

Clinical Dermatology and Other Cutaneous Disorders

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Clinical evaluation of 168 Korean patients with rosacea: Sun exposure correlates with erythematotelangiectatic subtype

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Background: Though rosacea is a chronic cutaneous inflammatory disorder commonly seen in adults, the etiology and pathogenesis still remain unclear. Well established diagnostic classification and grading system may play a critical role in performing research and would serve diagnostic reference in clinical field.

Objectives: We sought to classify the patients with new standard classification and grading system and find peculiar features and relationship of each subtype. Also we analyzed the relationship between degree of sun exposure and each subtype.

Methods: We reviewed medical records, and clinical photos of 168 patients diagnosed with rosacea from 2002 to 2007. Standard classification and grading system suggested by National Rosacea Society (NRS) Expert Committee were adopted to evaluate each patient's subtype and severity.

Results: The male:female ratio was 1:2.29. Mean age at diagnosis was 47.8 years. Mean duration of disease was 3.5 years. Sun exposure and hot bath/exercise were two most common precipitating factors, while majority of patients did not have specific relieving factors. By NRS classification and grading system, patients were classified into four subtypes. One hundred sixty two (96.4%) patients were diagnosed with erythematotelangiectatic subtype irrespective of severity. Eighty five (50.6%) patients had papulopustular subtype and 24 (14.3%) patients had ocular rosacea. Eight (4.8%) patients had mild phymatous change. Degree of sun exposure had significant correlation with development and severity of erythematotelangiectatic subtypes ($p < 0.05$), while no correlation with papulopustular, ocular and phymatous subtypes.

Conclusion: Though erythematotelangiectatic subtype was the most common subtype of rosacea, many patients also had other subtypes of rosacea simultaneously. Especially, based on our result, we proved that ocular rosacea is an extension of clinical spectrum of erythematotelangiectatic rosacea. In addition, the result suggests that sun exposure influences each subtype differently

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A dramatic presentation of metastatic adenocarcinoma of the skin

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Background: Adenocarcinoma metastasizing to the skin is an uncommon, but well-documented entity associated with a poor prognosis. We discuss the presentation of a patient with skin metastasis presumed to be pancreatic in origin manifesting as nodular growths on the left upper eyelid and scalp.

Observation: A 76-year-old Caucasian man presented for excision of a 3-mm x 2.7-mm erythematous papule located on his left upper eyelid of one-month duration. A biopsy performed by the referring physician revealed adenocarcinoma and was presumed to be a primary tumor of the meibomian glands. Two scalp nodules were noted on physical examination on the posterior parietal scalp and overlying his right mastoid process measuring 3-cm and 2-cm respectively. Biopsies of the nodules were also consistent with metastatic adenocarcinoma and stained positive for both cytokeratins 7 and 20. Imaging studies demonstrated two poorly defined lung nodules on chest radiography; multiple chest wall, axillary and abdominal masses including a 5.8-cm mass at the tail of the pancreas on computed tomography scans; and increased uptake in the tail of the pancreas and axillae with several smaller foci within the liver, lungs, thoracic vertebrae and occipital bone on PET scan. The pancreatic mass was presumed to be the site of origin. The patient was treated with palliative radiation therapy and succumbed to his disease within two months of his initial presentation.

Comment: Metastatic carcinoma to the skin presents as flesh-colored, erythematous, or violaceous nodules and is associated with a poor prognosis. Skin metastases can occur through direct extension, implantation from a procedure or dissemination through the vasculature. Impressive papulonodular lesions involving the eyelid and scalp were the presenting feature in our patient with the pancreas as the presumed site of origin. We present the patient to demonstrate the many guises of metastatic disease and to encourage physicians to perform complete physical examinations and appropriate imaging studies if a cutaneous nodule is consistent with adenocarcinoma.

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A case of eruptive vellus hair cyst developed on the labium major

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A 64-year-old woman was presented with the unknown onset of several pinhead-to-matchhead-sized yellowish papules on the inner side of labium major. She had felt itching on the both labium majors for 3 years when she visited the hospital. However, the papules on the labium major were asymptomatic and she didn't know when the lesions had appeared. She had no notable family history of any such occurrences. She had two normal, uncomplicated spontaneous vaginal deliveries, with both pregnancies going full term. A biopsy specimen from the yellowish papule showed a mid-dermal cyst, which was lined by a stratified squamous epithelial cells and filled with laminated keratin materials and cutting vellus hair shafts. These findings were consistent with eruptive vellus hair cysts.

