MICRO LABS LIMITED

DERMA

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Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "Derma Today" which contains latest and interesting news in the field of Dermatology.

This issue contains:

1. **A Case Report of Dermoscopy and Reflectance Confocal Microscopy describing Amyloidosis cutis Dyschromica**
2. **First Human Trial to treat patients with photosynthetic cells, supporting the translation of photosynthetic therapies into clinics**
3. **Short Term risk of developing Psoriatic arthritis treated with guselkumab**

Should you require any article or, medical information, please feel free to contact us
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Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited.

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A Case Report of Dermoscopy and Reflectance Confocal Microscopy describing Amyloidosis cutis Dyschromica

Introduction:

Primary localized cutaneous amyloidosis, a chronic pruritic skin disease characterized by amyloid deposition in the upper dermis. Amyloidosis cutis dyschromica is a rare type of Primary localized cutaneous amyloidosis. Mutations of the glycoprotein non-metastatic melanoma protein B was scientifically proven to be linked with Amyloidosis cutis dyschromica. For early diagnosis of Amyloidosis cutis dyschromica, evidence through imaging is necessary. There are only few reports concerning the imaging of Amyloidosis cutis dyschromica, and no article has provided a unified description of the imaging characteristics.

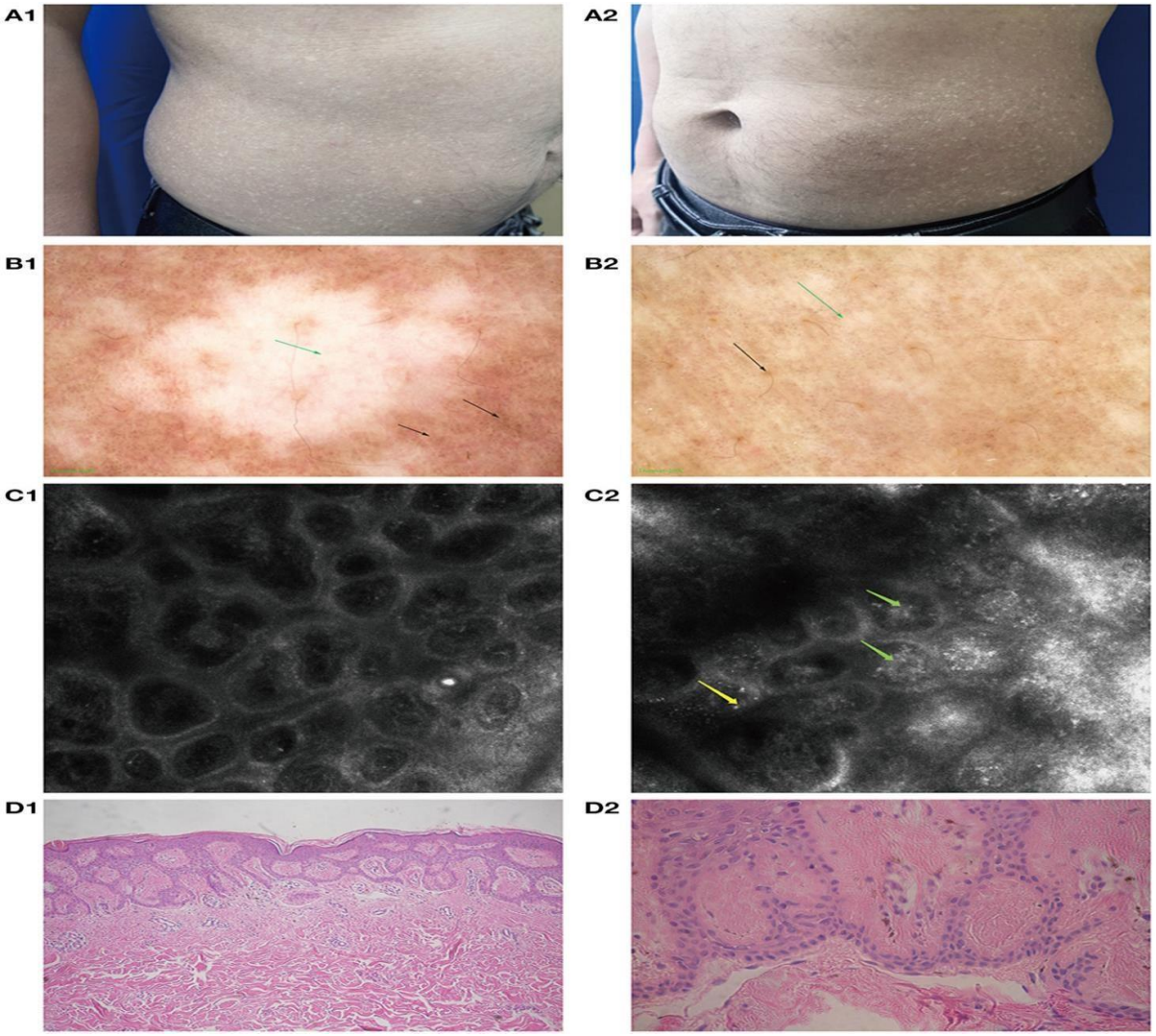
Objective:

