatitis before developing their acute episodes. Both patients were taking dupilumab when they presented with acute pancreatitis. Patient 1 was also taking cyclosporine, doxycycline, and tapering doses of prednisone while on dupilumab. Although doxycycline is considered class I, reported doxycycline or tetracycline derivatives linked to pancreatitis have had doses ranging from 1 to 2 g/d^{4,6}; patient 1 was only on 200 mg/d. Patient 1 also had previously been exposed to multiple trials of cyclosporine and prednisone without the manifestations of acute pancreatitis. At the time of onset of acute pancreatitis, patient 2 was also completing a prednisone taper while on treatment with dupilumab. Patient 2 had been exposed to prednisone on numerous occasions without the development of acute pancreatitis.

Demonstrating the causative association between a drug and development of pancreatitis is difficult, as pancreatitis may occur within weeks to months after initiation of a medication. With no recurrence on rechallenge, variable latency, and confounding medication use, it is not possible to draw a definitive conclusion on the direct causality of dupilumab and pancreatitis in these cases. However, the development of acute pancreatitis while on dupilumab in these otherwise healthy adolescent boys is striking. It is interesting to note that neither of these patients with severe AD had a positive response to dupilumab therapy.

To our knowledge, dupilumab has not been otherwise associated with the development of acute pancreatitis. More long-term data on the safety profile of dupilumab are needed and may provide clarity on the potential existence and mechanisms of uncommon adverse effects, such as acute pancreatitis.

Ryan C. Stoner, PhD
School of Medicine
Oregon Health and
Science University, Portland

Solveig Ophaug, MD
Eric Simpson, MD
Jon Hanifin, MD
Department of Dermatology
Oregon Health and Science
University, Portland
hanifinj@ohsu.edu

REFERENCES

1. Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med* 2016;375:2335–2348.
2. Ou Z, Chen C, Chen A, et al. Adverse events of dupilumab in adults with moderate-to-severe atopic dermatitis: a meta-analysis. *Int Immunopharmacol* 2018;54:303–310.
3. Vinklerova I, Prochazka M, Prochazka V, et al. Incidence, severity, and etiology of drug-induced acute pancreatitis. *Dig Dis Sci* 2010;55:2977–2981.
4. Badalov N, Baradarian R, Iswara K, et al. Drug-induced acute pancreatitis: an evidence-based review. *Clin Gastroenterol Hepatol* 2007;5:648–661; quiz 644.
5. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981;30:239–245.
6. Moy BT, Kapila N. Probable doxycycline-induced acute pancreatitis. *Am J Health Syst Pharm* 2016;73:286–291.

Hidradenitis Suppurativa Caused by Vedolizumab

Dear Editor,

Inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn disease (CD), is characterized by chronic intestinal inflammation, mucosal ulceration, and tissue damage. The treatment of patients with IBD has been changed by the development of biological therapies, such as tumor necrosis factor α (TNF- α) blockers and a new biological target therapy vedolizumab (VDZ). Vedolizumab is a gut-selective, monoclonal antibody targeting $\alpha_4\beta_7$ integrin.¹

Here, we report, to our knowledge, the first case of hidradenitis suppurativa (HS) induced by VDZ.

A 40-year-old woman was diagnosed in 2012 for UC located in the entire colon. The diagnosis was confirmed by colonoscopy and biopsies. She was previously treated with mesalazine, thiopurines, and corticosteroid. However, due to an insufficient response to steroids and persistent vomiting during thiopurine

use, treatment with VDZ was started. After 8 months of treatment with VDZ and mesalazine, the patient showed remarkable improvement in her UC condition, but she developed erythematous, painful inflamed nodules and cysts on her axillae and inguinal regions. Because of the suspected iatrogenic side effect, the gastroenterologist team decided to discontinue VDZ and continue therapy with mesalazine, resulting in complete resolution of cutaneous clinical manifestations after 2 months. Four months after discontinuation of VDZ, they decided to reintroduce VDZ again for better control of UC, with the consequent reappearance of skin manifestations. Therefore, they decided to send the patient to us for a dermatological consultation.

On dermatological examination, numerous painful and suppurating nodules and cysts with some fistulous tracts on the axillae and inguinal areas were observed (Figs. 1A, B). These clinical features confirmed the diagnosis of HS (Hurley stage II), and considering the clinical history, a diagnosis of drug-induced HS by VDZ was made. The patient was treated with tetracycline hydrochloride 250 mg 4 times a day for 2 months and topical clindamycin cream twice a day for 2 months, resulting in improvement of the HS.

Extraintestinal manifestations are present in 15% to 20% of UC patients and 20% to 40% of CD patients. Dermatological extraintestinal manifestations include a broad spectrum of skin diseases, such as erythema nodosum, pyoderma gangrenosum, psoriasis, and HS.² Hidradenitis suppurativa affects approximately 13% of the CD patients, but in the literature, there are no data about UC patients.³ The treatment of patients with IBD has been changed by the development of biological therapies, such as TNF- α blockers. Nevertheless, TNF- α blockers can trigger HS manifestations.¹

Vedolizumab is unique among biologics used to treat IBD because it specifically targets the gastrointestinal tract. This permits the reduction of extraintestinal side effects, including dermato-

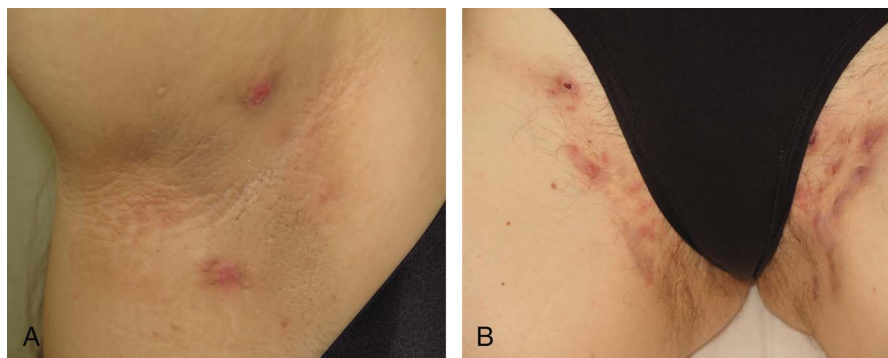


Figure 1. Numerous painful and suppurating nodules and cysts on the axilla and some fistulous tracts on the inguinal areas.

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logical ones. Vedolizumab is considered to have a good side effect profile, and no dermatological side effects have been reported in literature, but a few recent case reports mention exacerbation of