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Journal Watch

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Histologic features associated with an invasive component in lentigo maligna lesions

Moreno A, Manrique-Silva E, Viros A, Requena C, Sanmartin O, Traves V, et al.
JAMA Dermatol 2019;155:782-8.

This retrospective cross-sectional study aimed to identify the histological characteristics associated with lentigo maligna melanoma (LMM) in patients with lentigo maligna (LM) diagnosed by a partial diagnostic biopsy. This retrospective cross-sectional study recruited 266 patients with primary cutaneous melanoma in the form of either LM or LMM who had undergone surgical treatment, a complete histologic examination of the whole tumor, and an initial diagnostic partial biopsy of LM between January 1, 2000, and December 31, 2017. This study performed comparisons between invasive samples and samples without an invasive component. Ninety-six patients had sufficient histological material that could be evaluated, of which 63 patients (65.6%) were diagnosed with LM and 33 patients (34.4%) had LMM diagnosis.

The following histologic features were associated with an invasive component: subepidermal clefts (OR, 2.8; 95% CI, 1.0-7.9; P=0.049), melanocytes forming rows (OR, 11.5; 95% CI, 1.4-94.1; P=0.02), or nests (OR, 3.0; 95% CI, 1.1-8.6; P=0.04), and a non-chronic sun damage degree of elastosis (OR for chronic sun damage, 0.4; 95% CI, 0.1-1.1; P=0.07). Melanocytes forming rows were more frequently present in LMM samples than in LM samples (97% vs 63.5%; P<0.001). Compared to the in-situ stage, subepidermal clefts was more common in cases with an invasive component (16 (48.5%) vs 13 (20.6%); P=0.005). In contrast to LM, LMM was more frequently associated with at least 25% of intraepidermal melanocytes arranged in nests (16 (48.5%) vs 11 (17.5%); P=0.001). Solar elastosis not to the degree of chronic sun damage was more common in lesions with an invasive component than those with LM (12 (36.4%) vs 11 (17.5%); P=0.04).

The author concluded the above findings may be useful in classifying early LM specimens at higher risk of invasion.

Prevalence of advanced liver fibrosis in patients with severe psoriasis

Maybury CM, Porter HF, Kloczko E, Duckworth M, Cotton A, Thornberry K, et al.
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The aim of this study was to describe the prevalence of and evaluate the clinical factors associated with advanced liver fibrosis in people with severe psoriasis. Four hundred adults with severe psoriasis were recruited in this prospective observational cohort study. The primary outcome was a diagnosis of advanced liver fibrosis determined by transient elastography. Psoriasis-specific and metabolic indices, alcohol use, and methotrexate exposure were evaluated.

Three hundred and thirty-three of the 400 patients had transient elastography scans that were suitable to be evaluated. Advanced hepatic fibrosis was present in 47 of 333 patients (14.1%; 95% CI, 10.4%-17.9%). The best performing multivariate model for advanced fibrosis included the following: insulin resistance, reduced alcohol consumption, psoriasis severity, platelet count, increased central obesity (waist circumference), and aspartate aminotransferase level.

The authors concluded that these study findings suggest that advanced fibrosis is common in severe psoriasis. People with severe psoriasis should be screened for advanced liver fibrosis irrespective of which systemic medication they are receiving.

Dupilumab provides important clinical beneits to patients with atopic dermatitis who do not achieve clear or almost clear skin according to the Investigator's Global Assessment: a pooled analysis of data from two phase III trials

Silverberg JI, Simpson EL, Ardeleanu M, Thaci D, Barbarot S, Bagel J, et al.
Br J Dermatol 2019;181:80-7.

Dupilumab is a monoclonal antibody that inhibits the interleukin 4 and 13 pathway and was approved to treat moderate to severe atopic dermatitis (AD). Investigator's Global Assessment (IGA) is a common tool in measuring the outcome for treatment of eczema. IGA 0 (clear) or 1 (almost clear) was defined as treatment success in many studies. This study investigated the efficacy of dupilumab for AD patients through both IGA and other outcome measures. Patients were randomised to dupilumab 300 mg weekly, dupilumab 300 mg every 2 weeks or placebo. Loading dose (600 mg) on day 1 was given to patients in all dupilumab regimens.