To analyse the characteristic imaging changes of Amyloidosis cutis dyschromica under dermoscopy and reflectance confocal microscopy and to investigate gene mutations in a Chinese Han pedigree of Amyloidosis cutis dyschromica and analyse the correlation
Between genotype and phenotype.

Case Presentation:

A 35-year-old male patient presented with dense hyperpigmentation and hypopigmented spots on the trunk and limbs. Patient complaint of progressive, asymptomatic, diffused pathological changes since 8 years old. Initially, patient complained of having hyperpigmentation on his back, later it affected the abdomen, limbs, and palmoplantar regions. No history of systemic diseases or other skin diseases was recorded. Patient's son and daughter reported no such symptoms, but patient's 32-year-old brother complaint of having similar skin lesions. Dermoscopy revealed the hypopigmented areas which showed big white patches with poorly defined margins, surrounded by small white spots and hyper pigmented blotches. The hyper pigmented areas were the patches composed of brownish spots, intermixed with striped or patchy white areas of hypopigmentation. Reflectance confocal microscopy, revealed hyperkeratosis in the epidermis: a highly refractive substance with clumpy, dotted, and linear structures inside the papillary dermis, and widening of the ring structure of the dermal papilla. Parts of the hypopigmented areas showed highly refractive round cells scattered in the superficial dermis. Histopathology report revealed sparse melanophages and focal pigment incontinence beneath the epidermis, mild hyperkeratosis in parts of lesions, and homogenous eosinophilic deposits in the papillary dermis that stained positive with CR and was consistent with amyloidosis. A missense mutation and a frameshift mutation were identified.

Clinical manifestations, imaging changes, and pathological changes in amyloidosis cutis dyschromica (ACD).



Conclusion:

Analyzing the genotype–phenotype correlation of Amyloidosis cutis dyschromica, it was hypothesized that the blisters could be associated with some gene mutations such as c.565C>T and c.660T>G. But no significant relevance was recorded. The characteristic changes under dermoscopy and Reflectance confocal microscopy provides the possibility of early diagnosis of Amyloidosis cutis dyschromica. More studies with larger samples are required to verify the genotype–phenotype correlation in Amyloidosis cutis dyschromica.

Reference:

Gao M, et al. Amyloidosis Cutis Dyschromica: Dermoscopy and Reflectance Confocal Microscopy and Gene Mutation Analysis of a Chinese Pedigree. Frontiers in Medicine.:2354.

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First Human Trial to treat patients with photosynthetic cells, supporting the translation of photosynthetic therapies into clinics

Introduction:

Oxygen, is the major molecule required for aerobic metabolism and at the same time, it plays a key role in cellular processes including mitochondrial respiration and reactive oxygen species production. Every step of the wound healing process, for example cell proliferation, synthesis of collagen, angiogenesis requires oxygen. Hypoxia, a lower concentration of oxygen in arterial blood is responsible for the leading cause for chronic wounds. Traditional systemic oxygen therapies, like supplemental oxygen or hyperbaric oxygen therapy provides only modest support of wound healing. translation of these technology. As, oxygen is produced by the process of photosynthesis, the use of photosynthetic cells highlights an amazing alternative for local delivery of oxygen either in vitro or in vivo. Study has also shown that the presence of photosynthetic cells allows the development of thicker 3D cardiac structures in vitro and improves the cardiac function after heart ischemia in vivo. Uses of photosynthetic cells for the local oxygen delivery has become a promising approach and, there has been an increasing interest in the advances of photosynthetic biomaterials and therapies as explained by numerous published articles, where the potential of this novel concept is highlighted.

