DERMA TODAY

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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. Determination of serum sRAGE levels in children with atopic dermatitis
2. Assessment of the burden of itch and its dimensions across patients with epidermolysis bullosa
3. Relationship between pigment granules and their representative pathological features
4. A case report on Spitz lesions.

Should you require any article or, medical information, please feel free to contact us medicalservices@microlabs.in

Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited

1. Determination of serum sRAGE levels in children with atopic dermatitis

Introduction

Atopic dermatitis (AD) is a recurrent, chronic skin disease that presents with a wide range of clinical symptoms and signs, including severe itching. While it mostly affects children from infancy forward, it is also very common in adults.[1] Clinically, it manifests as dry, itchy skin, scratching, exudation, thickness, and discolouration of the skin. Advanced glycation end products (AGEs) have distinct structural characteristics. All types of molecules, including proteins, lipids, and nucleic acids, are included in the phrase "AGEs." AGE is a member of the immunoglobulin superfamily, which functions as a model recognition receptor for both glycated and non-glycated ligands. Inflammatory responses are influenced by the receptor for advanced glycation end products (RAGE). RAGE's soluble form (sRAGE), functions as a decoy to prevent RAGE interactions. Patients suffering from asthma, allergic airway disease, bronchiolitis, chronic obstructive pulmonary disease, adult AD, and psoriasis had lower serum levels of sRAGE. In paediatric AD patients, this was unclear.[2] The purpose of this study was to assess serum sRAGE levels in children with AD.

Types Of Atopic Dermatitis

Methods

This was a randomized, prospective, case-control study included patients with current AD in children aged 4–24 months (patient group). Hanifin and Rajka's criteria were used to make the AD diagnosis. The disease severity was determined using the Scoring Atopic Dermatitis

(SCORAD) index. Skin prick testing (SPT), IgE levels, and eosinophil counts were analyzed. Venous blood samples were taken in test tubes without anticoagulant to determine sRAGE. The sRAGE levels were measured using the ELISA method.

Results

About 65 AD children, aged 0.4 to 2.0 years, were divided into two groups based on whether they had SPT positive (AD+/Atopy+ [n = 40]) or negative (AD+/Atopy− [n = 25]). The comparisons were done with a healthy control group matched for age and gender. The median sRAGE levels in patients and controls were 8.43 (1.04-18.37) and 14.09 (6.35-28.64), respectively ($p < 0.001$). The median sRAGE levels in the AD+/Atopy+, AD+/Atopy−, and control groups were 8.5 (3.1-17.27), 7.75 (1.04-18.37), and 14.09 (6.35-28.64), respectively ($p = 0.004$) (Fig 1). Correlation study revealed no significant relationship between illness severity, sRAGE levels, total IgE levels, and eosinophil counts.

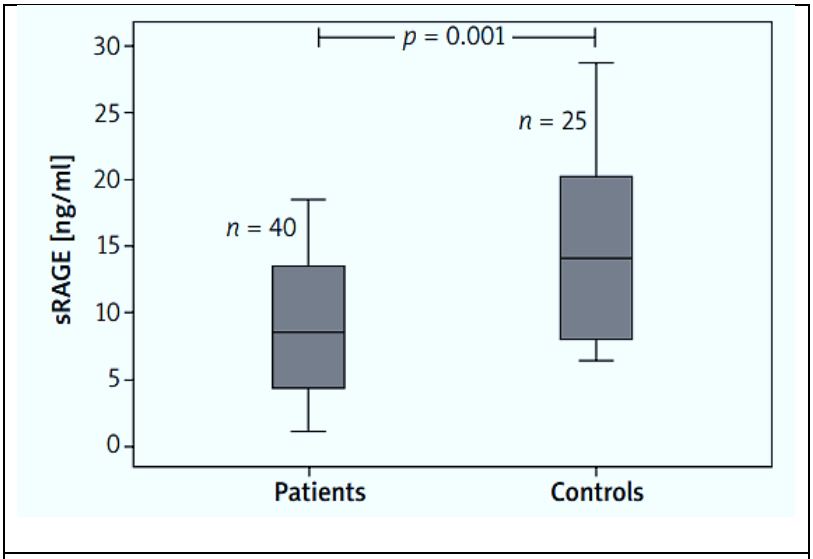

Figure 1. sRAGE levels in children with atopic dermatitis vs healthy controls.

