Sturge-Weber syndrome and portwine stains caused by somatic mutation in GNAQ

Portwine stain (PWS) is a congenital malformation that affects 0.3% of all newborn infants. Sturge-Weber syndrome (SWS) is a neuro-cutaneous disorder characterised by PWS over the distribution of the ophthalmic branch of the trigeminal nerve, and concomitant underlying leptomeningeal vascular abnormalities. In this genome study, the authors tested the longstanding hypothesis that PWS and SWS were caused by the same somatic mutation. They performed whole-genome sequencing of the DNA collected from three patients with SWS to identify the candidate culprit gene. A somatic mosaic mutation was then tested from 50 persons (97 samples in total) with PWS, SWS or controls (nil abnormality). The authors demonstrated that PWS and the closely-related SWS were caused by an activating somatic mutation in the guanine nucleotide-binding protein G (q) subunit alpha (GNAQ) gene. They also identified a non-synonymous single-nucleotide variant (c.548G→A, p.Arg183Gln) in the GNAQ and hypothesised that such mutation would cause a moderate activation of the extracellular signal-regulated kinase (ERK). It was the subsequent selective downstream signalling processes that would possibly lead to the non-oncogenic proliferation in PWS and SWS. The authors further hypothesised that a late origin of the somatic GNAQ mutation during development of the vascular endothelium would be the cause of the non-syndromic PWS, whereas the same somatic mutation may occur earlier during the development of the progenitor cells in SWS. This novel recovery is expected to lay a solid foundation for future research in the field of vascular malformation.

Characteristics of primary cutaneous lymphoma according to WHO-EORTC classification in Korea

Primary cutaneous lymphoma (PCL) is a form of non-Hodgkin lymphoma with primary skin involvement. The other important feature of PCL is the absence of extracutaneous or systemic involvement at the time of diagnosis or initial staging. PCL has been classified by the joint World Health Organisation/European Organisation for Research and Treatment of Cancer classification (WHO-EORTC). Although several epidemiological studies have been performed to study the demographic, clinical and histopathological features of PCL, data in Asians is however lacking. This was a retrospective review on 93 patients with PCL in Korea over a 16-year period. The authors suggested that there were geographical and racial differences in the epidemiology of PCL. In this study, the common subtypes of PCL observed were primary cutaneous CD30+ lymphoproliferative disorders, extranodal natural killer/T-cell lymphoma and primary cutaneous diffuse large B-cell lymphoma. A higher percentage (81.6%) of PCL of the T-cell or natural killer-cell lineage was observed in this Korean study, as compared to that reported in Europe (77.5%) and the USA.
Primary cutaneous B-cell lymphoma occurred in 16.2% while precursor haematological neoplasms occurred in 2.2% of patients. Other notable differences of this Asian study were the lower rate of mycosis fungoides but a higher frequency of CD30+ lymphoproliferative disorders. In the current study, a median age of 52 years (3-95 years) was observed. In contrast to other previous large-scale studies, a slightly higher female predominance was found in this retrospective analysis (M:F=1:1.16). In agreement with the literature, the overall prognosis of PCL was good with a five-year survival rate of 92.5% in the present study.

Prevalence and clinical significance of anti-laminin 332 autoantibodies detected by a novel enzyme-linked immunosorbent assay in mucous membrane pemphigoid


Mucous membrane pemphigoid (MMP) is a heterogeneous group of autoimmune subepithelial blistering diseases that predominantly affects the mucous membranes resulting in scarring and significant morbidity. It is characterised by circulating autoantibodies directed against various components of the basement membrane zone. The two major autoantigens in MMP are bullous pemphigoid (BP) 180 antigens and laminin (Lam) 332 antigens. Patients with anti-Lam332 autoantibodies cannot be differentiated clinically from patients with other forms of MMP. This form of anti-Lam332 MMP seems to be associated with an increased risk of malignancy and thus it is necessary to identify this group of patients. Immunoprecipitation and immunoblot studies have been employed to detect IgG anti-Lam332 autoantibodies in patients with MMP. Lately, enzyme-linked immunosorbent assay (ELISA) has been used to serve this purpose.

This was a multicentre retrospective study investigating the prevalence and clinical significance of anti-Lam332 autoantibodies in patients with MMP. Serum samples from 154 patients with MMP and 89 control subjects were obtained to test for Lam332 ELISA scores and other anti-basement membrane zone autoantibodies. The Lam332 ELISA scores were assessed with reference to the clinical presentations of the patients with MMP.

