

## Foreign Body Granuloma: A Neglected Splinter

Assia EL Bouhmadi<sup>1</sup>, El Fatoiki Fatima Zahra<sup>1</sup>, Hali Fouzia<sup>1</sup>, Chiheb Soumiya<sup>1</sup>

<sup>1</sup>Chu Ibn Rochd, Dermatology, Morocco

## **Introduction & Objectives:**

Foreign objects within soft tissues are frequently encountered in children, particularly in the hands. If unnoticed, these objects may give rise to a granulomatous inflammatory response, potentially linked to a regional aseptic bone reaction. The development of foreign body granulomas can be initiated by various particles that are relatively insoluble and minimally immunogenic.

#### **Materials & Methods:**

Here, we present a case of a 40-year-old woman, highlighting the diagnostic complexities associated with this phenomenon.

#### **Results:**

A 40-year-old woman without notable medical history presented to the dermatology department with a painful swelling on the outer aspect of her left knee, evolving over the past 2 months. Despite a fall one month prior without immediate pain, she reported no fever, skin rash, or altered consciousness. Clinical examination revealed a hard and painful subcutaneous nodular lesion without tenosynovitis or edema. Standard X-rays and joint ultrasound were normal, and no signs of infection were found in laboratory tests. Soft tissue ultrasound identified a linear hyperechoic foreign body surrounded by a heterogeneous hypoechoic thick-walled area consistent with a foreign body granuloma. The foreign body measured 3 cm in length, with a distance of 8 mm from the skin surface. Soft tissue infiltration and a small fluid collection containing air bubbles were observed. Surgical exploration revealed a splinter with tissue inflammatory reaction, and symptoms rapidly resolved.

In the discussion, foreign body granulomas, chronic inflammatory lesions, were explored. These lesions involve the accumulation of cells from the monocyte and macrophage lineage, along with other inflammatory cells. Various particles, both inorganic and organic, can induce the formation of foreign body granulomas. The clinical presentation varies, including papules, nodules, or violet erythematous plaques, often becoming harder over time due to fibrosis. A complex interplay between non-immunological xenogenic granulomas and allergic granulomas challenges a clear clinical distinction. The latency period between foreign body inclusion and nodule formation can span several years. Diagnosis, particularly when the foreign body is radiotransparent, requires meticulous approaches such as ultrasound for localization and excision, leading to clinical and radiographic cure.

## **Conclusion:**

In conclusion, foreign body granulomas pose diagnostic challenges, often arising from unnoticed objects within soft tissues. This case highlights the complexities associated with these granulomas, emphasizing the importance of considering diverse etiologies. The study underscores the significance of imaging modalities, particularly ultrasound, in accurate localization and excision of suspected foreign bodies. Timely surgical intervention can lead to a swift resolution of symptoms and clinical cure, emphasizing the need for a multidisciplinary approach in managing such cases.



## Circulating tumor DNA: a promising biomarker in stage III BRAF+ melanoma

Gabriele Roccuzzo<sup>1</sup>, Eleonora Bongiovanni<sup>1</sup>, Sara Marchisio<sup>2</sup>, Alessia Andrea Ricci<sup>3</sup>, Ada Funaro<sup>2</sup>, Simone Ribero<sup>1</sup>, Rebecca Senetta<sup>4</sup>, Pietro Quaglino<sup>1</sup>

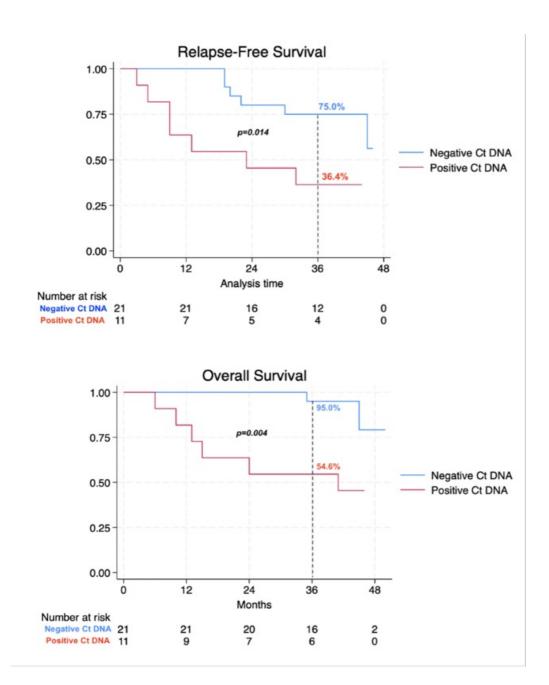
<sup>1</sup>University of Turin, Section of Dermatology, Turin, Italy, <sup>2</sup>Laboratory of Immunogenetics, Department of Medical Sciences, University of Turin, Turin, Italy, <sup>3</sup>Pathology Unit, Medical Sciences, University of Turin, Turin, Italy, <sup>4</sup>Pathology Unit, Oncology, University of Turin, Turin, Italy