Discussion

This study found that sRAGE levels were lower in AD patients compared to healthy controls.[2] Egron et al. conducted a prospective, observational, and analytical investigation including 93 infants. The authors found that acute bronchiolitis patients had considerably lower sRAGE levels than controls, although this did not correspond with clinical severity. There was no association detected between serum sRAGE and severity score, respiratory infections, or recurrent wheeze after one year.[3] This study indicated that individuals with AD had lower sRAGE levels than healthy controls, which was consistent with previous studies. However, no correlation was established with disease severity.[2]

Conclusion

This study suggested that sRAGE may be involved in the pathophysiology of AD based on these data. The drop in sRAGE may indicate continued inflammation and apoptosis. sRAGE can serve as a marker for AD. Future therapeutic treatments may target the topical or systemic administration of certain compounds, such as sRAGE and its derivatives.

The decrease in sRAGE (RAGE's soluble form) may suggest continued inflammation and apoptosis. sRAGE can be used as an Atopic dermatitis (AD) marker.

Reference

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2. Assessment of the burden of itch and its dimensions across patients with epidermolysis bullosa

Introduction

Epidermolysis bullosa (EB) is a genetic condition that causes skin and mucosal fragility. There are four forms of classical EB: EB simplex (EBS), Junctional EB (JEB), Dystrophic EB (DEB), and Kindler EB. EB can cause burning, scarring, poor wound healing, discomfort, and itching. One of the most significant unmet requirements for children with severe EB is itching (pruritus).[1] Pruritus is described as an uncomfortable sensation that causes a desire to scratch. Pruritus, a typical symptom of inflammatory skin conditions, can disrupt sleep and everyday activities, significantly affecting patients' quality of life.[2] A previous study indicated that itch was prevalent among all EB patients, particularly those with severe forms. It is essential to recognize and understand the effects of pruritus on EB patients in order to reduce this burden and enhance the patients' quality of life.[1] The purpose of this study was to evaluate the impact of itching and discuss its various components in EB patients.

Methods

This was a cross-sectional study included patients with EB. The Leuven Itch Scale (LIS) patient questionnaire was used in this study to assess the effects of itching. The LIS is an 11-item questionnaire that is an established and dependable measure for itch specificity. Subscale scores on six domains (itch frequency, duration, severity, distress, repercussions, and surface area) can be computed by adding together the raw values and converting them into a scale from 0 to 100 using certain algorithms. Higher scores indicate more itchiness.

Results

The study included 46 EB patients ranging from 2 months to 37 years old, with an average age of 9.8 years. There were 23 males (50%) and 23 females (50%) with the same gender distribution. Five patients had EB simplex (EBS), three had junctional EB (JEB), thirty-four had dystrophic EB (DEB), and four had an unknown form. Of the patients, 97.8% had itchy skin, with only one patient never having itchy skin. Out of 45 patients, 33 (73.3%) reported

having itchy skin either frequently or always. Most patients (59.1%) experienced an itching episode that lasted for less than half an hour. JEB and RDEB experienced longer than two-hour itching episodes (66.7% and 3.2%, respectively). The itch profile of EBS patients was lower than that of JEB or DEB patients. In the entire group of EB patients, the majority of them had itching in hot environments (80%) and when sweating (71.1%), however just 2.2% of them experienced itching in cool environments. A total of 18 patients (40%) experienced itching throughout wound healing, with 16 (35.6%) experiencing it during dressing changes. The characteristics of itch, including frequency, duration, intensity, distress, consequences, and surface area, exhibit relationship as indicated by the correlation matrix. The correlations range from 0.48 to 0.82 (Fig 1). A correlation was discovered between the age group of EB patients and the itching profile. Pruritus was more prevalent among older EB patients.

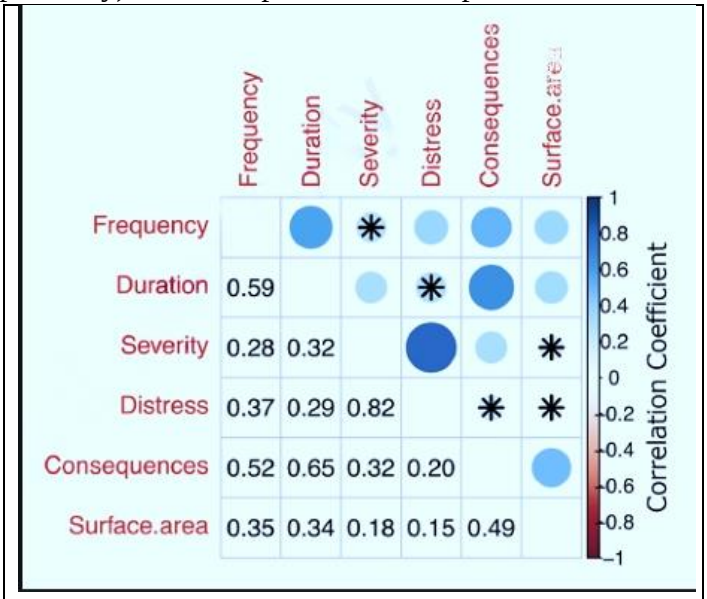

Figure 1. The correlation matrix of the itching dimensions indicates the strength of the relationship between two variables.