A total of 892 patients were treated with dupulimumab or placebo. At 16 weeks, about 171 of 448 (38.1%) of AD patients treated with dupilumab achieved the primary endpoint of IGA score ≤1 while this was seen in only 47 of 443 (10.6%) placebo treated patients. Patients with IGA score >1 also showed significant improvement their outcome measures. The dupilumab group had greater improvement with respect to other outcome measures than the placebo group: Eczema Area and Severity Index (EASI) -48.9% vs -11.3%, Pruritus numerical rating scale (NRS) -35.2% vs -9.1%, Body surface area (BSA) -23.1% vs -4.5%, Patient-Oriented Eczema Measure (POEM) score ≥4-point improvement 57.4% vs 21%, Dermatology Life Quality Index (DLQI) score ≥4-point improvement 59.3% vs 24.4%. In conclusion, dupilumab has a significant benefit in treatment of moderate to severe atopic dermatitis with respect to both IGA score and other clinical outcomes. Even patients with IGA score >1 showed significant improvement in other outcome measures.

Efficacy and safety of mirikizumab (LY3074828) in the treatment of moderate-to-severe plaque psoriasis: results from a randomized phase II study

Reich K, Rich P, Maari C, Bissonnette R, Leonardi C, Menter A, et al.
Br J Dermatol 2019;181:88-95.

Interleukin (IL) 23 is a key cytokine involved in pathogenesis of psoriasis. Mirikizumab (LY3074828) is a humanised monoclonal antibody that inhibits the p19 unit of IL23. This was a double-blinded study on the efficacy and safety of different doses of mirikizumab for the treatment of moderate or severe psoriasis. Two hundred and five patients were randomised to receiving placebo, 30 mg, 100 mg or 300 mg mirikizumab subcutaneously at week 0 and week 8. Psoriasis Area and Severity Index (PASI) 90 at week 16 for placebo, 30 mg, 100 mg or 300 mg mirikizumab was measured and found to be 0%, 29% ($P=0.009$), 59% ($P<0.001$) and 67% ($P<0.001$) respectively. PASI 90 response rate at week 16 was better for higher dose of mirikizumab and higher than placebo.

Common side effects of mirikizumab were viral upper respiratory tract infection, other upper respiratory tract infection, injection site pain, hypertension, diarrhoea. No deaths were reported. One patient with history of hypercholesterolaemia and alcohol abuse had elevated liver enzyme which returned to normal after discontinuation of mirikizumab. He was also found to have alcohol abuse and elevated liver enzymes again after this study. It was concluded that mirikizumab is a safe and effective treatment for moderate or severe psoriasis.

Pharyngeal Chlamydia and gonorrhea: a hidden problem

Gaspari V, Marangoni A, D'Antuono A, Roncarati G, Salvo M, Foschi C, et al.
Int J STD AIDS 2019;30:732-8.

Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) are the commonest agents of bacterial sexually transmitted infections (STIs) worldwide. Besides the common urogenital infections, they can also infect extra-genital sites, such as pharyngeal and ano-rectal mucosa, especially in women and men having sex with men (MSM). In this cohort study, 893 cases reporting unprotected oral sex were enrolled. A pharyngeal swab was taken from each patient for the molecular detection of CT and NG. Genotyping of positive CT samples by an *omp1* gene PCR was performed. Overall, 155 cases had pharyngeal infection (17.4%). There was a total of 134 cases of gonorrhea (15%) and 34 chlamydial infections (3.8%) detected in the pharyngeal site. There were no significant differences between males and females. Four cases of L2 serovar infection, (all in MSM) giving a 0.4% overall prevalence of pharyngeal lymphogranuloma (LGV) were detected on CT genotyping. There was a significant association between CT/NG pharyngeal infections and HIV positivity ($P=0.01$), history of sexual contacts with a partner positive for CT and/or NG ($P<0.0001$), and the presence of concurrent genital and/or rectal infections ($P<0.0001$). It should be noted that over 90% of the infections were completely asymptomatic, suggesting that symptoms were not predictors of a pharyngeal infection ($P=0.7$). These findings suggest that pharyngeal screening for CT/GC should be considered if there is a history of unprotected oral sex even in asymptomatic cases.

Neurosyphilis is more common in malignant syphilis: a case series and review of the literature

Zhu L, Shi M, Peng RR, Gu X, Guan Z, Xu H, et al.
Int J STD AIDS 2019;30:779-85.

Malignant syphilis is also known as lues maligna or nodular-ulcerative syphilis, is a rare form of secondary syphilis and is believed to be more common in immunocompromised patients because there has been an increase in the reported cases with the appearance of HIV population. This study aimed to investigate the relationship between HIV infection, malignant syphilis, and neurosyphilis through a systematic chart review of 26 malignant syphilis patients seen at our hospital. All cases were of secondary syphilis consisting of five females and 21 males, aged 20-68 years. Of these, 18 cases (69%) were HIV positive. Six patients were diagnosed with neurosyphilis and malignant syphilis but were HIV negative. A literature review of 83 reported malignant syphilis cases since 1987 revealed no association between HIV infection and malignant syphilis or neurosyphilis. It was concluded that these findings suggested that there was a strong association between malignant syphilis and neurosyphilis in general and that there was no association between HIV infection, malignant syphilis and neurosyphilis. This should be borne in mind when managing these cases.

