Got Warts? Try the MMR Vaccine

Intralesional Immunotherapy of Plantar Warts: Report of a New Antigen Combination.

Gamil H, Elgharib I, et al:

J Am Acad Dermatol 2010; 63 (July): 40-43

The measles, mumps, and rubella vaccine may work as well or better than *Candida* antigen for the treatment of warts.

Background: Think of all the different ways we treat warts and you have an overview of the stark fact that nothing works all that well. One common technique used especially in primary care is immunotherapy with *Candida* antigen. There have been literature reports of success also with mumps, *Trichophyton*, and tuberculin vaccines.
Objective: To test the effectiveness of the use of measles/mumps/rubella (MMR) vaccine intralesional therapy for plantar warts.
Design/Participants: Unblinded cased series of 40 patients with single or multiple plantar warts.
Methods: The subjects were tested for existing immunity with 0.5 cc of intradermal injection of MMR vaccine. Wart dosing was based on the response to the test. The MMR vaccine was injected into single warts or the largest wart in case of multiple lesions at 3-week intervals until complete clearance occurred or for a maximum of 3 treatments. Follow-up was done every 3 months for a total of 9 months to detect any recurrence.
Results: 23 patients completed the study; the other patients discontinued for a variety of reasons including nonreactivity to MMR vaccine, failure to follow-up, and side effects such as flu-like symptoms and pain of the procedure. Single lesions were present in 13 patients and multiple lesions were found in 10 patients. Eight patients had recalcitrant warts and 6 had warts distant from the plantar warts. The duration of the lesions ranged from 3 to 20 months with a mean of 7.4 months. Fourteen patients received previous treatment in the form of keratolytics, cryotherapy, or electrocautery. For those who completed the study, complete clearance of the warts occurred in 20 patients, with >50% clearing in 1 patient and <50% clearing in 2 patients. Complete response was achieved in 6 of 8 patients with recalcitrant plantar warts and in 5 of 6 patients with warts at sites other than the soles. Side effects included pain during injection and flu-like symptoms, which occurred in 1 patient.
Conclusions: Intralesional immunotherapy by MMR vaccine seems to be a simple, effective, and safe treatment modality for plantar warts.
Reviewer's Comments: This study reported higher response rates with fewer treatments than previous studies. The authors speculated that this might be because of the use of 3 viral antigens that might potentiate each other. The obvious problems with the study are an absence of a control population, small numbers, absence of blinding, and possibly lead bias. Still, this study presents some modest efficacy data and the therapy is significantly cheaper, safer, and easier than some other intralesional therapies including bleomycin. (Reviewer-David L. Swanson, MD).

Keywords: Warts, Immunotherapy, HPV

Print Tag: Refer to original journal article

Lamp or Laser -- Which Would You Use to Treat Vitiligo?

308-nm Excimer Lamp Vs. 308-nm Excimer Laser for Treating Vitiligo: A Randomized Study.

Le Duff F, Fontas E, et al:

Br J Dermatol 2010; 163 (July): 188-192

In this study, the 308-nm excimer lamp and laser showed similar efficacy in treating vitiligo. For the same fluence, the lamp induced more erythema suggesting photobiological differences between the 2 devices.