**Introduction & Objectives:** In recent years, various melanoma biomarkers have undergone investigation in both preclinical and clinical settings. Among these, circulating tumor DNA (ctDNA) has emerged as a promising candidate. However, in the adjuvant setting, only a limited number of exploratory analyses have been conducted, and uncertainties persist regarding the link between ctDNA detection and patients' relapse.

Materials & Methods: A cohort of 32 patients with resected stage III BRAF+ melanoma, who were diagnosed and underwent adjuvant therapy with either anti-PD1 or dabrafenib/trametinib, was collected from 2019 to 2021 and followed up until December 2023. Clinical, histological, and serological data were recorded. A sensitive multiplexed digital droplet (dd)-PCR was used to detect and quantify the three most common hotspot mutations in codon 600 (V600E, V600R, V600K) of the BRAF oncogene in circulating free DNA isolated from plasma. Blood samples were retrieved monthly post-surgery, starting from the initial administration of adjuvant therapy until therapy completion or relapse. Samples were classified as mutated when the number of copies/reaction exceeded the limit of blank (LOB = meanblank + 1.645\*SDblank). The number of mutated DNA copies per reaction was employed to calculate copies per milliliter (ctDNA copies/mL) of plasma.

Results: The overall 36-month recurrence-free survival (RFS) for the cohort was 61.6% (95% CI 42.3%-76.1%). Stratifying by basal ctDNA status, individuals with negative basal ctDNA exhibited a significantly higher 36-month RFS of 75.0% (95% CI 50.0%-88.8%) compared to 36.4% (95% CI 11.2%-62.7%) in the positive group (p=0.014) (Fig.1). Cox univariate analysis for RFS identified in-transit metastasis (HR 4.20, 95% CI 1.11-15.87, p=0.034) and positive basal ctDNA status (HR 3.79, 95% CI 1.20-12.00, p=0.023) as significant risk factors. The 36-month overall survival (OS) rate for the cohort was 80.8% (95% CI 62.2%-90.9%), with a significant difference observed between the negative basal ctDNA (95.0%, 95% CI 69.5-99.3) and the positive (54.6%, 95% CI 22.9-77.9) groups (p=0.004) (Fig.2). Cox univariate analysis for OS identified age (HR 1.07, 95% CI 1.01-1.14, p=0.015), stage IIID (HR 8.81, 95% CI 1.68-46.21, p=0.010), in-transit metastasis (HR 9.44, 95% CI 1.89-47.16, p=0.006), relapse during adjuvant therapy (HR 24.58, 95% CI 2.65-228.08, p=0.005), brain relapse (HR 100.69, 95% CI 1.14-100.80, p=0.039), and positive basal ctDNA (HR 7.92, 95% CI 1.56-40.36, p=0.013) as significant variables. Interestingly, clinical stage showed no correlation with basal ctDNA status (p=0.324, Spearman test), which was confirmed at logistic regression (p=0.1621, Pseudo R2=0.0993). At last, the examination of basal LDH levels (normal range 250-450 UI/L) demonstrated no association with relapse, death, or basal ctDNA.

**Conclusion:** Basal ctDNA status proved to be an effective tool for predicting relapse and survival in stage-III melanoma patients, surpassing the predictive value of clinical stage and basal LDH values, traditionally recognized prognostic factors in melanoma. This biomarker exhibits considerable potential in forecasting both response and survival outcomes, warranting comprehensive evaluation across a broader cohort of patients undergoing adjuvant therapy.