It was found that 20.1% of patients with MMP with active disease at the time of diagnosis had serum anti-Lam332 autoantibodies. On the contrary, only one out of fifty patients with bullous pemphigoid, none out of seven patients with pemphigus, and three out of thirty-two patients without autoimmune bullous disease were test positive. It was also noted that patients with positive Lam332 ELISA score MMP frequently had more severe disease. However, no association was found between a positive Lam332 ELISA score and the occurrence of internal malignant neoplasm or the manifestations of mucosal involvement in MMP. The authors suggested that this novel Lam332 ELISA assay appears to be a relevant diagnostic and prognostic tool for the identification of a subset of patients presented with a more severe form of MMP.

Factors predictive of recurrence and death from cutaneous squamous cell carcinoma. A 10-year, single-institution cohort study


This was a 10-year single-institution retrospective cohort study investigating the risk factors associated with a poor outcome (e.g. local recurrence, nodal metastases, disease-specific death) of cutaneous squamous cell carcinoma (CSCC).
A total of 1,832 CSCC in 985 patients from January 2000 to December 2009 were traced by searching the electronic database at Brigham and Women's Hospital. Any occurrence of local recurrence (LR), nodal metastases (NM), distant metastases (DM), disease-specific death (DSD) and all-cause death (ACD) were identified. Characteristics of the primary tumour such as the anatomical location, differentiation, depth of invasion, infiltrative or desmoplastic growth pattern and the presence of perineural or lymphovascular invasion were retrieved from the pathology reports.

It was found that LR, NM and DSD occurred in 45 patients (4.6%), 36 patients (3.7%) and 21 patients (2.1%) respectively. Five risk factors associated with poor outcomes of CSCC were identified. Tumour diameter of 2 cm or larger was associated with an increased risk of LR, NM and DSD. Poor tumour differentiation predicted LR, NM, DSD and ACD. Tumour invasion beyond subcutaneous fat was associated with an elevated risk of LR, NM, DSD and ACD. Perineural invasion predicted LR and DSD. Tumour location on the ear or temple was associated with LR, NM and DSD. Anogenital location, despite of the small number of cases, was also significantly associated with NM and death.

In conclusion, a subset of CSCC was associated with a significant risk of metastasis and death. The authors suggested that five aforementioned risk factors may be the most significant determinants of a poor outcome in CSCC. It was also recommended that clinical trials regarding nodal staging and adjuvant therapy may be targeted at patients with one or more of these risk factors.

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**Trends and antibiotic susceptibility patterns of methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* in an outpatient dermatology facility**

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This was a retrospective observational study to investigate the trend of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *Staphylococcus aureus* (MSSA) infections and their antibiotic susceptibility profiles in an outpatient dermatology clinic in Miami, Florida.

The data was collected from skin culture isolates annually between January 2005 and December 2010, and monthly during the six-month period of January 2011 to June 2011 from patients at the University of Miami Hospital outpatient dermatology clinic. The overall relative proportion of MRSA and MSSA was 35.7% and 64.3% respectively. The relative proportion of MRSA increased by 17.0% during the last three years (2008 to 2010) of this study compared with the previous three years (2005 to 2007). Regarding antibiotic resistance, it was noted that MSSA was becoming more resistant to many antibiotics, namely ciprofloxacin, clindamycin, gentamicin, and trimethoprim-sulphamethoxazole. The increase in resistance of MSSA to these antibiotics may be due to empirical antibiotics usage or genetic recombination. However, for MRSA infections, there was an increase in the sensitivity of MRSA to ciprofloxacin and a trend toward an increase, despite not statistically significant, in its sensitivity to clindamycin, levofloxacin, rifampin, and tetracycline.

The authors suggested that the best empirical antibiotic to cover both MRSA and MSSA infections is trimethoprim-sulphamethoxazole or tetracycline. Moreover, it is crucial to obtain cultures from infected sites before administering an antibiotic. The antibiotic therapy should also be adjusted according to the clinical response since in vitro susceptibility testing does not necessarily predict in vivo efficacy.
Treatment of high-grade anal dysplasia in high-risk patients: outcome at an urban community health centre


High-grade anal intraepithelial neoplasia (HGAIN) which is defined as anal intraepithelial neoplasia (AIN) grade 2 or higher including carcinoma in situ, is the likely precursor of invasive anal squamous cell carcinoma. The incidence is estimated to be 70-100 per 100,000 person years in US among HIV infected men-who-had-sex-with-men (MSM). The aim of this study was to describe the outcome of treating incident biopsy-proven HGAIN in HIV infected and non-HIV infected MSM by ablation in a community-based clinic.

