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Journal Watch

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Mucocutaneous findings and course in an adult with zika virus infection

Derrington SM, Cellura AP, McDermott LE, Gubitosi T, Sonstegard AM, Chen S, et al.
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Zika virus (ZIKV) is an enveloped, single-stranded RNA flavivirus that is transmitted by the mosquito vector *Aedes aegypti*. Recent outbreaks of ZIKV infection have occurred in Brazil and different regions of the world since 2015. Association of ZIKV infection with Guillain-Barré syndrome and microcephaly was reported in 2015. According to the case definition by the World Health Organisation, a person is suspected of being infected with ZIKV if there is an erythematous eruption and/or fever with at least one of the following features: arthritis, arthralgia and/or conjunctivitis. This case report describes the mucocutaneous morphological features and histological features of ZIKV infection.

A traveller who had returned from Puerto Rico developed headache and lethargy three days after his return. The patient developed a skin eruption the next day which initially affected the upper extremities and then spread to the trunk and lower extremities. Physical examination revealed numerous tiny pink and erythematous papules diffusely affecting the head, neck, trunk, the palms, soles and extremities. There were also petechiae on the hard palate and non-purulent injection of the sclerae. There was a mild and focal moderate perivascular lymphocytic infiltrate in the upper dermis on skin biopsy of a skin lesion. Both the deep dermis and subcutis were unaffected. No eosinophils or neutrophils were present in the infiltrate and no viral cytopathic changes were seen in the tissue. ZIKV RNA was detected by real-time polymerase chain reaction in the urine but not the serum and enzyme linked immunosorbent assay on serum was reactive for IgM.

The exanthem of ZIKV infection has been described as "maculopapular" or morbilliform. The eruptions were noted to be comprised of small papules in this case, starting on the trunk and spreading to involve the lower body. Petechiae on the palate and hyperaemic sclerae were also present in this case. The author suggested that a detailed examination of mucocutaneous findings associated with ZIKV infection will enable early recognition and will facilitate elimination of Zika infection.

Laser treatment of nongenital verrucae. A systematic review

Nguyen J, Korta DZ, Chapman L, Kelly KM.
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Warts are benign neoplasms caused by human papillomavirus (HPV) infection of keratinocytes. Treatment modalities of warts include the application of salicylic acid, chemical agents (e.g. cantharidin, formaldehyde), chemotherapeutics (e.g. podofilox, fluorouracil, bleomycin sulphate), contact sensitizing agents (e.g. dinitrochlorobenzene, squaric acid dibutyl ester), immunomodulators (e.g. interferon, imiquimod), cryotherapy, surgical excision, curettage and laser therapy. Various lasers have been used in the treatment of warts, including carbon dioxide (CO_2), erbium:yttrium-aluminum-garnet (Er:YAG), pulsed dye (PDL), and Nd:YAG

lasers. This is a systematic review of 35 studies (2149 patients), investigating the use and efficacy of different types of lasers for treating nongenital cutaneous warts.

Simple and recalcitrant common, palmar, plantar, periungual and subungual warts have been successfully treated with CO_2 laser, with response rates ranging from 50% to 100%. However, adverse effects including scarring, hypopigmentation, postoperative pain, and prolonged wound healing can occur. Pulsed dye laser (PDL) therapy has been used to treat simple and recalcitrant common, palmar, plantar and flat warts, with studies reporting remission rates ranging from 47% to 100%. Although multiple treatment sessions are generally required for disease remission, PDL has significantly fewer adverse effects than CO_2 laser. Adverse effects of PDL therapy include local pain during and after the procedure, bullae, crusting, scarring, and temporary pigmentary changes. Combination therapies with lasers and other agents including bleomycin, salicylic acid and light-emitting diode have shown some success.

The lack of established treatment guidelines limits the use of laser treatment for warts. Optimal treatment protocols are required as well as further studies comparing the efficacies of different laser modalities and non-laser treatment options.

High prevalence of psychiatric disorders in patients with skin-restricted lupus: a case-control study

Jalenques I, Rondepierre F, Massoubre C, Haffen E, Grand JP, Labeille B, et al.
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Patients with systemic lupus erythematosus (SLE) were noted to be associated with psychiatric problems. On the contrary, the prevalence of psychiatric problems in patients with skin-restricted lupus (SRL) remains less well known.