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## Reverse transcription polymerase chain reaction in the assessment of fungal viability in onychomycosis

Yanina Kutasevych<sup>1</sup>, Iryna Oliinyk<sup>1</sup>, Kseniia Suprun<sup>1</sup>, Oksana Sokol<sup>1</sup>

<sup>1</sup>State Establishment "Institute of Dermatology and Venereology of the NAMS of Ukraine", Dermatology, Kharkiv

# **Introduction & Objectives:**

Despite the high sensitivity of the polymerase chain reaction (PCR) method, difficulties arise in establishing the fact of onychomycosis pathogen elimination, because this method detects even single copies of DNA of a non-viable pathogen. The detection of RNA in the studied material of nail plates indicates the viability of the pathogen, but the methodological determination of RNA is a difficult task. The aim of the study was to isolate complementary DNA (cDNA), which is a copy of the RNA molecule and is produced by reverse transcriptase, from the genetic material (biological samples) of nail plates.

#### **Materials & Methods:**

Determination of cDNA was performed by reverse transcription PCR (RT-PCR). For this purpose, 47 patients with onychomycosis after treatment were selected by randomization. The study was conducted in two stages. At the first stage, PCR detected the genetic material of fungi in the scales of the affected nail plates. In the second stage, when genetic material was detected in the biological samples, a RT-PCR reaction was performed to determine the viability of the fungi.

## **Results:**

PCR revealed that 31.9 % of the samples contained fungal genetic material, and 68.1 % were negative. According to the results of RT-PCR, cDNA was detected in 60.0% of patients, indicating the absence of fungal elimination, and therefore treatment of such patients was continued. cDNA was not detected in 40.0% of patients, indicating the absence of viable fungi, i.e., the onset of mycological negativity, so these patients did not require further treatment.

#### **Conclusion:**

The molecular study of RT-PCR allows to determine the viability of onychomycosis pathogens, reduce the percentage of false-positive results of traditional PCR and makes it possible to establish mycological elimination.



developing a New Multivariate Predictive Model for Oral Lichen Planus Diagnosis: Combining Medical History and Direct Immunofluorescence

Katarzyna Osipowicz\*1, Patrycja Łazicka<sup>2</sup>

<sup>1</sup>Klinika przeszczepiania i leczenia włosów sp. zoo, dermatology, Warszawa, <sup>2</sup>Poland, dermatology, Warszawa, Poland

## **Introduction & Objectives:**

Around 25% of adults experience mouth ulcers, which can be caused by various factors, including lichen planus, a chronic inflammatory and autoimmune disorder affecting the oral cavity. According to literature, differential diagnosis of oral lichen planus and oral lichenoid lesions can be aided by the use of direct immunofluorescence (DIF). The diagnostic criteria for oral lichen planus, which were first published in 1978, are still being refined, with the most recent diagnostic algorithm proposed in 2019 based on clinical signs and medical history. Our study aimed to develop a new multivariate predictive model by combining medical history and DIF.

#### **Materials & Methods:**

The study included patients who presented to the Department of Dermatology in 2019-2022 with erosive lesions in the oral cavity or were referred there by their dentists. The following variables were collected: DIF IgG, DIF IgA, DIF IgM, DIF C3, DIF F1, DIF F2, histopathology, gender, age on the day of lesion onset, stress during the study period, stress at onset, localization of white patches and erosions, previous treatment, taking supplements, herbs, or any medication, dental status, smoking, using mouthwash. Statistical analysis was performed using Statistica 13. For neural networks we used default parameters of the Statistica software.

## **Results:**

The study group consisted of 80 patients: 63 (78.8%) women and 17 (21.2%) men. Lichen was confirmed by histopathology in 4 (5.0%) of the study participants and not confirmed in 57 (71.2%); it was not excluded in 30 subjects (37.5%) and excluded in 31 (38.8%). The incidence of DIF IgG, DIF IgA, DIF IgM, DIF C3, DIF F1, DIF F2 positivity did not differ significantly between either subjects with confirmed or unconfirmed lichen, or between subjects with lichen excluded or not excluded. Data Mining module suggested four significant predictors to create a multivariate model for dependent variable 'lichen planus not excluded by histopathology' and none for 'lichen confirmed'. It were: stress at onset (0.017), white patches under a tonque (p=0.029), erosions on mandibular gingiva (0.041), and erosions under a tonque (0.049). Neural networks created on this basis had 74% correct classifications for learning, 85% for testing, and 71% for validation

#### **Conclusion:**

In some populations, DIF is not a significant predictor of the diagnosis of lichen planus, regardless of whether strict diagnostic criteria for this disease were used in histopathological examination or whether results potentially indicative of lichen planus were also included. By using neural networks, interview data can establish a diagnosis with approximately 70% certainty compared to histopathology as the reference test. Further optimization of variables included in the model may allow for the creation of a clinically useful tool.