This was a retrospective cohort study including the MSM who were diagnosed to have HGAIN during 1996 to 2010 and received treatment in the study centre. For those with a history of prior anal or colorectal cancer and with anal dysplasia treated at other institutions were excluded. Patients with a previous history of major colorectal surgery was also excluded. A total of 153 MSM patients with HGAIN were included and 64% of them had anogenital warts of which 56% were HIV-infected. The mean duration of HIV diagnosis was 11.7 years and median CD4 count 514 cells/mm³ with a range of 21-1308 cells/mm³. Of these patients, 77% were on HAART. Eighty (52%) patients received ablative treatment of high frequency desiccator or CO₂ laser destruction in the clinic and 49 (61%) of those treated in clinic returned for follow-up in nine months. Twenty-six (53%) were free of high-grade disease, 19 (39%) still had high-grade disease and four (8%) had unknown grading. Logistic regression analysis revealed that less extensive anal disease was associated with a lower probability of high-grade disease. The HIV status and age of patients were not found to be significantly associated.

In summary, this study showed that identification and ablative treatment of HGAIN could be managed in a clinic-based setting and the authors suggested further studies would be needed on the long-term outcome of treating HGAIN in the community setting.

Liver involvement in HIV-infected patients with early syphilis


Impairment of liver function is common in HIV infected patients. It may be caused by opportunistic infections such as mycobacterium infection, cryptosporidium, Kaposi sarcoma, anti-retroviral therapy, viral hepatitis, alcohol and hepatic steatosis. Early syphilis may be another cause of liver impairment in HIV patients. The aim of this study was to review the prevalence of liver involvement and related factors in HIV-infected patients diagnosed with early syphilis. This was a seven-year multicentre case series study of HIV patients co-infected with early syphilis. Liver involvement is defined as an increase above the normal range of aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamytransferase (γGT) or alkaline phosphatase during syphilis infection or doubling of the previous values that were already high before the diagnosis of syphilis. The time frame was defined as "before" (3-9 months before the diagnosis of syphilis), "during" (12 weeks before and 2 weeks after the diagnosis of syphilis) and "after" (3-9 months after the diagnosis and treatment of syphilis). For those with acute hepatitis during infection with syphilis, incomplete treatment and missing data were excluded. A total of 147 patients were included and 86.4% were men-who-had-sex-with-men (MSM). The mean CD4 count was 497 cells/mm³, 70.7% were on combination antiretroviral therapy and liver involvement was found in 45 (30.6%) patients. Only one of these patients presented with symptomatic hepatitis such as jaundice and vomiting. The only statistically significant associated factor was RPR >1:64. Other factors including CD4 count, HIV viral load, co-infection with viral hepatitis and clinical presentation of early syphilis were not associated. Thus, the authors concluded that syphilis should be screened in HIV patients with liver impairment.
Androgenetic alopecia and risk of prostate cancer: a systematic review and meta-analysis


Androgenetic alopecia (AGA) is caused by follicular hypersensitivity and miniaturisation by dihydrotestosterone, a testosterone metabolite, in predisposed patients. Since both AGA and prostate cancer share some biological risk factors, (namely age, genetic inheritance and hormonal factors), the potential association between these two entities has been studied.

In this review, the authors searched through MEDLINE and Cochrane Library and identified studies that examined the association of AGA with the risk of prostate cancer. Studies that did not use standard tools for examining hair loss were excluded.

Seven case-control studies were included, which consisted of 4078 cases and 4916 controls. No statistically significant association between AGA of any pattern and prostate cancer was found. However, vertex baldness was shown to be associated with prostate cancer (OR 1.25, 95%CI 1.09-1.44).

This association might be explained by the previous findings showing that vertex baldness was associated with higher levels of circulating testosterone. Also, patients with vertex baldness were found to have higher levels of insulin-like growth factor (IGF-1), which were also shown to be associated with prostate cancer. Finally, microRNAs, which are found in hair follicle formation, were down-regulated in prostate cancer. All these findings may give a potential explanation about the association between vertex baldness and prostate cancer. The authors concluded that vertex AGA at any age was at a significantly higher risk of developing prostate cancer. However, further prospective or randomised controlled trials were needed to confirm this observation.