Background: 308-nm excimer lasers and lamps are FDA-approved indications for excimer devices. Both are effective, but which is better? How do they compare head to head? Until now, that question has never been studied for vitiligo, although it has for psoriasis. It's an important question to answer for people contemplating purchasing the devices since lasers are much more expensive than lamps.
Objective: To compare the effectiveness and tolerance of the 308-nm excimer lamp to the 308-nm excimer laser in vitiligo.
Design: This is a randomized side comparison study unblinded to the therapist but blinded to the evaluators. This trial was funded by Quantel Medical, a company that makes both excimer lasers and excimer lamps.
Participants: 20 nonsegmental vitiligo patients, of whom 17 completed the study.
Methods: 104 symmetric paired vitiligo lesions were treated. These lesions were at least 10 cm2 in area. In a randomized fashion, one lesion was selected for treatment with the 308-nm lamp and one with the laser. Minimal erythemal dose (MED) was assessed for both lamp and laser and the lower dose was chosen as reference for the initial treatment dose. Doses were then increased by 50 mJ cm2 every 2 sessions. If erythema lasted >48 hours or if blisters were observed, the doses were decreased to the highest doses without those side effects. Treatment was conducted twice weekly on nonconsecutive days (every Tuesday and Friday) for 24 sessions. The diameter of the laser beam was 25 mm and the surface area of treatment with the lamp was 16 cm2. Digital photographs with direct and UV light were used for analysis by blinded evaluators.
Results: The 2 treatments were equivalent in effectiveness, although more erythema occurred with the lamp. In total, 70% of patients showed some repigmentation; only 15% of the patches obtained a repigmentation of >50%. The treatment was well tolerated with both modalities. The fluence delivery times were slightly longer with the lamp, although the differences were typically a matter of seconds.
Conclusions: The 308-nm lamp and laser were equivalent in efficacy.
Reviewer's Comments: My only real criticism of this study is the short duration of treatment for the vitiligo subjects. We have found treating patients with narrow band UVB or PUVA that it can take 6 to 12 months before really impressive repigmentation occurs. It's conceivable that over time differences would have become evident between the 2 technologies. (Reviewer-David L. Swanson, MD).

Keywords: Laser, Excimer, Lamp, Vitiligo, Psoriasis

Print Tag: Refer to original journal article

Ipilimumab Improves Survival in Melanoma Patients

Improved Survival With Ipilimumab in Patients With Metastatic Melanoma.

Hodi FS, O'Day SJ, et al:

N Engl J Med 2010; June 14 (): epub ahead of print

Although adverse events with ipilimumab can be severe and long-lasting, most are reversible with appropriate treatment.

Background: Improving the long-term survival of patients with metastatic melanoma has been a mostly unrealized goal. Ipilimumab is a fully humanized monoclonal antibody against CTLA-4. CTLA-4 is thought to down-regulate pathways of T-cell activation. Ipilimumab is thought to increase antitumor activity by blocking this suppressive pathway.
Objective: To compare ipilimumab administered with or without a glycoprotein 100 (gp100) peptide vaccine to gp100 alone in patients with previously treated metastatic melanoma.
Design/Methods: This was a prospective randomized trial with 3 arms. Arm 1 received ipilimumab plus gp100 vaccine, arm 2 received ipilimumab alone, and arm 3 received gp100 vaccine alone. In total, 676 unresectable progressive stage 3 or 4 melanoma cases were randomly assigned in a 3:1:1 ratio. The treatments were administered every 3 weeks for up to 4 treatments. Eligible patients could receive another course of therapy.
Results: Median overall survival was 10.0 months for patients receiving ipilimumab plus gp100, 6.4 months for patients receiving gp100 alone, and 10.1 months for ipilimumab alone. No difference in overall survival was detected between the ipilimumab groups (hazard ratio with ipilimumab plus gp100, 1.04; P =0.76). There were 14 deaths related to the study drugs (2.1%), and 7 were associated with immune-related adverse events.
Conclusions: Ipilimumab improved survival compared to gp100 vaccine given alone in patients with previously treated metastatic melanoma.
Reviewer's Comments: The long-term survival with ipilimumab demonstrated 1- and 2-year survival rates of 45.6% and 23.5%, which is slightly higher than rates reported for other trials in which no clinical benefit was found for the studied intervention. Most adverse events were immune-related, supporting the purported mechanism of action of the medication. Though this is a good first step, one must keep in mind the survival was only 4 months longer with this medication than without. Similar results were reported with interferon some time ago, only to be later called into question with subsequent trials and meta-analyses. Hopefully, this is just the first of many more effective medications to come. (Reviewer-Daniel Eisen, MD).

Keywords: Melanoma, Biologics, Chemotherapy

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Chest Compressions Override Rescue Breathing in Layperson CPR

CPR With Chest Compression Alone or With Rescue Breathing.

Rea TD, Fahrenbruch C, et al:

N Engl J Med 2010; 363 (July): 423-433

Rescue breathing does not improve survival for patients receiving cardiopulmonary resuscitation by laypersons.