Fig. 1. ROC curve for 'lichen not excluded'.



## Unveiling the Spectrum of Struge-Weber Syndrome: A Case Report Analysis

Mrike Bunjaku<sup>1</sup>, Artina Pajaziti\*<sup>2</sup>, Gramoz Bunjaku<sup>3</sup>

<sup>1</sup>Radiology, Prishtina, Kosovo, <sup>2</sup>Dermatovenerology, Prishtina, Kosovo, <sup>3</sup>Infectious Diseases, Prishtina, Kosovo

**Introduction & Objectives:** Struge-Weber syndrome (SWS), also known as encephalotrigeminal angiomatosis, is a rare neurocutaneous disorder characterized by the triad of capillary malformations involving the face, typically in the distribution of the trigeminal nerve, leptomeningeal angiomatosis and ocular abnormalities. The incidence of SWS is estimated to be around 1 in 50.000 live births. Clinical features of SWS vary widely among affected individuals and can range from mild cutaneous involvement to severe neurological complications. Diagnostic evaluation of SWS typically involves a combination of clinical examination, neuroimaging studies and ophthalmological assessment. Magnetic resonance imaging of the brain is the imaging modality of choice for evaluation leptomeningeal angiomatosis and associated structural abnormalities. We aim to describe a case of SWS presented with extensive hemifacial and forehead dermal capillary venous malformation, ipsilateral glaucoma and cerebral capillary venous leptomeningeal angioma.

**Materials & Methods:** We report a case of a 30 year-old female with an extensive hemifacial and forehead port-wine stain birthmark: violaceous macules and patches involving completely the right side of the face with sharp borders, involving mucosal surfaces as well. The patient's anamnestic data indicated a history of focal epilepsy since the age of 2, necessitating continuous treatment with antiepileptic medication. Additional to dermatological examination the patient has sent for a fundoscopy, EEG and brain MRI.

**Results:** Intraocular pressure of the right eye showed a value of 23.0mmHg, indicating secondary glaucoma. Brain magnetic resonance showed discrete cortico-subcortical high signal intensity in FLAIR sequence, mixed with discrete cortical low signal intensity located in the parieto-occipital region of the right brain hemisphere. In the posterior aspect of the right orbit crescentic high signal of intensity was also noticed. After gadolinium contrast administration, increased vascular leptomeningeal enhancement following the sulcal pattern in the same region was detected. Moreover, enhancement on the posterior aspect of the orbit was suggestive of choroidal enhancement. SWI sequence detected right gyral parieto-occipital low signal intensity indicating cortical calcifications. A large right soft tissue neck heterogenous tissue concordant with imaging appearance of hemangioma was described. EEG showed diffuse deceleration in the form of theta waves, without paroxytic discharge.

**Conclusion:** This case report highlights the diverse spectrum of manifestations seen in Struge-Weber syndrome (SWS), emphasizing the importance of thorough clinical evaluation and diagnostic imaging techniques in its management. The presented case underscores the significance of recognizing the triad of cutaneous, ocular and neurological features characteristic of SWS, as well as the potential complications such as secondary glaucoma and epilepsy. Further research and awareness are warranted to improve early diagnosis and optimize treatment strategies for individuals affected by this rare neurocutaneous disorder.