The aim of this study was to assess the current and lifetime prevalence of Axis I psychiatric disorders among outpatients with SRL and to examine the factors associated with psychiatric disorders among such patients.

The authors conducted a multicentre case-control study including outpatients with SRL and controls matched for sex, age and education level. The Mini International Neuropsychiatric Interview which was validated in general French population was used for evaluation.

The study evaluated 75 patients and 150 controls within a 3-year study period who were over 18 years old and had skin-restricted lupus at eight French university hospitals. Among these, 49% of patients vs. 13% of controls had met the criteria for at least one current psychiatric disorder ($p<0.001$). The following psychiatric diseases were significantly more common among patients than controls: generalised anxiety disorder (23% vs. 3%, $p<0.001$ and 35% vs. 19%, $p=0.03$), current and lifetime major depressive disorder (9% vs. 0%, $p<0.001$ and 44% vs. 26%, $p=0.01$), panic disorder (7% vs. 0%, $p=0.004$ and 21% vs. 3%, $p<0.001$), lifetime agoraphobia (20% vs. 9%, $p=0.01$), alcohol dependence (7% vs. 0%, $p=0.004$) and current suicide risk (24% vs. 7%, $p=0.003$).

In summary, the authors suggested that a high prevalence in suicidal risk, depression, anxiety and alcohol dependence was observed in SRL patients and the clinicians should not hesitate to refer such patients for psychiatric evaluation.

Do early-life exposures explain why more advantaged children get eczema? Findings from the U.K. Millennium Cohort Study

Taylor-Robinson DC, Williams H, Pearce A, Law C, Hope S.
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It is known that the incidence of eczema is higher in more advantaged populations. However, the factors that determined the difference in the incidence are not well studied.

The purpose of this study was to investigate the early-life risk factors for eczema, and to investigate how early-life risk factors could explain differences

in eczema. The authors estimated odds ratios (ORs) for ever having suffered eczema by age 5 years in 14499 children from the U.K. Millennium Cohort Study (MCS), with a focus on maternal, antenatal and early-life risk factors and socioeconomic circumstances (SECs). Risk factors were studied to assess if they weakened associations between SECs and eczema.

The results showed that overall 35.1% of children at some time had eczema by age 5 years. Eczema was more common in patients whose mothers had degree-level qualifications comparing with those with no educational qualifications (OR 1.52, 95% confidence interval 1.31-1.76). An increased risk of having eczema was seen in children who had a history of breast-feeding (1-6 weeks and ≥6 months), having been introduced solids under 4 months or cow's milk under 9 months, or antibiotic exposure in the first year of life and whose mothers had a history of atopy. Factors which reduced odds for eczema included female sex, Pakistani and Bangladeshi ethnicity, smoking during pregnancy, having more siblings and exposure to environmental tobacco smoke. After controlling for maternal, antenatal and early-life characteristics e.g. maternal smoking during pregnancy, breastfeeding and the number of siblings, the OR for eczema was reduced to 1.26 (95% confidence interval 1.03-1.50) in the group with the highest educational qualifications compared with the lowest.

The authors concluded that in a U.K. child cohort, the incidence of eczema was higher in the more advantaged children. This could be due to early-life factors including having fewer siblings, not smoking during pregnancy and breastfeeding.

Ustekinumab in hidradenitis suppurativa: clinical results and a search for potential biomarkers in serum

Blok JL, Li K, Brodmerkel C, Horvatovich P, Jonkman MF, Horvath B.
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Severe cases of hidradenitis suppurativa (HS) are difficult to treat. Traditional medications and even surgical treatment may not be helpful. The aim of this study was to evaluate the efficacy of ustekinumab which was a newly launched biologic and to find a potential biomarker for HS. The authors recruited 17 patients in this open-label study. They were treated with 45 mg or 90 mg ustekinumab at weeks 0, 4, 16 and 28. Proteomic technology and enzyme-linked assay analysis were used to test the sera.

Of the 12 patients who completed the protocol, moderate to marked improvement of the modified Sartorius score was noted in 82% of patients at week 40 and the Hidradenitis Suppurativa Clinical Response 50 in 47% cases. This study showed that good responders had milder disease and lower expression of leukotriene A4- hydrolase (LTA4H). Interleukin (IL)-2R, tumour necrosis factor-alpha, IL-17A and IL-17F were not elevated and did not change during treatment.