Methods:

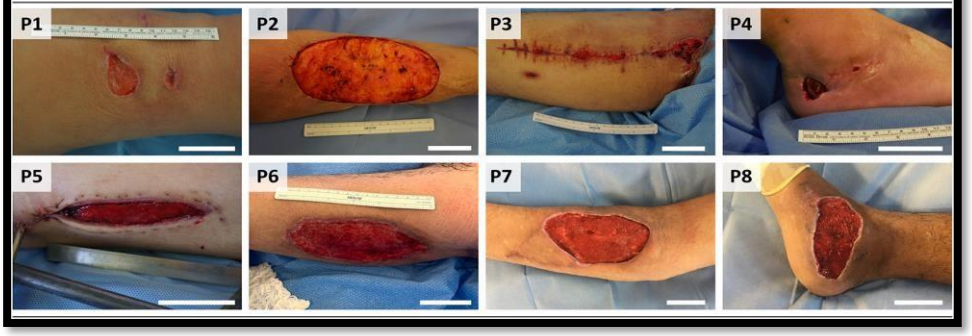
At 20◦C, C. reinhardtii strain was grown photomixotrophically in sterile liquid "Tris-Acetate-Phosphate medium" and agitation was kept constant, in the exponential growth phase and constant white illumination. Photosynthetic scaffolds were fabricated following optimized protocol. Briefly, 25 cm 2 scaffolds were slightly dried on a sterile gauze, and placed silicone-face down on a sterile cell culture plate. Then, 1.25× 108 cells were re suspended in 850 µL of sterile TAP, and mixed in a 1:1 ratio with human fibrinogen. Around, 850 µL of human thrombin were homogeneously mixed to the scaffolds, and the microalgae fibrinogen was added. For 1 hour, Scaffolds were left undisturbed to ensure complete polymerization, and was covered with 20mL of sterile TAP. During the testing period, it was made sure that scaffolds remains undisturbed at room temperature with constant white illumination for 4 to 6 days. Once the results confirmed, scaffolds were packaged and transported to the operating room. Kruskal Wallis test and Dunn's post-test with Graph Pad Prism 5 software were used the compare the results. Oxygen production of the scaffold was then detected upon light stimulation with oxygen metabolic rate of 12.3 ± 1.1 n mol cm−2 min−1, while oxygen was consumed in the absence of light at a rate of 10.2 ± 1.1 nmol cm−2 min−1

Study Design and Participants

A total of 8 Patients with 21 to 63 years old were enrolled in this study, according to specific inclusion and exclusion criteria. After the wound bed was cleaned, scaffolds were implanted and illuminated for 7 days with a specially designed device. On day 21, an autologous partial skin graft was performed on patients, except for few cases where the 2nd intervention was not required. Blood samples along with biopsy were taken to detect the systemic and local immune response of the patients throughout the study period. On day 7, 21, and 27 of post implantations, histological and immune histochemical analysis, biopsy samples were taken and analysed. Of the enrolled patients, most wounds corresponded to single full thickness skin defects, except for 1 patient who was treated for multiple wounds. The etiology of the wounds as well as the body location were diverse but, all wounds were located on the right extremities. The wound area seen to be highly variable among patients, with a range of 4.1–134.2 cm2.

Characteristics of the enrolled patients.

Patient	Age	Gender	Wound etiology	Wound location	Area (cm^2)
P1	30	F	Laceration	Right thigh, lower third, lateral	8.7
P2	56	F	Burn scar contracture	Right arm, elbow crease	134.2
P3	21	M	Traumatic injury	Right thigh, higher third, medial	13.8
P4	31	M	Traumatic injury	Right ankle, lateral, retromalleolar	4.1
P5	46	M	Exposed fracture	Right thigh, lower half, lateral	12.8
P6	31	M	Loxocelism	Right leg, higher half, posteromedial	48.8
P7	63	M	Flap necrosis	Right forearm, ventral area	49.1
P8	31	M	Attrition	Right ankle, medial	40.4



Results:

No clinical signs of local inflammation such as edema or erythema was shown in any patient in the surrounding healthy skin between the scaffold and the wound edge. After 90 days of scaffold implantation, the Clinical outcome showed complete integration of the skin