# Original study: evaluation of serum and fecal calprotectin levels in patients with moderate-to-severe plaque psoriasis

Karina Polak<sup>1</sup>, Tomasz Muszyński<sup>2</sup>, Aleksandra Frątczak<sup>1</sup>, Mikołaj Łanocha<sup>3</sup>, Bartosz Miziołek<sup>1</sup>, Beata Bergler-Czop<sup>1</sup>

<sup>1</sup>Chair and Department of Dermatology, Medical University of Silesia, Katowice, Poland, <sup>2</sup>Brothers Hospitallers of Saint John of God Hospital in Cracow; Doctoral School of Medical and Health Sciences, Jagiellonian University, Cracow, <sup>3</sup>Public Independent A. Mielecki Clinical Hospital, Department of Dermatology, Katowice, Poland

## **Introduction & Objectives:**

Serum calprotectin levels have been shown correlate with several inflammatory biomarkers and may serve as an indicator of psoriatic arthritis severity. As the risk of Crohn's disease is 2,5x higher and the risk of ulcerative colitis is 1,64x higher in psoriatic patients than in general population, it is important to understand the link between the pathogenesis of these diseases. The aim of the study was to investigated if the calprotectin concentration in blood and stool may correlate with the severity of moderate-to-severe plague psoriasis.

#### **Materials & Methods:**

20 patients and 20 sex, age, BMI-matched healthy controls were enrolled in the study. Inclusion criteria: confirmed diagnosis of moderate-to-severe plaque psoriasis, age between 20-40 years old, no past or current systemic treatment, no current or past (during the last 60 days) systemic therapies with antibiotics, probiotics, non-steroidal anti-inflammatory drugs. Exclusion criteria: pregnancy or breastfeeding, bacterial, viral, fungal infections of the skin, mucosae membranes, upper respiratory tract, gastrointestinal tract during last 60 days, smoking or other addiction, any systemic immunosuppressive therapy in the past (excluding steroids), a diagnosis of concomitant psoriatic arthritis, a diagnosis of inflammatory bowel disease, in females, menstruation. The disease severity and psoriatic patients' quality of life had been assessed using appropriate questionnaires: Psoriasis Area and Severity Index (PASI) Score, Body Surface Area (BSA) and Dermatology Life Quality Index (DLQI). A sample of blood and stool had been collected from each participant. The fecal calprotectin concentration had been analyzed using the LIAISON ® XL instrument (CLIA Systems, DiaSorin) using chemiluminescence analysis method with the result expressed in units of μg/g, ELISA method had been used in order to determine blood calprotectin concentrations expressed in ng/ml. The results were analysed using Statistica 13.1 StatSoft. Student's T-tests for variables were used for normal distribution independent, and for data without normal distribution, the Mann-Whitney test.

## **Results:**

Mean calprotectin blood level in the study group was 112.24ng/ml, while in the control group 60.31ng/ml. The stool levels were 15 µg/g and 13 µg/g, accordingly, yet the differences were not statistically significant. There was no correlation between Tau b Kendall and Spearman's rho for PASI, BSA, DLQI scores and calprotectin concentration in blood and feces in the study group; also, lack of correlation between calprotectin concentration in blood and feces and overweight, hypertension, obesity and smoking was observed in the control group. However, the results showed that in the study group, there is a relationship between smoking and BSA scale score (rho = 0.467; p<0.038).

#### **Conclusion:**

Despite many promising results suggesting blood and stool calprotectin levels may serve as a biomarker of psoriasis severity, our study did not confirm this thesis. Although the mean calprotectin levels were higher in psoriatic patients than healthy controls, the results were not statistically significant. More studies on larger groups with multiple sampling are needed in order to investigate this topic.



cutaneous lechmaniasis still a health problem in Morocco about a case F. Mohamed Sidi, Y.Zemmez, R.Frikh, N.Hjira Department of Dermatology and Venereology Mohamed V Military Training Hospital, Rabat

Fetima Med Sidi<sup>1</sup>

<sup>1</sup>RABAT AGDAL, agdal, Rabat, Morocco

## **Introduction & Objectives:**

Leishmaniasis is a group of parasitic diseases caused by flagellate protozoa of the genus Leishmania, with a tropism for cells of the reticuloendothelial system, and transmitted to many mammalian species by the bite of an insect vector = the sandfly. This tropism determines several forms of the disease, with varying prognoses. Therapeutic difficulties are particularly acute in diffuse and cutaneomucosal forms. These treatments have several disadvantages: they require hospitalization for several weeks and have marked side effects. But the major problem with antimony-based drugs is the growing emergence of resistant strains of parasites.