Eruptive vellus hair cysts(EVHC) are asymptomatic, flesh-colored-to-bluish, 1-to-4 mm-sized papules that are usually located on the chest and extremities of children and young adults. Histologically, small cysts are revealed in the mid-dermis containing multiple hair shafts and keratinous materials. The uniqueness of this case is its atypical location. Until now, there have been reports of EVHC on the chest, extremities, face, neck, and buttocks but not on the labium major. To our knowledge, this is first case report of eruptive vellus hair cysts arisen on the labium major. The cause that the lesions are localized only on the labium major in this case is obscure. Some studies postulated that cystic lesions may be formed by the triggers such as minor trauma or scratching, but there is no clear evidence about it. In our case, the scratching for 3 years might have been a triggering factor for the EVHC of the area.

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Injectable poly-L-lactic acid for human immunodeficiency virus-related facial lipoatrophy: 1-year interim 5-year study results

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Background: Injectable poly-L-lactic acid (iPLLA) is approved for restoration and/or correction of the signs of facial lipoatrophy in people with human immunodeficiency virus (HIV).

Objective: The primary objective of the study was to evaluate the long term safety of iPLLA in subjects with HIV-associated facial lipoatrophy by Fitzpatrick skin type (FST) and gender.

Methods: This 1-year interim analysis of a 5-year, multicenter, open-label study included adult HIV-positive subjects with facial lipoatrophy. Subjects received up to 6 treatments at 4- to 6-week intervals, with adverse event (AE) assessments at weeks 4, 12, 24, and 1 year after initial treatment session. Yearly posttreatment evaluations included AEs, clinical evaluation of facial lipoatrophy using the James scale (grade 1 = mild; grade 4 = severe) and completion of a Likert-based Physician and Subject Satisfaction questionnaire using baseline photographs for comparison.

Results: Results from 290 treated subjects, mean age, 47.8 years, (female/FST I-III: n=70; female/FST IV-VI: n=70; male/FST I-III: n=74; male/FST IV-VI: n=76) were analyzed. Majority of AEs were mild or moderate; most frequently reported AEs being injection site nodule (8.6%), injection site papule (6.2%), injection site bruising (6.2%). Subjects of either gender with FST IV-VI had numerically lower rates of nodules and papules (female/FST I-III: papule/nodule 6/6; female/FST IV-VI: papule/nodule 4/2; male/FST I-III: papule/nodule 6/12; male/FST IV-VI: papule/nodule 2/5). Hypertrophic scars or keloids were not reported in any subject group. The overall rate of serious adverse events (SAEs) was 9.7%; none related to iPLLA treatment. At year 1 visit, all groups demonstrated significant improvement from baseline in James scale facial lipoatrophy units (-1.4 units overall, $P < 0.0001$). The overall Satisfaction With Treatment was "very good" or "excellent" for 96.2% physicians and 89.8% patients, and comparable among all groups.

Conclusions: Overall subjects with FST IV-VI reported numerically lower rates of product-related AEs. No subject developed hypertrophic scars or keloids on or before year 1 and no treatment-related SAEs were observed. Treatment with iPLLA resulted in statistically significant improvements from baseline in James scale facial lipoatrophy scores. High physician and subject satisfaction also was reported similarly among all groups.

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Successful treatment of necrolytic acral erythema with zinc supplementation

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Background: Necrolytic erythemas are a group of disease processes with an association to nutrient deficiencies or systemic illnesses. One of the more well known entities within this classification is necrolytic acral erythema (NAE). NAE has been associated with hepatitis C infection and recent studies have shown improvement with empiric treatment with zinc. Herein we discuss a case of NAE with a rare lab documented zinc deficiency successfully treated with oral supplementation, a review of the literature, and discussion of questions that still remain in this ever more prevalent condition.