Background: The effectiveness of rescue breathing during cardiopulmonary resuscitation (CPR) by laypeople is unknown. Animal models suggest that CPR without rescue breathing may be more effective for cardiac causes of arrest, but not for respiratory ones.
Objective: To compare outcomes when dispatcher instructions to bystanders consist of chest compression alone with outcomes when instructions consist of chest compression plus rescue breathing.
Methods: Callers to 911 centers who were willing to perform CPR were randomized to receive instructions with chest compressions or without. Exclusion criteria included: arrest due to trauma, drowning, or asphyxiation and those aged <18 years. Those in the compression-only arm received cycles of 50 compressions followed by reassessment of signs of life. For the arm including rescue-breathing, patients received 2 breaths followed by 15 compressions. To be eligible for analysis, patients had to receive care from emergency medical services (EMS) personnel. The primary outcome measure was survival to hospital discharge. Secondary measures were the return of spontaneous circulation following EMS care and favorable neurologic status at time of discharge.
Results: 1941 patients met the inclusion criteria. In total, 12.5% with compressions alone survived to discharge and 11.0% with rescue breathing and compressions survived. The difference was nonsignificant. A total of 14.4% and 11.5% survived with favorable neurologic status in the compression-only and rescue breathing groups, respectively. This difference was also nonsignificant. In those with cardiac causes of arrest (15.5% vs 12.3%) and shockable rhythm (31.9% vs 25.7%), there were nonsignificant trends toward survival with compressions only.
Conclusions: Chest compressions alone did not significantly increase survival, though there was a trend toward better outcomes in important clinical subgroups. Results support an emphasis on compressions and a move away from rescue breathing for layperson CPR.
Reviewer's Comments: Over the past several years, chest compressions have been emphasized more and rescue breathing less in formally taught CPR classes. Based upon the results of this study, expect that trend to continue. Though most dermatologists do not expect to run a code as part of their normal office routine, as physicians most members of society expect us to have rudimentary resuscitative knowledge that includes CPR. Certainly, many of our patients are elderly and we can reasonably expect to need to perform this service at some point in our careers. Even if one has not recertified in some time, most should be able to remember to administer 50 compressions followed by repeat assessments until emergency medical personnel arrive. (Reviewer-Daniel Eisen, MD).

Keywords: Cardiopulmonary Resuscitation, Compressions, Rescue Breathing, Layperson CPR

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FMF Has Poor 5-Year Overall Survival Rate

Folliculotropic Mycosis Fungoides: Single-Center Study and Systematic Review.

Lehman JS, Cook-Norris RH, et al:

Arch Dermatol 2010; 146 (June): 607-613

Folliculotropic mycosis fungoides has distinct clinical and microscopic features and is associated with a poor 5-year overall survival rate.