However, this study had several limitations. First, all studies included were case-control studies, which were subjected to recall bias. Also, not all included studies investigated the association between male pattern hair loss with prostate cancer.

A randomised phase 2a efficacy and safety trial of the topical Janus kinase inhibitor tofacitinib in the treatment of chronic plaque psoriasis


This multicentre, double-blind study to investigate the efficacy, local tolerability, systemic safety and pharmacokinetics of Janus kinase (JAK) inhibitor tofacitinib ointment was performed in ten specialties institutions from Canada and USA between February and November 2011. Seventy-one adult patients with mild-to-moderate plaque psoriasis from these centres were included and randomised 2:1:2:1 to 2% tofacitinib ointment 1 (differed by penetration enhancer); vehicle 1; 2% tofacitinib ointment 2; or vehicle 2 for 4 weeks twice daily treatments to a single fixed 300 cm² target plaque with or without one or more non-target plaques and normal skin. Target Plaque Severity Score (TPSS), target plaque area (TPA) and the Itch Severity Item (ISI) score change were used to assess the outcome and 2% tofacitinib ointment 1 demonstrated significant improvements in TPSS [least squares mean (LSM) -54.4%] vs. vehicle 1 (LSM -41.5%) , TPA (LSM-19.04%) and ISI, but ointment 2 did not achieve any significant differences. Mild or moderate adverse events were similar across treatment groups, occurring in 25 (35%) out of 71 patients but none were serious. The authors thus concluded that tofacitinib ointment 1 was well tolerated and efficacious and had the potential to provide an additional therapeutic option for patients with plaque psoriasis.
Evaluation of MYC status in oral lichen planus in patients with progression to oral squamous cell carcinoma


This study was performed in Hospital del Mar at Barcelona to analyse MYC status in patients with oral lichen planus (OLP) who had oral squamous cell carcinoma (OSCC). Ten OLP patients who developed OSCC were included in the study (group I) and eleven OSCC samples (group IA) and 17 OLP samples from these OSCC patients (group IB) were retrospectively selected. Thirteen biopsy specimens from 12 patients with OLP that had no OSCC were also included as control (group II). Fluorescence in-situ hybridisation (FISH) evaluation of the MYC gains was determined in 100 non-overlapping nuclei per sample and immunohistochemical evaluation was determined by calculating the percentage of C-MYC expression in the epithelial cells. Gains of MYC were observed in 10 out of 11 (91%) OSCC samples (group IA) and seven out of 15 samples (47%) in group IB, but no MYC gains were detected in group II. Nuclear over-expression of C-MYC was observed in eight out of 11 (73%) OSCC lesions, 13 out of 15 cases (87%) in group IB and only four out of nine (44%) in group II. The authors concluded that OLP lesions from patients with OSCC showed MYC gains and C-MYC overexpression and suggested that determining MYC status on some OLP lesions might predict a subgroup of patients with a higher risk of progression to OSCC.

Proactive maintenance therapy with a topical corticosteroid for vulvar lichen sclerosus: preliminary results of a randomized study

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This randomised double-blind study was conducted at a university dermatology vulva unit in Italy between December 2009 and May 2012 to investigate the effectiveness of proactive twice weekly maintenance mometasone furoate 0.1% ointment in preventing the exacerbation of vulvar lichen sclerosus (VLS). Twenty-seven eligible subjects entered an open-label active treatment phase of 12 weeks duration and the treatment responsive patients were then randomised to apply either mometasone furoate 0.1% ointment twice weekly (8 patients), once daily cold cream or topical vitamin E for the 52-week maintenance phase. Finally twenty-five patients entered the maintenance phase. Ten patients (40%) experienced relapse at the end of the study: five patients in the vitamin E group (5/9, 56%), and five patients in the cold cream group (5/8, 62%), while no patient in the mometasone furoate 0.1% ointment group relapsed (OR=0.0951, 95% CI 0.0177-0.5106). The median time to relapse of 21.6 weeks was the same for the vitamin E and the emollient groups. The authors concluded that proactive treatment with a topical corticosteroid twice weekly might be an effective, safe and reliable therapy for the long-term prevention of relapse in VLS.