Observation: A 47 year old female with history of hepatitis C and Grave disease presented with a several month history of hypertrophic, hyperpigmented plaques and erosions of her dorsal feet, heels, and toes. Plaques had an erythematous border and were exquisitely painful and pruritic. Previous treatment for suspected tinea pedis with a terbinafine/hydrocortisone mixture was unsuccessful. Other unresponsive treatments included lactic acid and betamethasone ointment for suspected contact dermatitis versus hypertrophic lichen planus. Serum zinc level was found to be 29, far below average value of 60-130. Hepatitis C quantitative value was 166,000. Treatment with zinc gluconate 220mg twice per day resulted in noticeable patient improvement in as little as ten days. All erosions had healed and plaques were markedly reduced by two week follow up. Zinc dosage was reduced by half at one month follow up with continued improvement. Patient was further referred to gastroenterology for treatment of her hepatitis C.

Comment: Necrolytic acral erythema has been well described in the literature as a cutaneous marker of hepatitis C. While the association of zinc deficiency and NAE has been delineated, the exact mechanism of pathogenesis is still unknown. Leading theories support that the disease process, by way of an unknown mechanism, causes the kidneys to excrete excessive amounts of zinc into the urine. There has also been a case reported of NAE in a hepatitis C negative patient, further complicating the picture. Only a handful of cases of NAE have been published in the United States, with even fewer containing lab documented zinc deficiencies. Given the prevalence of hepatitis C in the US and around the world, NAE is a clinical entity that warrants further study and is becoming more likely to be encountered in a clinical setting.

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Cutaneous lupus erythematosus and TNF α therapy: A case report with review of the literature

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Background: Anti-tumor necrosis factor- α (TNF α) immunotherapy is revolutionizing the treatment of immune disease, particularly Crohn's disease, rheumatoid arthritis, psoriatic arthritis, and psoriasis. The role of anti-TNF α agents in the management of cutaneous lupus erythematosus (LE), however, is not as clear.

Objectives: We sought to study the available literature to determine the mechanisms of action and efficacy of the three currently available anti-TNF α agents, etanercept, infliximab, and adalimumab, on cutaneous LE.

Methods: We present a case of a patient whose persistent discoid LE (DLE) was exacerbated by a trial of adalimumab, conducted a literature search of Pubmed, and identified 26 reports to date, to our knowledge, of anti-TNF α agents used to treat cutaneous LE.

Results: Only two reports demonstrated successful use of these medications in patients with SLE and sub acute cutaneous lupus erythematosus (SCLE), while 24 cases identified, induced at least one cutaneous manifestation of LE or lupus-like rash. In all 24 cases, the skin lesion regressed upon discontinuation of the anti-TNF α medication.

Limitations: Additional long-term observational studies of patients treated with anti-TNF α therapy for immune diseases would further help us understand the role of TNF α in LE.

Conclusions: After analysis, we consider three mechanisms whereby this arguably paradoxical effect may occur. We conclude that despite the suggested role of TNF α in promoting LE immunopathogenesis, anti-TNF α agents appear to exacerbate, not ameliorate, the disease.

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Hydroxyurea dermatopathy: Report of a case

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Hydroxyurea dermatopathy, also called pseudo-dermatomyositis or dermatomyositis-like reaction, is the most common adverse cutaneous reaction to hydroxyurea and generally occurs after several years of treatment. The classic presentation is scaly erythema over the dorsa of the hands with atrophic and telangiectatic changes, along with scaly or erythematous plaques over the bony prominences. These lesions are similar clinically and histologically to the Gottron's papules commonly seen in dermatomyositis. The reddish-violaceous heliotrope eruption around the upper eyelids that is considered the most specific skin manifestation of dermatomyositis is rare in hydroxyurea dermatopathy, but has been reported. Other dermatological changes include xerosis and cutaneous atrophy, which are almost constant with long-term treatment, as well as photosensitivity, palmoplantar hyperkeratosis, necrotic hand and leg ulcerations, multiple actinic keratoses, and squamous cell carcinomas. Myositis is generally not present, and thus muscle strength and creatinine kinase levels are normal.

Many of the manifestations of hydroxyurea dermatopathy are benign, and alternatives to hydroxyurea for treatment of polycythemia vera are limited, so any decision to withdraw hydroxyurea should be made on an individual basis, taking into account the patient's complete medical picture. Interferon alpha is one alternative treatment for polycythemia vera that has been successfully used in some patients.