In summary, the majority of patients improved with ustekinumab clinically. There was no specific biomarker discovered in HS. However, low LTA4H concentrations with mild disease might be related to the effectiveness of ustekinumab in patients.

Syphilis serology in pregnancy: an eight-year study (2005-2012) in a large teaching maternity hospital in Dublin, Ireland

McGettrick P, Ferguson W, Jackson V, Eogan M, Lawless M, Ciprike V, et al.
Int J STI AIDS 2016;27:226-30.

Syphilis is a well-known sexually transmitted infection causing intrauterine growth retardation, pre-term delivery, birth defects and perinatal death. The aim of this study was to identify pregnant ladies with positive syphilis serology and characterise this cohort to identify the high-risk groups and to highlight potential interventions during pregnancy.

During the eight-year period, the records of 194 women who had positive syphilis serology during pregnancy were reviewed. The prevalence was 0.28% (N=66038 where N is the total pregnancies during that period). The median

maternal age was 30 years. Most cases (127/194, 65.46%) were diagnosed to be positive for syphilis at the second trimester. The remaining cases were diagnosed at first (32/194, 16.5%) and third (32/194, 16.5%) trimesters and one case was diagnosed at the post-partum period. Almost all cases were late latent syphilis (LLS) (192/194, 98.97%) and only two (1.03%) were early syphilis.

There were a total of 186 babies delivered; 91.9% and 8.06% of these deliveries were full term and pre-term respectively. Except for two full term babies who had a low birth weight of <2.5 kg, all other babies were healthy and normal. There was one miscarriage at 20 weeks for a case who had LLS and documented previous treatment. There was one stillbirth at 28 weeks for a case with LLS in whom treatment was completed. There was one neonatal death. A 25-year-old African woman presented to Emergency Department at 24 weeks in advanced labour without any antenatal check-up. She had a twin pregnancy and blood screening results during labour which subsequently confirmed early syphilis with an RPR titre of 1:128. Twin one, a baby girl, had signs of intrauterine growth retardation, gross oedema and ascites. The baby succumbed around one hour after delivery; post-mortem was refused but placental histology demonstrated lymphohistiocytic vasculitis, focal acute vasculitis with foetal artery occlusion, sclerosis and associated villous fibrosis that was consistent with active treponemal infection. Twin two, a baby boy, was found to have an RPR titre of 1:4 at birth and 10 days of IV penicillin was given. There was no feature of congenital syphilis and follow-up serology was negative.

As for the treatment, 24.2% babies received no treatment, 52.1% babies received single dose of IM penicillin and 12.4% received 10 days of IV penicillin treatment. The treatment status of the remaining babies were unknown. Finally, only one baby (neonatal death) was confirmed to have congenital syphilis while the remaining 185 babies were not infected.

Herpes simplex virus type 2 (HSV-2) genital shedding in HSV-2/HIV-1 co-infected women receiving effective combination antiretroviral therapy

Pere H, Rascanu A, LeGoff J, Matta M, Bois F, Lortholary O, et al.
Int J STD AIDS 2016;27;178-85.

Although there is a good correlation between blood and genital tract HIV-1 viral load, sustained suppression of plasma HIV-1 virus such as viral load <50 copies/mL would not exclude the HIV-1 virus in the genital tract. Herpes simplex virus type 2 (HSV-2) may increase the infection risk of HIV-1 by increasing HIV-1 genital viral shedding during clinical and subclinical herpetic infection. This study assessed herpes seroprevalence and the dynamics of genital shedding of HSV-2 DNA in HIV-1 infected women taking combination antiretroviral therapy (cART) and its potential link with HIV-1 residual genital shedding retrospectively.