#### **Materials & Methods:**

We report the case of a 42-year-old woman, with no previous history, who consulted us for a 9-month history of non-painful, pruritic facial ulceration resistant to antibiotic treatment. The patient's history revealed a stay in an endemic area without protective measures. Clinical examination revealed a patient in relatively good general condition, apyretic and hemodynamically stable. Skin examination revealed a "wet" infiltrated papulo-nodular lesion on an erythematous background with a central +/- deep ulceration with a sanitized background showing papillomatous buds, bordered by a peripheral bulge, mainly located on the chin of the face. Dermoscopy revealed erythema, hyperkeratosis, crusts, ulceration, yellow tears = granulomas, salmon-coloured ovoid structures = granulomas and stippled vessels, then a hypochromic peri-lesional halo. A smear with needle puncture was taken, and a skin biopsy confirmed the diagnosis of stage I cutaneous leishmaniasis.

## **Results:**

The patient was started on intra-lesional glucantine 1 ml per session at the four cardinal points of the lesion twice a week for four weeks. The course was favorable, with clinical improvement and healing of the skin lesions.

**Conclusion:** \*\* Cutaneous leishmaniasis can be difficult to recognize due to its clinical polymorphism and multiple differential diagnoses, so a skin biopsy is recommended in the presence of any persistent, antibiotic-resistant chronic skin lesion. Diagnosis is based mainly on smears and histology, with compulsory reporting of the disease.



## Scalp punch biopsy in the final diagnosis of cicatricial alopecia

Iryna Chaplyk-Chyzho, Orysya Syzon, Marianna Dashko, Nataly Ivanyushko-Nasarko, Svitlana Volbyn, Iryna Vozniak

**Introduction & Objectives:** Cicatricial alopecia is a severe form of hail loss that affects both men and women. As this pathology develops, the hair follicles die completely, therefore, making a correct diagnosis rapidly affects the possibility of preserving the hair follicles that have not yet been damaged. The disease occurs in 3% of all alopecia patients and is characterized by a rapid hair loss, with focal lesions in different areas of the scalp.

The cause of cicatricial alopecia is not only injuries or burns, but also a number of skin diseases that can start affecting the scalp. The punch biopsy followed by histopathological examination is usually the key research method to make or confirm the final diagnosis of cicatricial alopecia and preserve healthy hair follicles.

**The objective** is to study the feasibility and effectiveness of skin punch biopsy in cicatricial alopecia to make the final diagnosis and prescribe effective therapy in time.

**Materials & Methods:** We performed the scalp punch biopsy for 24 patients with unknown cause of cicatricial alopecia aged 18 to 60 y/o, including 14 women (58%) and 10 men (42%), within 5 years. The disease lasted more than 5 years in 7 patients (29.2%), 1 to 5 years in 7 (29.2%) and less than a year in 10 (41.6%) patients. The provisional diagnoses were divided as follows: lupus erythematosus was diagnosed in 4 (17.7%) patients, lichen planus - in 5 (20.8%), Hoffmann's dissecting folliculitis - in 8 (33.3%), Pseudopelade of Brocq - in 3 (12.5%), scleroderma - in 1 (4.1%) and sarcoidosis - in 1 (4.1%) patient. The Microsporum caused disease was suspected as the cause of cicatricial alopecia in 2 (7.5%) patients.

**Results:** In 22 patients (91.6%), the punch biopsy of the skin allowed making the final diagnosis, which corresponded to the provisional one, and, sadly, in 2 (8.4%) patients, it did not, which forced us to expand the diagnosis using other, more highly specialized and expensive methods.

In 21 patients (87.5%), the provisional diagnosis corresponded to the final one (lupus erythematosus - in 3 (12.5%) patients, lichen planus - in 5 (20.8%), Hoffmann's dissecting folliculitis - in 7 (29.1%), Pseudopelade of Brocq - in 3 (12.5%), squamous cell carcinoma - in 1 (4.1%), sarcoidosis - in 1 (4.1%), and Microsporum caused disease - in 1 (4.1%) patient).

In 6 patients (25%), the final diagnosis did not correspond to the provisional one and allowed prescribing the patients an effective pathogenetic therapy.