We report a case of a 56-year old woman who presented with an eruption on the dorsal aspect of her hands and lower legs as well as brown hyperpigmentation on the sides of her face. Her medical history was significant for hypertension, hypothyroidism, polycythemia vera, depression, anxiety, and paranoia. Medications included atenolol, lisinopril, felodipine, levothyroxine, hydroxyurea, escitalopram, lorazepam, and quetiapine.

Physical exam showed thin, pink, non-tender, scaly papules and plaques on the dorsal surface of the metacarpal, proximal, and distal interphalangeal joints bilaterally (Fig 1). Additionally, brown hyperpigmented macules were notable along the sides of her face, and diffuse, extensive telangiectasias were prominent over the lower legs extending to the dorsal surfaces of her feet (Fig 2).

Histopathologic examination of the skin biopsy specimen (Fig 3) revealed mild vacuolar interface dermatitis and perivascular inflammation consistent with Gottron's papule.

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Use of topical tretinoin and the development of non-localized adverse events: Evidence from a systematic review of the literature

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Background: To investigate the safety of topical retinoids, we conducted a systematic literature review of non-teratogenic, non-localized adverse events (AEs) among patients treated with topical retinoids.

Methods: We sought all studies published in English through September 2008 and accepted trials reporting the development of a non-teratogenic non-localized AE among patients treated with topical retinoids for any indication.

Results: The literature search yielded 2,778 citations of which 25 studies reported the occurrence of an AE. Tretinoin was used in 23 of the studies. The most common AEs were headache (32%), infections (23%) and nausea (19%). None of the AEs were considered serious, and none was judged by the investigator to be related to treatment. Three reports (one case report, two randomized controlled trials) reported the occurrence of malignancies. The case report described a patient treated with tretinoin cream for a pigmented skin lesion which was subsequently found to be malignant. One randomized trial assessed the use of isotretinoin cream for the treatment of actinic keratosis in which two patients in the isotretinoin group developed skin cancer compared with five patients in the placebo group. The other randomized trial studied the use of topical tretinoin for the prevention of non-melanoma skin cancer. This trial was stopped early due to an imbalance in mortality between the treatment and the placebo groups. The imbalance was not specific to any particular illness and the authors conclude that a causal association with topical tretinoin and mortality is unlikely.

Conclusion: This review is consistent with other published data indicating the safety of topical retinoids. The majority of the AEs reported consisted of non-severe, nonspecific symptoms, and no AEs were judged by investigators to be related to retinoid treatment. Based on this review it can be concluded that there is no clear published evidence of a relationship between the use of topical retinoids, especially tretinoin, and the development of non-localized AEs.

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Giant cell fibroblastoma

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Giant cell fibroblastoma (GCF) is a rare superficial soft tissue tumor first reported in 1982. Several additional cases have been reported since, many with genomic analyses, suggesting that GCF is likely related to the more common dermatofibrosarcoma protuberans (DFSP). Here, we report a case of this uncommon tumor occurring in a young female.

A 13-year old Caucasian female presented complaining of an asymptomatic slowly growing nodule of her inner left thigh which began one year prior following trauma from a bicycle accident. Physical examination revealed a well appearing young female with a 1.7 by 2.5 cm brownish-red irregular nodule of the left superior medial thigh. The lesion was soft, non-tender and the patient had no inguinal lymphadenopathy.

A biopsy of the lesion revealed a spindle cell neoplasm filling the entire dermis and expanding the subcutaneous septae. The tumor was composed primarily of bland spindle cells with admixed stellate and multinucleated giant cells, arranged in a loose, myxoid stroma. The cells demonstrated mild nuclear atypia. Scattered pseudovascular spaces lined by floret-type giant cells were present. Lesional cells stained diffusely positive with CD34.

Giant cell fibroblastoma is a rare dermal and subcutaneous mesenchymal tumor that predominantly affects children and is more common in males, although it has been described in all age groups. It is a locally aggressive tumor that tends to recur following excision, but does not metastasize. GCF is characterized by a chromosomal translocation (17;22) which leads to the fusion gene COL1A1-PDGFB. This t(17;22) also characterizes DFSP and recent studies demonstrate that the gain of extra copies of the fusion gene may be associated with the histologic evolution of GCF into DFSP; this gain in copies is also a common oncogenic mechanism for fibrosarcomatous transformation of DFSP. CD99 positivity has also recently been demonstrated in both GCF and DFSP.