Discussion

Papanikolaou M et al. showed that pruritus was a prevalent symptom across all EB subtypes and significantly impacted patients' quality of life.[3] This study found that 73.3% of individuals with EB experienced itch on a regular or frequent basis. The pathogenesis of EB pruritus was not entirely understood.[1] It's likely that dysregulated activation of systemic proinflammatory cytokines and barrier failure are all involved in pathophysiology of EB pruritus.[3]

Conclusion:

The prevalence of pruritus increased with age. Overall, this study showed that EB pruritus requires specialized therapy since itching is one of the most severe signs for people with EB.

Controlling itching is crucial for Epidermolysis bullosa (EB) patients, since it is one of the most distressing symptoms.

Reference

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3. Relationship between pigment granules and their representative pathological features

Introduction

Dermoscopy is a non-invasive in vivo imaging method that can reveal disease in superficial tissues. Dermoscopy serves as a bridge between clinical evaluation and dermatopathology.[1] The dermoscope, often known as the dermatologist's "stethoscope", has become an important instrument in dermatological clinical practice due to its capacity to reveal complications not

visible to the naked eye. Dermoscopy is becoming more widely recognized in the range of non-tumoral skin conditions, such as inflammatory, pigmentary, infectious, and infiltrative dermatoses, despite its traditional use in the assessment of both melanocytic and non-melanocytic proliferative lesions as well as hair disorders. As a result, fewer cases requiring biopsy are reported when using dermoscopy.[2] Polarized dermoscopy (PD) and non-polarized dermoscopy (NPD) are the two types of dermoscopy. In general, PD and NPD offer comparable pictures for the majority of pigmented and non-pigmented lesions. NPD is more suited for detecting granularity in various disorders. Granular regions can appear in a variety of disorders, including inflammatory skin diseases. Under dermoscopy, black-brown-gray pigment granules are frequently seen in clinical practice. However, there is little information concerning their clinical importance.[1] The purpose of this study was to investigate the correlation between pigment granules and their associated pathological characteristics.

Methods

This retrospective study reviewed the clinical database and included patients with complete information on pigment granules, demographics, and pathological findings. Cases were analysed to assess the pathological and dermoscopic patterns. To investigate the relationship between certain histologic characteristics and known diagnoses, Fisher's exact test was employed. A nonparametric test was used to assess the non-normal distribution of pigment granule depths. In this investigation, a FotoFinder Medicam 800/1000 dermoscope was utilized.

Results

This study examined 38 males and 45 females, with a mean age of 47.2 years. Among 83 patients, the most common clinical diagnoses were post-inflammatory hyperpigmentation, solar dermatitis, and eczema. Pigment granules seen during dermoscopy strongly suggested pigment incontinence or basal cell death (91.5%, 76/83). The size, color, and distribution of the pigment granules inside the lesions were classified into uniform and non-uniform patterns. Eosinophils (many or in aggregation, $P<0.001$) or perifollicular inflammatory infiltration in the dermis ($P=0.008$) were more likely to be linked to uniform granular pigmentation. Notably, the

likelihood of drug induction was higher for brown pigment granules (P = 0.024) and homogeneous granular pigmentation (P < 0.001) (Table 1).