**Conclusion:** The scalp punch biopsy is a reasonable diagnostic method for cicatricial alopecia, as it allowed to make an accurate diagnosis in 87.5% of cases. Thus, the scalp biopsy, being used to confirm or refute diagnoses, allows recommending the necessary pathogenetic therapy in time. The cooperation between a dermatovenerologist and a histopathologist affects the efficiency and results of the diagnostic search of a punch biopsy.



## Blastic plasmacytoid dendritic cell neoplasm - clinical, dermoscopic and reflectance confocal microscopy features

Jakub Żółkiewicz\*<sup>1</sup>, Patrycja Rogowska<sup>1</sup>, Biernat Wojciech<sup>1</sup>, Michał Sobjanek<sup>1</sup>, Martyna Sławińska<sup>2</sup>

<sup>1</sup>Medical University of Gdańsk, Department of Dermatology, Venereology and Allergology, Gdańsk, Poland, Medical University of Gdańsk, Department of Pathology, Gdańsk, Poland

## **Introduction & Objectives:**

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematologic malignancy with an aggressive clinical course and poor prognosis. The underlying cause of BPDCN has not been explained so far. It is postulated that premalignant clonal precursors migrate from bone marrow to the skin, where they undergo malignant transformation. The majority of patients initially present with non-tender skin lesion(s), most commonly erythematous, violaceous or brownish papules, infiltrated patches or nodules, often with a bruise-like appearance. Concomitant cytopenias, lymphadenopathy and splenomegaly are often encountered. The minority of patients present with disease limited to the bone marrow and leukemic dissemination, without tangible skin lesions. Initially, associated systemic symptoms such as fevers, chills, weight loss and night sweats are absent, however, they may develop along with the progression of the disease. Current knowledge on dermoscopic features of BPDCN skin lesions is scarce and PubMed literature search performed on 16.02.2024 revealed no reports on reflectance confocal microscopy features. This case report aims to present the clinical, dermoscopic and RCM features of BPDCN.

#### **Case presentation:**

An 83-years-old male presented to the Outpatient Clinic with recently developed asymptomatic scattered nodules. Nodules located on the face, trunk and upper extremities were erythematous and infiltrative, whereas those located on the lower extremities were purpuric. There was no history of associated systemic symptoms. On dermoscopy polymorphous vessels over a homogenous pinkish background were identified. RCM examination revealed a typical honeycombed pattern in the epidermis and the presence of multiple blurred and relatively monomorphic and large cells intermingled with the elastic fibers in the superficial part of the dermis. Histopathological evaluation led to the diagnosis of BPDCN and the patient was referred to the Department of Haematology for further diagnostics and treatment.

#### **Discussion:**

BPDCN is a rare entity that should be included in the differential diagnosis of rapidly progressing, disseminated skin lesions. More observations are needed to define the diagnostic role of dermoscopy and RCM in this entity.



## Ultrastructural features of actinic cheilitis-Clinical Implications

Doinita Temelie-Olinici<sup>1</sup>, Walther Bild<sup>1</sup>

<sup>1</sup>"Grigore T. Popa" University of Medicine and Pharmacy Iasi, Romania, Morpho-Functional Sciences II, IAŞI

# **Introduction & Objectives:**

Actinic cheilitis, inflammatory lesions of the lips, is one of the most common premalignant precursor pathologies of invasive desmoplastic squamous cell carcinoma specific to the cutaneous-mucosal transition zone, especially in the 5th decade of life. Quantification of the risk of malignant transformation is conditioned by the clinico-morphological and etiopathogenic variability of these lesions, with a negative impact on the individualization of diagnostic and therapeutic management.

#### **Materials & Methods:**

In this sense, the main objective of the present research was to characterize from an ultrastructural perspective the specific tumour microenvironment, using a technique with a resolution power higher than optical microscopy. Fragments of oral mucosa from 40 patients clinically and histopathologically diagnosed with various types of actinic cheilitis were excised from healthy tissue in order to be processed by means of classical electron microscopy and examination with the Philips CM100 microscope.

## **Results:**

The electron microscopic study revealed structural details suggestive of malignant transformation, capturing changes both at the level of cytoplasmic organelles responsible for cellular energetics and secretion and at the level of cell-cell and cell-extracellular matrix junctional complexes.

# **Conclusion:**

The identification and description of the ultrastructural morphological substrate favouring the evolution and progression of the studied lesions correlates directly with the improvement of the prognosis and quality of life of these patients