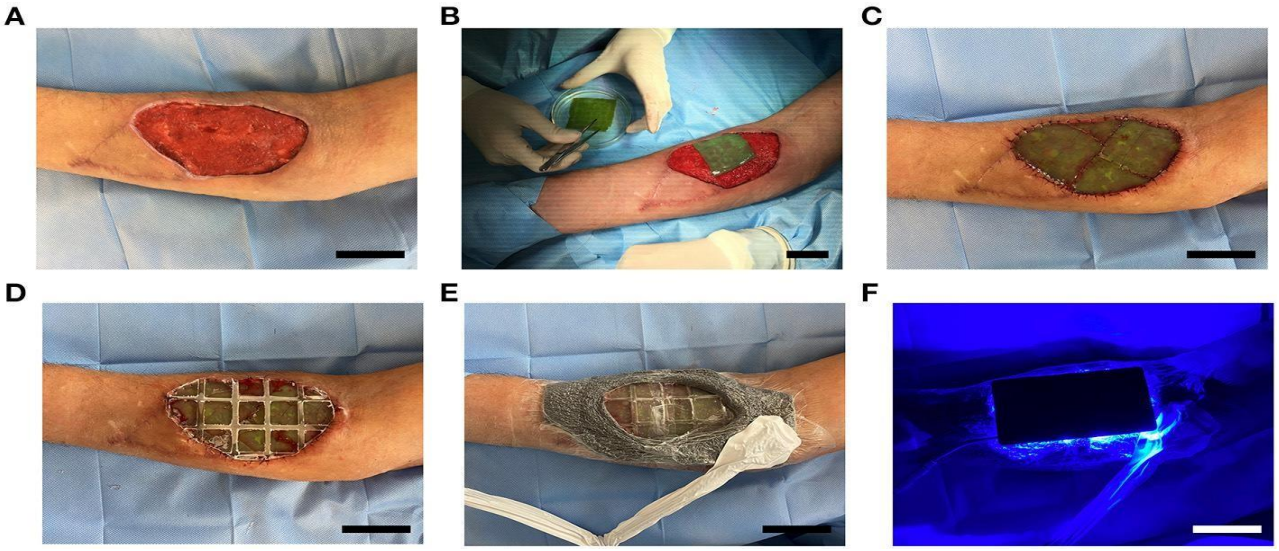
graft, no signs of morbidity and functional recovery of the wound area was observed. Overall clinical outcome of all patients were similar, as all wounds closed at the expected time and, when corresponded, the autologous graft was integrated with the previously implanted scaffold. This trial showed the presence of the photosynthetic microalgae

Chlamydomonas reinhardtii in the implanted scaffolds doesn't trigger any deleterious local

or systemic immune responses in a 90 days' follow-up, allowing full tissue regeneration

in humans.

Photosynthetic scaffold implantation. Wound bed was cleaned and prepared for scaffold implantation (A). Photosynthetic scaffolds were sutured between them and to the wound edges (B,C), and covered with a flexible and transparent PDMS membrane (D), which was then secured with negative pressure wound therapy, leaving a window over the scaffold to allow illumination (E). Light device was then placed on top and illumination intensity was controlled (F). Scale bars represent 5 cm.



Conclusion:

This study represents the safety of implanting microalgae as an important approach to oxygenate tissues by photosynthetic therapy. The implantation of this therapy in all of the 8 patients, with full thickness skin wounds did not trigger any immune response within the 90 days' follow-up, and helped in full tissue regeneration. Results obtained from this study, significantly going to utilise photosynthetic biomaterials and therapies into clinical settings, and will play an important role in understanding the potential symbiotic relationships between

humans and photosynthetic cells. This results represent the 1st attempt to treat patients with scaffold implantation, supporting the translation of photosynthetic therapies into clinics.

Reference

Obaíd ML, et al. A First in Human Trial Implanting Microalgae Shows Safety of Photosynthetic Therapy for the Effective Treatment of Full Thickness Skin Wounds.Frontiers in Medicine.2088.

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Short Term risk of developing Psoriatic arthritis treated with guselkumab

Introduction:

Psoriatic arthritis, a major extra cutaneous manifestations of psoriasis with 20–30% of patients suffering from psoriasis develops this condition. Joint involvement typically follows psoriasis onset, although Psoriatic arthritis are seen less commonly with skin lesions. Some growing evidence highlights that the patients with Psoriasis go through 3 clinically silent and progressive stages before developing clinically evident Psoriatic arthritis: stage (1) immunological phase, stage (2) subclinical phase and stage (3) prodromal phase. This model of progression helps in early intervention aiming to treat patients with Psoriasis. in patients with Psoriasis, 2 categories of predictors for developing Psoriatic arthritis have been identified, including medium or long-term and short-term.

Objectives:

To evaluate the efficacy of guselkumab in psoriasis patient with short term risk of psoriatic arthritis development.