Background: Folliculotropic mycosis fungoides (FMF) is a variant of mycosis fungoides that can be challenging to diagnose.
Objective: To expand existing knowledge regarding clinical, histopathologic, and therapeutic observations, and biologic behaviors of FMF.
Design: Retrospective clinicopathologic study.
Participants: The authors included patients diagnosed with FMF in the Mayo Clinic from 1995 to 2007.
Methods/Results: The authors identified 50 patients who met the study inclusion criteria, which included persistent cutaneous lesions compatible with FMF and histologic findings of atypical lymphoid infiltrate surrounding or involving the perifollicular epithelium and CD4 predominance of lymphocytic infiltrate. Follicular mucinosis was a supportive criterion. The most common initial diagnoses for FMF were dermatitis, follicular mucinosis, and dermatophyte infections. The mean interval between onset of symptoms to diagnosis of MF was 3.9 years. The mean age of diagnosis in women was age 63 years, which is significantly older than that in men of 55 years. Although the head and neck areas are commonly spared in classic MF, these locations are involved in 58% of cases in FMF. The authors also determined that 24% of patients with localized disease had distant lymph node involvement. Furthermore, among the 37 patients who had peripheral smears, 30% had circulating Sézary cells. Comorbid malignancies were observed in 14% of patients, which included chronic lymphocytic leukemia and breast cancer. On histology, the neoplastic lymphoid cells had a CD3+ CD4+ CD8- immunophenotype. Tissue eosinophilia was specific but not sensitive for predicting pruritus. Syringotropism was found in 56% patients. Of the 21 patients who had polymerase chain reaction or flow cytometry studies on their lesional skin, clonality was identified in 71% of specimens. The overall survival rates at 1, 2, and 5 years after diagnosis of FMF were 96%, 90%, and 65%, respectively. Disease-specific survival rates could not be calculated due to the small number of cases. FMF appears to be less responsive to treatment than classic MF, which might be attributed to the deep extension of lymphocytes into the hair follicles limiting response to superficial topical steroid or light therapies.
Conclusions: FMF is associated with a poor 5-year overall survival rate.
Reviewer's Comments: FMF is a rare variant of MF that can be easily misdiagnosed clinically. On histology, the significance of the intrafollicular mucin for diagnosis has been a source of discussion. I tend to agree with the authors that intrafollicular mucin deposition is primarily a secondary phenomenon that can accompany either neoplastic or non-neoplastic lymphocytic infiltrates in the follicular epithelium. Therefore, clinicopathologic correlations, additional immunohistochemical studies, and longer-term observation may be necessary in some equivocal cases. (Reviewer-April W. Armstrong, MD).

Keywords: Folliculotropic Mycosis Fungoides, Pilotropic Mycosis Fungoides, Mycosis Fungoides

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Beta2-Microglobulin Levels Are Useful Marker for SLE Activity

Beta2-Microglobulin Can Be a Disease Activity Marker in Systemic Lupus Erythematosus.

Kim H-A, Jeon J-Y, et al:

Am J Med Sci 2010; 339 (April): 337-340

Beta2-microglobulin is only one of many reliable tests to determine systemic lupus erythematosus activity, but comparative studies among these types of tests are lacking.

Objective: To report serum levels of beta2-microglubulin in patients with systemic lupus erythematosus (SLE).
Participants/Methods: 100 consecutive patients with SLE were compared with 50 healthy control subjects in Korea. Additionally, beta2-microglobulin levels were correlated with history and clinical findings, blood cell counts, serum chemistries, urinalysis, complement levels, and anti–double-stranded DNA (dsDNA) antibodies. Overall disease activity was calculated using the SLE Disease Activity Index.
Results: Patients and controls were similar in sex distribution, but SLE patients were significantly older (32 vs 29 years). Of SLE patients, 97% had a positive beta2- microglobulin level, while 100% of controls were negative. Among SLE patients, those with renal disease, oral ulcers, or serositis had higher beta2-microglobulin levels. There was a positive correlation between elevated beta2-microglobulin and erythrocyte sedimentation rate, C-reactive protein, anti-dsDNA antibodies, and the SLE Disease Activity Index. A negative correlation was documented between elevated beta2-microglobulin and complement and hemoglobin levels.
Conclusions: Beta2-microglobulin levels are a useful marker for disease activity in SLE.
Reviewer's Comments: The search for activity markers in SLE continues. Some markers such as anti-dsDNA antibodies and complement can be used to monitor disease activity, but they correlate better with certain clinical manifestations such as renal disease. Among systemic markers of inflammation, C-reactive protein is elevated in patients with rheumatoid arthritis but not in those with lupus. Also, various disease activity indices available, such as the Systemic Lupus Activity Measure, the British Isles Lupus Assessment Group, and the SLE Disease Activity Index, are too complex for routine clinical use. This paper indicates that beta2-microglobulin can be a good and reliable marker, as it correlated well with the SLE Disease Activity Index, oral ulcers, serositis, anemia, hypocomplementemia, and anti-dsDNA antibodies. These findings confirm those of previous reports showing a correlation between elevated beta2-microglobulin and renal, extrarenal, and serologic activity; dsDNA autoantibodies, hypocomplementemia, and between active versus non-active lupus patients. So, beta2-microglobulin joins a growing list of tests that have shown good correlation with lupus symptoms and disease activity including anti-chromatin antibodies, thrombomodulin, lymphocytotoxic antibodies, anti-C1q antibodies, and anti-nucleosome antibodies. The latter is useful in the diagnosis and assessment of disease activity in lupus patients who are negative for anti-dsDNA antibodies. Nevertheless, optimal use of these tests or their combinations is still unknown. (Reviewer-Carlos Garcia, MD).