	Dermoscopy/Histological features	DIH, n(%)	Non-DIH, n(%)	SL, n(%)	Unspecified, n(%)	*P** value
Dermoscopy features	Large-middle pigment granules	19(79.2)	32(72.7)	7(58.3)	1(33.3)	0.250
	Vasodilation	17(70.8)	27(61.4)	4(33.3)	2(66.7)	0.176
	Perifollicular distribution	5(20.8)	15(34.1)	2(16.7)	1(33.3)	0.510
	Black pigment granules	19(43.2)	3(3.6)	6(50)	0	***0.024***
	Pigment granule equidistribution	22(26.2)	7(15.9)	8(66.7)	2(66.7)	***0.000***
Histological features	Destruction of basal cells	23(95.8)	38(86.4)	11(91.7)	3(100)	0.707
	Pigment incontinence	24(100)	41(93.2)	8(66.7)	3(100)	0.095
	Eosinophils	23(95.8)	2(4.5)	2(16.7)	0	***0.000***
	Plasma cells	1(4.2)	6(13.6)	0	0	0.491
	Perivascular infiltrates	15(62.5)	25(56.8)	6(50)	2(66.7)	0.889
	Necrotic keratinocytes	7(29.2)	12(27.3)	2(16.7)	1(33.3)	0.859
	Parakeratosis	7(29.2)	11(25)	4(33.3)	1(33.3)	0.628
	Epidermal atrophy	5(20.8)	3(6.8)	0	0	0.198
	Psoriasiform changes	1(4.2)	2(4.5)	0	0	1.000
	Perfollicular inflammation	10(41.7)	6(13.6)	1(8.3)	2(66.7)	***0.008***
	Erythrocyte l extravasation	3(12.5)	2(4.5)	1(8.3)	2(66.7)	***0.021***
	Depth of pigment granules (mm)	0.54±0.22	0.32 ±0.14	0.41±0.37	0.23±0.09	***0.032***

Table 1: Histological characteristics, dermoscopy, and a summary of the statistical analysis (using Fisher's exact test)

Discussion

Dermoscopy is a valuable tool for evaluating dermoscopic observations about pigment granules. A two-dimensional projection of the skin structure at various depths can be obtained using dermoscopy. Dermoscopy is a valuable diagnostic method for detecting superficial skin disorders.[1] In previous studies by Phillips M et al. and Zakria D et al. showed that dermoscopy can only reveal structure and color in the dermal papilla layer or middle dermis due to its limits. Dermoscopy was not able to show abnormalities when a lesion has pathological change deeper than the lower dermis. Therefore, for the right diagnosis, a biopsy should be performed in addition to a clinical evaluation.[3,4]

Conclusion:

In conclusion, pigment granules may be classified into uniform and non-uniform patterns. The pigment granules' size, color, and distribution were all uniform when there was a uniform

pattern. A thorough investigation was required because uniform granular pigmentation during dermoscopy was a unique sign of drug response.

Under dermoscopy, uniform granular pigmentation is a unique sign of a drug reaction.

Reference

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4. Case report on Spitz lesions

Introduction

Spitz lesions are a variety of melanocytic proliferations, which include benign Spitz nevi, atypical Spitz tumors with intermediate malignant potential, and malignant Spitz melanomas. Spitz nevi are the most prevalent lesions in children and adolescents.[1] Spitz nevi are melanocytic proliferations that contain epithelioid, spindle, or both types of melanocytes. Spitz proliferations can range from benign Spitz nevi (SNs) to atypical Spitz tumors (ASTs) and malignant melanomas (MM), making differentiated diagnosis challenging.[2] Atypical Spitz tumors are less common than Spitz nevi, although they also occur in the same age group. They are classified into two types: low- and high-grade. Managing atypical Spitz tumors is hard and typically needs a multidisciplinary approach due to the lack of recognized therapeutic options.[1] This study presented the case of a young patient with a high-grade atypical Spitz tumor, including the diagnostic procedure and subsequent care.

Case Presentation

A 23-year-old female patient came to the dermatology department with a persistent pink nodule on her right thigh (Fig 1). After inconclusive clinical and dermatoscopic exams, the patient was referred for histological analysis and complete excision of the lesion. A low-magnification pathological examination showed a tiny, symmetrical, and well-defined compound melanocytic tumor (Fig 2). Pathological investigation at high magnification revealed extensive nests of melanocytes and short fascicles. The component melanocytes were plump and ranged in morphology from epithelioid to spindle-like. Melanocytes formed vertical nests at the dermoepidermal junction. The lesion had numerous melanocytes in a pagetoid pattern throughout the epidermis and a non-brisk lymphocytic infiltration in the center.

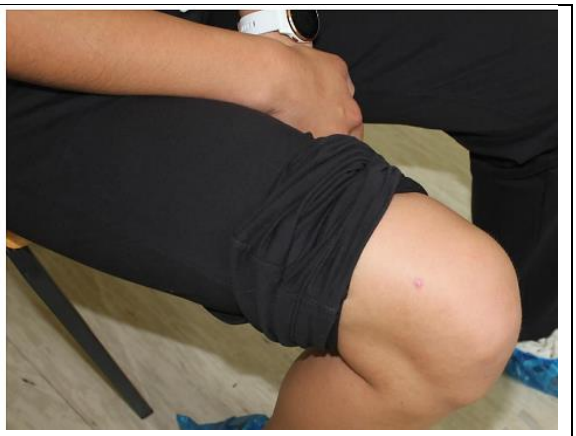

Figure 1. The patient has a pink papule on her right thigh.