Mohs excision of the tumor was recommended but the patient chose to undergo a local wide resection with a medial thigh flap repair under general anesthesia. She is doing well post-operatively without sign of residual or recurrent neoplasm.

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Persistent acantholytic dermatosis in the setting of end-stage renal disease and hemodialysis

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A 69-year-old Caucasian male with a history of end-stage renal disease (ESRD) on hemodialysis presented to the dermatology clinic with a three month history of a pruritic eruption. In addition to ESRD secondary to polycystic kidney disease, the patient's medical history was significant for coronary artery disease, hypertension, hypercholesterolemia, anxiety and gout. He denied any history of eczema, psoriasis or skin cancer. He described his itch as so intense that it kept him awake at night.

Hemodialysis itself seemed to exacerbate the pruritus, recently to the extent that several hemodialysis sessions had to be shortened prematurely because the itch became intolerable. Topical triamcinolone cream brought no relief. Physical examination revealed scattered 2-4 mm pink papules, some with overlying hemorrhagic crust, distributed over the chest, back and extremities. Biopsy of two such lesions revealed suprabasilar acantholysis with dyskeratosis, consistent with Grover's disease (transient acantholytic dermatosis). Gram stain showed no microorganisms. The skin findings and symptoms improved markedly following continued triamcinolone topical therapy plus gabapentin 100 mg nightly. (Medications with anti-cholinergic side effects were avoided due to a history of associated delirium.) Grover's disease that persists or recurs over months to years is more aptly termed 'persistent acantholytic dermatosis.' The etiology of these eruptions is not known. A possible link between ESRD and persistent acantholytic dermatosis has been postulated in the literature. Chua has reported two cases of persistent acantholytic dermatosis with chronic renal failure, in the setting of both hemodialysis and peritoneal dialysis. Casanova et al. describe four hemodialysis patients who developed lesions clinically and histologically consistent with Grover's disease, but that persisted chronically; in one, the lesions resolved following kidney transplantation.

Given that conditions like asteatotic eczema, atopic dermatitis, and cutaneous irritation have been shown to be associated with Grover's disease to a statistically significant degree, the xerosis and decreased sweating of ESRD have been suggested as possible factors predisposing to persistent acantholytic dermatosis. Regardless of disease pathogenesis, the possibility of persistent acantholytic dermatosis should be entertained when evaluating ESRD patients with complaints of pruritus.

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Mucocutaneous side effects associated with liposomal doxorubicin therapy: A case series of six patients

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Polyethylene glycol-coated liposomal doxorubicin (Caelyx) is a new form of doxorubicin which is an anthracycline antineoplastic agent causing antitumour activity through inhibition of DNA synthesis. It has been approved for AIDS-related Kaposi sarcoma, aggressive Non-Hodgkin lymphoma, refractory ovarian cancer and breast cancer. Compared to free doxorubicin, liposomal form has been associated with increased efficacy, reduced myelosuppression and cardiac side effects. However, mucocutaneous side effects still occurs and can be dose-limiting. The most common mucocutaneous side effects of this drug are acral erythrodysesthesia, diffuse follicular eruption, intertrigo-like eruption, stomatitis and development of new melanotic macules. Herein, we report six consecutive patients who were referred to Dermatology department between January-December 2008 because of various mucocutaneous side effects attributed to liposomal doxorubicin therapy. A basic severity scale of I through IV was adopted for toxic effects to the skin, based on National Cancer Institute common toxicity criteria.

Acral erythrodysesthesia was observed in all six patients. Intertrigo-like eruption was identified in four of them. One patient developed diffuse follicular eruption with stomatitis, and one showed new melanotic macules on the palms. Two of the patients developed Grade III skin lesions, one of which was compatible with acral erythrodysesthesia and the other with intertrigo-like dermatitis. Mucocutaneous side effects occurred after third chemotherapy cycle in 3 patients, and after second cycle in the remaining 3 patients (median time interval of appearance was 15 days (range: 10-19 days). Dermatologists should be aware of the potential mucocutaneous side effects of liposomal doxorubicin therapy which is increasingly being used in certain types of cancer.