Keywords: Beta2 Microglobulin, Lupus Disease, Activity Markers

Print Tag: Refer to original journal article

Scarring Is Not Issue With PDT

Photodynamic Therapy in Dermatology: State-of-the-Art.

Babilas P, Schreml S, et al:

Photodermatol Photoimmunol Photomed 2010; 26 (June): 118-132

Photodynamic therapy does not affect fibroblasts or collagen fibers; therefore, scarring is not an issue.

Discussion: Both aminolevulinic acid (ALA) and methyl aminolevulinate (MAL) photodynamic therapy (PDT) have proven effective for treatment of actinic keratosis (AK). Response rates for PDT are similar to those for cryotherapy (about 70% to 90%) and superior to those for placebo. Complete clearance rates for basal cell carcinoma (BCC) are 87% to 92% for superficial BCC and 53% to 71% for nodular BCC. The response rate for Bowen's disease is 80%. The response rate of individual plaques of psoriasis varies from 30% to 80%. For plantar warts, ALA-PDT with incoherent light resulted in 75% improvement. Both visible and blue light and ALA- and MAL-PDT are effective to treat acne. Beneficial effects are sustained for ≥20 weeks. PDT resulted in significant clinical improvement in 10 patients with morphea. Additionally, it improved pruritus in 10 of 12 patients with lichen sclerosus. ALA-PDT with intense pulsed light, red light, blue light, and diode lasers lead to significant improvement of photodamaged skin during treatment of AK. A great advantage of PDT is that it does not produce scars or hypopigmentation. A randomized controlled trial of 60 patients showed clinical resolution in 93% and parasitological cure in 100% of leishmania lesions (*Clin Exp Dermatol* 2006).
Reviewer's Comments: PDT with ALA or MAL results in the production of inflammatory mediators, necrosis, and apoptosis of cells mainly through production of highly reactive oxygen radicals. ALA is more effective if lesions do not exceed 2 to 3 mm in depth. Use of newer liposomal forms allows for reduced ALA concentrations and better penetration. Recently, ALA patches have also been used, and results when treating AK were better than with cryotherapy. Use of MAL requires curettage prior to application but has advantages of more rapid accumulation in target tissues and less pain at time of irradiation. In terms of light sources, the Food and Drug Administration approved blue light in combination with ALA for treatment of non-hypertrophic AK, but research has demonstrated that other wavelengths and sources are also effective, including red light, intense pulsed light, and various lasers. The most important side effects of PDT are burning and stinging pain. (Reviewer-Carlos Garcia, MD).

Keywords: Photodynamic Therapy

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Elderly at Particular Risk of Death Due to PAN

Clinical Features and Outcomes in 348 Patients With Polyarteritis Nodosa: A Systematic Retrospective Study of Patients Diagnosed Between 1963 and 2005 and Entered into the French Vasculitis Study Group Database.

Pagnoux C, Seror R, et al:

Arthritis Rheum 2010; 62 (February): 616-626

Patients with hepatitis B virus-associated polyarteritis nodosa (PAN) have more severe disease as compared to patients with primary systemic PAN.