Risk factors and diagnostic markers of bacteremia in Stevens-Johnson syndrome and toxic epidermal necrolysis: a cohort study of 176 patients

Koh HK, Chai ZT, Tay HW, Fook-Chong S, Choo KJL, Oh CC, et al.
J Am Acad Dermatol 2019;81:686-93.

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are dermatological emergency conditions characterised by epidermal detachment and mucositis. SJS-TEN is a disease continuum differentiated on the basis of the percentage of body surface area (BSA) detached. The mortality rate of the two conditions ranges from 10% for SJS and up to 50% for TEN. The most common cause of death in SJS-TEN is sepsis, which accounts for 50% of the mortality. This retrospective cohort study was done to validate potential risk factors for bacteraemia that were present in patients upon admission and to identify clinical and laboratory findings that might enable rapid prediction of positive blood cultures.

A total of 176 patients were recruited in this study in which 33.5%, 29% and 37.5% were cases of SJS, SJS-TEN and TEN respectively. The most common organisms identified were *Acinetobacter baumannii*, followed by *Staphylococcus aureus*, other Gram-positive bacteria and Enterobacteriaceae. Bacteraemia occurred in 29.5% of the patients during hospitalisation. The overall in-hospital mortality rate was 23.9%. Patients with bacteraemia were more likely to require ICU admission, invasive mechanical ventilation, dialysis and had longer hospital lengths of stay. Patients who received cyclosporine and intravenous immunoglobulin were not found to be significantly associated with bacteraemia. In the multivariate analysis, significant risk factors on admission associated with bacteraemia included haemoglobin <=10 g/dL (OR 2.4, 95% CI 2.2-2.6), BSA >=10% (OR 14.3, 95% CI 13.4-15.2) and existing cardiovascular disease (OR 2.1, 95% CI 2.0-2.3).

One limitation of this study was the retrospective study design which included the flaws inherent in that design choice. Secondly, the study location was the national reference centre for SJS-TEN, in which the data are prone to referral bias. Finally, in the setting of a burns unit and burns ICU, the microbial data might be skewed toward nosocomial organisms.

Coffee, tea, caffeine, and risk of nonmelanoma skin cancer in a Chinese population: The Singapore Chinese Health Study

Oh CC, Jin A, Yuan JM, Koh WP.
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The main environmental risk factor is ultraviolet (UV) radiation from the sun, there has been great interest in identifying other modifiable risk factors for skin cancer and new approaches for non-melanoma skin cancer (NMSC) prevention. A number of animal studies reported that caffeine intake or topical administration of caffeine on the skin inhibits UV-induced skin cancer and tumours.

This was a prospective cohort study of 61,321 subjects aged 45 to 74 years with a mean age of 74.3 years at diagnosis and the mean follow up of 18.3 years. There were 427 incident cases of BCC and 182 incident cases of SCC identified via linkage with the nationwide cancer registry. The authors found that coffee drinking was associated with reduced NMSC risk in a dose-dependent manner. The risk was significantly reduced in daily drinkers and with increasing number of cups/day. In the highest intake category of three or more cups per day, the hazard risk (HR) was 0.47 (95% confidence interval [CI], 0.29-0.75). Daily black tea drinkers also had a statistically significantly reduced NMSC risk (HR, 0.70; 95% CI, 0.52-0.94). Specifically, coffee drinking was associated with reduced risk of both BCC and SCC, whereas daily tea drinking reduced the risk of BCC only. Intake of green tea and intake of soda were not significantly associated with NMSC risk. The finding of a protective association of coffee and caffeine intake with BCC is consistent with all previous prospective studies in Australia, United States, and Europe. Moreover, this study showed an inverse association between coffee or caffeine and risk of SCC.

The strengths of this study include the population based, prospective cohort study design with long follow up period and a large number of incident NMSC cases. There were several limitations for this study as well. First, there may have been misclassification of intake of caffeine, coffee or tea with the questionnaire and the measurement was done only at baseline. Second, there was no information on decaffeinated coffee or tea. Moreover, there was no data on the following confounding risk factors: history of radiation, family history, chemical exposure, outdoor sun exposure, Fitzpatrick skin type, and whether sunscreen and/or protective outerwear were used. Finally, as the small number of black tea drinkers and as most them only drank one cup/day, the actual effect of black on risk of NMSC could not be fully evaluated.