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Quantitative sensation testing is abnormal in the majority of patients with erythromelalgia: Studies using computer-assisted sensory examination (CASE)

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Background: Erythromelalgia is a rare disorder characterized by burning pain and warmth and redness of the extremities. The etiology is unknown. The degree of pain is often severe. Computer-Assisted Sensory Examination (CASE) is a standardized quantitative sensory test; it can be used to detect altered pain threshold and sensory alteration in disease. CASE is composed of several testing measures, including vibratory detection threshold (VDT), cooling detection threshold (CDT), and heat-pain testing (HPT). In this way, CASE evaluates altered sensation for different classes of cutaneous receptors and their nerve fibers. VDT tests A-alpha-B receptors and long, large sensory neurons, CDT tests A-alpha fibers and small fiber neurons, and HPT tests drC unmyelinated large fiber neurons.

Methods: Retrospective study, examining the results of CASE studies in patients with definitive diagnosis of erythromelalgia.

Results: 43 patients with definite erythromelalgia were studied with CASE. 70% had abnormal CASE studies (VDT, CDT and/or HPT abnormalities), 9% had equivocal results and 21% had normal CASE studies. Isolated Vibration Detection (VDT) abnormality was found in 9.3% patients, isolated Cold Detection (CDT) abnormality was found in 9.3% patients, isolated Heat-Pain Test (HPT) abnormality in 18.6% patients, VDT + CDT abnormality in 4.7% patients, VDT + HPT abnormality in 11.6% patients, CDT + HPT abnormality in 4.7% patients and VDT + CDT + HPT (pan modality) abnormality in 7% patients.

Conclusions: The majority of patients with erythromelalgia have abnormal Quantitative Sensation Testing as measured by CASE; multiple modalities of sensation are altered.

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Prevalence of hidradenitis suppurativa and co-morbidities in a large patient care database

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Hidradenitis suppurativa (acne inversa) remains a poorly understood and understudied disease. The exact prevalence is unknown; most estimates based on small European patient cohorts and surveys range from 0.3%-4%. We sought to estimate the prevalence of hidradenitis suppurativa in the US and identify associated co-morbidities which might ultimately lead to early diagnosis, affect treatment options, and improve quality of life. We analyzed a retrospective cohort of 4.6 million patients affiliated with the Partners Health Care System with electronic records dating between 1/1/1979 and 11/30/2008. The overall prevalence of diagnosed hidradenitis suppurativa (ICD-9 code 705.83) was 0.05%. It was approximately three times more common among females, and over 80% of cases occurred in patients ages 18-60. As compared to the general patient population, patients with hidradenitis suppurativa were more likely to be black or Hispanic (19% and 12%, respectively). We also examined the frequency of chronic conditions previously hypothesized to be associated with hidradenitis suppurativa. Diabetes, dyslipidemia, thyroid disease, mental disorders, polycystic ovarian syndrome, and arthropathies were more common among patients with hidradenitis suppurativa ages 18 and older, compared to patients in the same age range in the general patient population. Obesity and smoking also appear to be more common among patients with hidradenitis suppurativa; however, these data may be biased by under-use of these diagnostic codes in electronic records. We conclude that in a large patient care population, hidradenitis suppurativa is associated with a variety of chronic co-morbidities and is more common among females and minorities.

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Acral erythema and neutrophilic dermatosis and induced by paclitaxel

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Paclitaxel is an antineoplastic agent in the class of microtubule-stabilizing antitumor agents. The taxanes are used for the treatment of advanced and refractory lung, breast, head and neck, bladder and other epithelial cancers. Cutaneous drug reactions associated with paclitaxel treatment are rare and include bullous fixed drug eruptions, acral erythema, erythema multiforme, pustular eruptions, scleroderma-like cutaneous lesions and onycholysis. Here the first case of neutrophilic dermatosis and acral erythema induced by paclitaxel is reported. A 77-year-old woman presented with painful red, round and scaly papules and plaques on dorsal hands and multiple tender erythematous crusted papules and nodules on anterior legs two weeks after the administration of paclitaxel for breast cancer. The diagnosis was confirmed by skin biopsy with dermatopathological evaluation and laboratory studies

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