Objective: To describe the main characteristics of and long-term outcomes in patients with well-characterized polyarteritis nodosa (PAN) diagnoses.
Methods: The authors performed a retrospective review of the French Vasculitis Study Group database and identified 348 PAN patients. Patients' charts were reviewed with respect to demographics and clinical, histologic, laboratory, and radiologic findings, and outcomes. Patient characteristics and outcomes were analyzed and compared according to hepatitis B virus (HBV) status.
Results: 63% of patients were male. The mean age at diagnosis was 51 years. Most patients (96%) were white. The most common clinical manifestations were fever, weight loss, myalgias, and arthralgias in 93%; mononeuritis multiplex and peripheral neuropathy in 79%; and cutaneous nodules, purpura, or livedo in 49% of patients. Other manifestations included abdominal pain in 35% and hypertension in 34%. Only 3.7% of patients had limited cutaneous PAN. Overall, 70% of patients had histologic evidence of PAN and 66% had renal artery microaneurysms. Patients with HBV-associated PAN had more severe disease as manifested by neuropathy, hypertension, cardiomyopathy, abdominal pain, and orchitis. Patients with primary PAN and cutaneous manifestations were more likely to relapse. Risk factors for death included hypertension, severe abdominal manifestations, and age >65 years.
Conclusions: The rate of mortality from PAN remains high, especially for the elderly, and relapses do occur, particularly in patients with non-HBV-related PAN with cutaneous manifestations.
Reviewer's Comments: Results showed that HBV-associated PAN leads to a more severe disease as determined by current disease activity scores and manifested by hypertension due to renal vasculopathy, skin nodules, peripheral neuropathy, abdominal pain, and orchitis. The overall mortality rate at 5 years was approximately 25%. There were no significant differences in mortality among groups, but there were significantly fewer relapses in patients with HBV-associated PAN. The worse prognosis and higher risk for death was documented in elderly patients who developed recent-onset hypertension and abdominal symptoms severe enough to require GI consult or surgery. Of interest to dermatologists, this series included only a few patients with limited cutaneous PAN. In my experience, cutaneous PAN comprises <10% of cases, except in children, in whom it is the most frequent type of PAN. Clinically, cutaneous PAN manifests by localized livedo reticularis, with or without nodules, and is often associated with mononeuritis multiplex of the affected extremity, and with mild general symptoms such as fever, arthralgias, and myalgias. The treatment of choice is topical or intralesional corticosteroids. Antibiotics are recommended for patients with evidence of streptococcal infection. I use oral prednisone only for extensive or progressive disease. (Reviewer-Carlos Garcia, MD).

Keywords: Polyarteritis Nodosa, Vasculitis, Medium-Sized Vessel Vasculitis

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Early Onset Lichenoid GvHD Is New Variant of Acute GvHD

Early-Onset Lichenoid Graft-vs.-Host Disease: A Unique Variant of Acute Graft-vs.-Host Disease Occurring in Peripheral Blood Stem Cell Transplant Patients.

Magro CM, Kerns MJ, et al:

J Cutan Pathol 2010; 37 (May): 549-558

An early onset lichenoid graft-versus-host disease is a new variant of acute graft-versus-host disease occurring within the setting of peripheral blood hematopoietic stem cell transplants.

Background: Chronic graft-versus-host disease (GvHD) may complicate stem cell transplantations. Cutaneous manifestations include lichenoid GvHD and scleroderma that may occur from at least 100 days post-transplant.
Objective: To characterize early onset GvHD.
Design: Retrospective study.
Participants: 17 recipients were selected (8 males, 9 females; age range, 24 to 61 years).
Methods: All patients received peripheral blood hematopoietic stem cell transplants (PBSCT) for primary diagnoses ranging from acute leukemias, lymphomas, and myelodysplasia. Donor and recipient were chosen with sex mismatch from a database of 130 cases of GvHD including acute and chronic cases. Light microscopy was performed. FISH XY assay was performed. A control group of patients with classic lichenoid GvHD with rash developing at >3 months was selected.
Results: Duration from transplantation to onset of symptoms ranged from 16 to 56 days (average, 35.3 days). Clinical presentation was heterogeneous and included erythema to lichenoid papules. Gastrointestinal GvHD was suspected in all patients and confirmed by gastrointestinal biopsy in 12 of 16 patients. A cytomegalovirus (CMV) hybrid capture assay was positive in the peripheral blood in 9 of 10 patients within 1 month of transplantation. FISH XY analysis in all 17 cases found the predominant lymphocyte population to be donor origin in 12 cases, host origin in 2 cases, and mixed origin in 3 cases. Histopathology revealed variable epidermal hyperplasia with hyperkeratosis and hypergranulosis, and variable subepidermal fibroplasia and interface changes, patterns that were similar to the control group of accelerated lichenoid GvHD.
Conclusions: An early onset lichenoid GvHD is a new variant of acute GvHD occurring within the setting of PBSCT. The pathogenesis appears to be mediated by donor lymphocytes as confirmed by FISH XY analysis.
Reviewer's Comments: Clinicians and dermatopathologists alike need to be aware of this new variant of acute GvHD with lichenoid features occurring within 60 days of a PBSCT. This histopathologic pattern was previously associated only with chronic GvHD. This paper provides an excellent summary and description of this new variant. The authors further point out that these cases were seen only with PBSCT and not bone marrow transplants (BMT), although the type of transplantation was not a study exclusion criterion. They hypothesize that PBSCT may contain more stem cells and T cells as compared to bone marrow transplantation. The authors further speculate that CMV immediate early, and early proteins may play a role-enhanced immunity by activating pro-apoptotic pathways. Since donor T-lymphocytes appear to be responsible for the pathophysiology, early therapeutic intervention may be possible. (Reviewer-Paul K. Shitabata, MD).