A total of 22 women had cervicovaginal secretions and sera were studied. The mean age was 33 years (range, 30-37). All cases were clinical stage A and the majority (n=20, 91%) had a non-B type HIV-1. Nineteen women (86%) showed circulating IgG antibodies of HSV-2. The cervicovaginal HIV-1 loads were highly correlated with plasma HIV-1 viral loads (Spearman's $r=0.63$, $p<0.0001$). The plasma HIV-1 viral loads were significantly correlated with cervicovaginal HSV-2 loads ($r=0.36$, $p=0.0008$). Multiple regression analysis showed only plasma HIV-1 viral load was highly associated with cervicovaginal HIV-1 load, however, cervicovaginal HSV-2 viral load was not associated with plasma or genital HIV-1 viral load. Therefore, the authors concluded that genital HSV-2 replication under cART does not influence cervicovaginal HIV-1 viral shedding.

The efficacy of 308-nm excimer laser/light (EL) and topical agent combination therapy versus EL monotherapy for vitiligo: A systematic review and meta-analysis of randomized controlled trials (RCTs)

Bae JM, Hong BY, Lee JH, Lee JH, Lee JH, Kim GM.
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Vitiligo is a challenging skin condition with no definite curative treatment. Phototherapy remains the mainstay of treatment with a variable clinical outcome. Recently excimer laser (EL) was introduced to provide targeted irradiance and was believed to be able to induce immature pigment cell development. It was shown to be more effective than NB-UVB. Combination use of topical agents like corticosteroids, calcineurin inhibitors, and vitamin-D3 analogues have been widely used with EL and were shown to have a synergistic effect. In this systematic review, the authors aimed to compare the efficacy of EL monotherapy versus EL and topical agent combination therapy.

RCTs comparing EL and EL with topical agents, with at least 10 subjects or patches in each treatment arm and treatment period of more than 12 weeks or 24 sessions, were selected from a computerised search of MEDLINE, EMBASE and Cochrane library till December 2014. A total of eight RCTs were included. A total of 214 patches or patients were on combination therapy and 211 patches or patients were treated with EL monotherapy. The combination of EL with topical calcineurin inhibitors was shown to be more effective than EL alone in terms of repigmentation in four RCTs (relative risk 1.93, 95% CI: 1.28-2.91). This combination therapy was also shown to significantly reduce treatment failure (RR 0.43, 95% CI: 0.24-0.76). However, there was insufficient evidence to support the combination use of topical vitamin D3 analogues and topical steroids in terms of repigmentation and reducing treatment failure when compared with using EL alone.

This study supported the use of combination therapy of topical calcineurin inhibitors and EL. However, there were several limitations in this study, namely small sample size, short treatment period, heterogenicity of vitiligo subtypes recruited and excimer laser machines used and the lack of blinding in some of the RCTs included might have caused bias in this systematic review.

Fractional carbon-dioxide (CO_2) laser-assisted topical therapy for the treatment of onychomycosis

AK Bhatta, U Keyal, X Huang, JJ Zhao
J Am Acad Dermatol 2016;74:916-23.

Onychomycosis is the most prevalent nail disorder. However, treatment options are limited. Topical agents are often ineffective due to the inability to penetrate the nail plate, while systemic antifungals may cause hepatotoxicity and potential drug interaction. Recently, light-based therapy had been explored and shown to be a potential alternative.

In this single-arm study, patients with onychomycosis confirmed with positive potassium hydroxide (KOH) and culture were included. All affected nails were treated with three sessions of laser therapy at 4-week intervals and once daily topical terbinafine cream for 3 months. The laser treatment regime was 2 to 6 passes of fractional CO_2 laser (2030CI) using pulse energy of 99 mJ, 410 spots/cm^2, pulse interval of 0.55 mm, pulse duration of 0.1 ms and rectangular spot size of 2 to 10 mm.

A total of 75 patients with 356 affected nails were included. Complete clinical resolution was observed in 11 and 25 patients at 3 and 6 month follow-up respectively. A greater than 60% response at 3 and 6 month follow-up was seen in 57% and 40% of patients. Mycological resolution was observed in more than 90% of patients at 3 months and 80% at 6 months. Based on the clinical scoring (scoring clinical index for onychomycosis, SCIO), among those who scored higher than 6 (i.e. candidate for systemic therapy), 98% showed response at 3 months and 78% at 6 months.

The authors concluded that fractional CO_2 laser was effective in treating onychomycosis, and it is especially suitable for older patients and those who are contraindicated for systemic therapy. However, this study was limited by the lack of control arm and relatively short duration of follow-up.