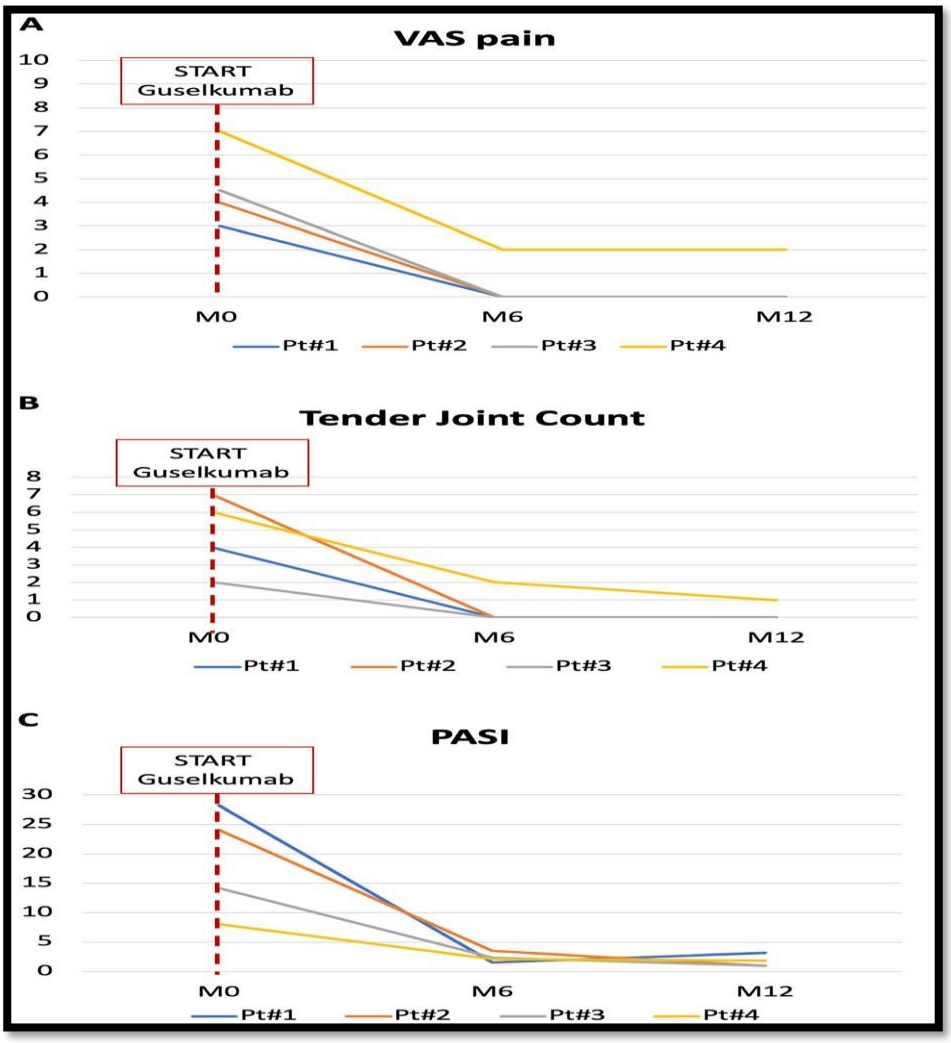
Methods:

This study enrolled 4 patients (2 women and 2 men) with a mean age of 53.3 years (38–65 years) and a mean Psoriasis duration of 13.3 years (8–25 years) carrying a short-term risk of developing Psoriatic arthritis treated with guselkumab for skin disease. Baseline mean Psoriasis Area and Severity Index score was 18.6 (SD 9.2), with figures ranging from 8 to 28.2, while nail involvement was seen only in 2 cases. All the patients reported arthralgia at baseline, with a mean tender joint count of 4.74 (SD 2.2), without swollen joints and a mean VAS pain of 4.6 (SD 1.7). Sonographic report revealed the evidence of subclinical active synovitis in patient 1 and patient 3. Guselkumab was considered as the first line treatment in all cases after the failure of at least one conventional treatment (methotrexate or cyclosporine). Follow up was done for almost 1-year, and no patient complaints of developing clinical arthritis and fulfilled classification criteria for Psoriatic Arthritis.

Results:

A significant reduction in VAS pain after 6 months of therapy, was seen in almost all patients and a complete regression of arthralgia was observed in 3 patients while 1 patient (case 4) reported a major regression of musculoskeletal pain and TJC. No sonographic sign of active synovitis was observed in the present cohort from month 6. Psoriasis Area and Severity
Index was observed 75 in all cases.

Variation of VAS pain (a), tender joint count (TJC) (b), and PASI score (c) over 1 year



Conclusion:

This study concluded that guselkumab might intercept Psoriatic Arthritis during a potential ‘‘window of opportunity’’ in individuals with moderate to severe Psoriasis having

short-term predictors of developing Psoriatic arthritis. More Randomized controlled trials are needed to confirm the preliminary findings.

Reference:

Zabotti A, et al. Arthritis Interception in Patients with Psoriasis Treated with Guselkumab. Dermatology and Therapy. 2021 Nov 27:1-4.