Keywords: Lichenoid Graft-vs-Host Disease, Early Onset, Peripheral Blood Stem Cell Transplant

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FISHing for Superficial Melanocytic Neoplasms

Superficial Melanocytic Neoplasms With Pagetoid Melanocytosis: A Study of Interobserver Concordance and Correlation With FISH.

Gerami P, Barnhill RL, et al:

Am J Surg Pathol 2010; 34 (June): 816-821

Fluorescence in-situ hybridization can be performed on both small and large indeterminate melanocytic lesions with lesional cells visualized by direct immunofluorescence microscopy.

Background: Superficial melanocytic neoplasms with pagetoid melanocytosis are a diverse group of diseases ranging from an intraepithelial Spitz nevus, an epithelioid de novo melanocytic dysplasia, or early pagetoid melanoma. Diagnostic concordance, even among expert dermatopathologists, may be poor. Comparative genomic hybridization (CGH) and fluorescence in-situ hybridization (FISH) have been used to assist in difficult melanocytic proliferations. While both methodologies may assist in discriminating between benign melanocytic nevi and melanomas, CGH is more practical for larger lesions where lesional cells may be micro-dissected, while FISH can be performed on both small and large lesions with lesional cells visualized by direct immunofluorescence microscopy.
Objective: To determine use of a targeted melanoma FISH-assay on superficial melanocytic neoplasms with pagetoid melanocytosis. The interobserver diagnostic reliability among reviewing dermatopathologists was also evaluated.
Design: Retrospective study.
Participants: 24 cases of superficial melanocytic neoplasms with pagetoid melanocytosis were selected.
Methods: A targeted FISH-assay using 4 probes (6p25, 6q23, Cep6, and 11q13) previously validated to be highly specific for melanomas were performed on all biopsies. Cases were scored as positive or negative by previously established criteria. Cases were biased to lesions that exhibited melanocytic nesting with at least 10 cells from each site for a maximum of 3 sites. Three additional experienced dermatopathologists independently scored lesions as clearly benign, benign with some atypia, atypical and melanoma cannot be excluded, or melanoma. The consultants' scores were summed and 3 categories were created: consensus diagnosis of melanoma, consensus diagnosis of benign, and indeterminate with no clear consensus.
Results: Consensus diagnosis yielded 7 melanomas, with FISH positive in 5 of 7 cases (71%). A benign consensus was diagnosed in 6 cases with a negative FISH in all cases. An indeterminate diagnosis was rendered in 11 cases, with FISH being positive in 2. In 1 of the FISH-positive indeterminate cases, the re-excision showed a definite melanoma.
Conclusions: When expert dermatopathologists agree on the diagnosis of either benign or malignant superficial melanocytic neoplasms with pagetoid melanocytosis, the FISH assay is sensitive and specific. The 2 indeterminate cases, reviewed in concert with FISH results, led to the conclusion that these represent early melanomas. The majority of indeterminate cases are usually FISH negative. In the hands of experienced dermatopathologists, FISH may be helpful in establishing a diagnosis in a subset of cases.
Reviewer's Comments: This is a practical application of the FISH assay for a diagnostically challenging area in dermatopathology. With more cases, an algorithm may be set up to assist in the triage of these cases, minimizing potentially disfiguring surgery for benign cases. Future studies should examine atypical junctional melanocytic proliferations overlying scars or other neoplastic dermal processes such as fibrous papules, dermatofibromas, and basal cell carcinomas. (Reviewer-Paul K. Shitabata, MD).