Diagnosing high-grade atypical Spitz tumor from melanoma might be challenging due to melanocyte atypia. Immunohistochemical

examination revealed no BRAF V600E or n-RAS positivity. MelanA/Ki67 did not indicate proliferative activity in intradermal melanocytes, and there was a mosaic pattern with maintained p16, negative HMB45, and positive junctional component. ALK, ROS1, and pan-TRK staining were negative. After inconclusive immunohistochemistry examinations, mutational studies employing RNA next-generation sequencing (NGS) identified an AGK-BRAF fusion. After analyzing all available data, the lesion was identified as a high-grade atypical Spitz tumor. BRAF fusion has a clear genetic background, with no additional mutations, deletions, or fusions present. After identification of a high-grade atypical Spitz tumor, re-excision with 10 mm margins was recommended. The patient had frequent follow-up visits every 6 months for at least 5 years, in line with modern guidelines. As a result of the AGK-BRAF fusion, she had twice-yearly locoregional lymph node sonography for 5 years. After a two-year follow-up, there was no recurrence or metastasis, and locoregional lymph node sonography was consistently negative.

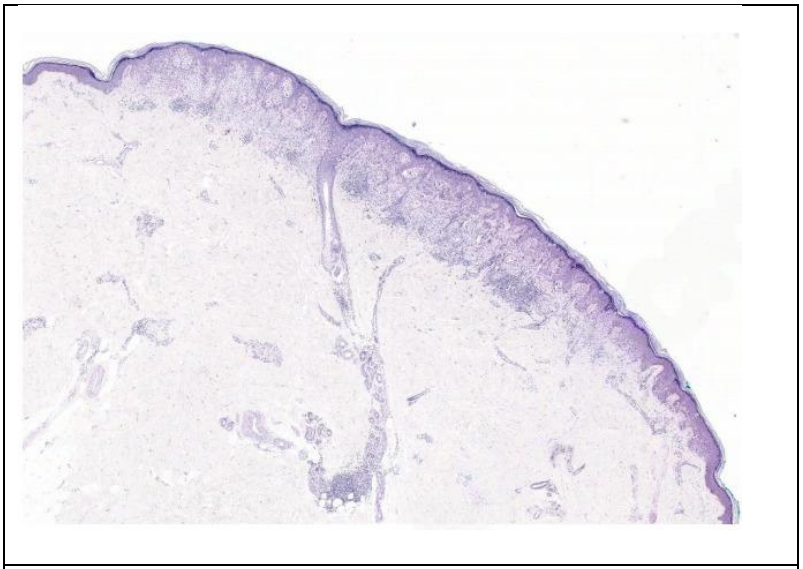

Figure 2. A low-magnification histological examination showed a tiny, symmetrical, and well-defined compound melanocytic neoplasm, which was diagnosed as an unusual high-grade Spitz tumour.

Discussion

Spitz nevi are uncommon, accounting for approximately 1-2% of excised melanocytic lesions across all age categories. It has an incidence of one to ten cases per 100,000 people.[1] Cheng TW et al. showed that Spitz nevi are often difficult to identify from melanomas. There are certain clinical distinctions that may help in distinguishing Spitz lesions. Clinical factors such as patient age, lesion location, color, shape, and size, and dermoscopic patterns are significant.[3]

The identification of BRAF mutations in malignancies, including melanoma, and the absence of these mutations in Spitz nevi, made it easier to distinguish between the two.[1] Furthermore, Newman S et al. showed that Spitz lesions often include kinase fusions and translocations, such as ROS1, ALK, RET, BRAF, NTRK1, MET, NTRK3, and MAP3K8, which might provide further information.[4]

Conclusion

Atypical Spitz tumors provide both a diagnostic and a management difficulty. In complex situations, a multidisciplinary approach was necessary due to persistent problems about diagnosis, prognosis, and treatment options. Further studies are needed to address current difficulties, including the malignant potential of atypical Spitz tumors, screening for metastases, and predicting metastatic illness.

Atypical Spitz tumors are challenging to diagnose and manage. A multidisciplinary approach is required in complicated situations due to persistent problems with diagnosis, prognosis, and treatment options.

Reference

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