Keywords: Melanoma, Pagetoid, Fluorescence In-Situ Hybridization, Spitz Nevi

Print Tag: Refer to original journal article

Can Switching to Sirolimus Reduce Skin Cancer Risks in Renal Transplant Patients?

Switch to a Sirolimus-Based Immunosuppression in Long-Term Renal Transplant Recipients: Reduced Rate of (Pre-)Malignancies and Nonmelanoma Skin Cancer in a Prospective, Randomized, Assessor-Blinded, Controlled Clinical Trial.

Salgo R, Gossmann J, et al:

Am J Transplant 2010; 10 (June): 1385-1393

Switching to sirolimus-based immunosuppression can reduce the incidence of actinic keratosis and skin cancers in renal transplant patients.

Background: Nonmelanoma skin cancers (NMSCs) are a common and important complication of immunosuppression used for organ transplantation. Currently, most immunosuppressive regimens are based on the calcineurin inhibitors, cyclosporine or tacrolimus, or on azathioprine. All 3 of these agents are known to promote NMSC. Sirolimus, an mTOR inhibitor, is a newer immunosuppressive agent with decreased nephrotoxicity relative to calcineurin inhibitors. Non-controlled trials have hinted that switching to sirolimus may decrease the incidence of cancer in transplant patients but, until now, prospective data have been lacking.
Objective: To determine if switching from conventional immunosuppression to sirolimus can prevent or reduce squamous cell carcinoma (SCC) and actinic keratosis (AK) in renal transplant patients.
Design: Prospective, randomized, assessor-blinded, controlled clinical trial.
Participants: 44 renal transplant patients receiving cyclosporine, tacrolimus, or azathioprine-based immunosuppression.
Methods: Patients were randomized to either continue their current immunosuppressive regimen or switch to a regimen of sirolimus and prednisone. Blinded skin assessments for AK and skin cancers were conducted by a dermatologist at 6 and 12 months.
Results: At 6 months, the AK score improved in 31% of the sirolimus group compared to 0% in the control group. At 12 months, 73% of the sirolimus group improved versus 0% in the control group. Improvement in AK was highly significant at 6 and 12 months. At 12 months, 1 new NMSC was seen in the sirolimus group, while 8 new skin cancers were seen in the control group. NMSCs were predominantly SCCs.
Conclusions: Sirolimus may be a valuable option for renal transplant recipients with multiple NMSCs.
Reviewer's Comments: This study suggests that malignant and premalignant skin lesions are not an inevitable consequence of long-term immunosuppression. Although this trial was small, the results seem believable because they are consistent with findings from a large clinical trial, the CONVERT trial, which was designed to compare renal function after switching to sirolimus. Although not a primary end point, this study also saw a reduction in cancer from 9% to 3% in those switched to sirolimus. In addition to a rapid decrease in new skin cancers, this study suggests that premalignant lesions will regress following switch to an mTOR inhibitor-based regimen. Although sirolimus lacks some of the renal toxicity of calcineurin inhibitors, it cannot be tolerated by all patients due to significant adverse effects including pneumonitis, proteinuria, and apthous ulcers. Based on this study, it seems reasonable to advise our patients with multiple SCCs or extensive AKs to discuss sirolimus-based immunosuppression with their transplant physicians. (Reviewer-Michael S. Kolodney, MD, PhD).

Keywords: Nonmelanoma Skin Cancer, Renal Transplant, mTOR Inhibitor, Sirolimus

Print Tag: Refer to original journal article