MICRO LABS LIMITED

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Dear Doctor,

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This issue contains:

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Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited.

Analysis of the clinical features and therapeutic characteristics of solar urticaria along with the evaluation of therapeutic outcomes of antihistamines and omalizumab

Introduction:

Solar urticaria (SU) is a photodermatosis and physical urticaria caused by exposure to ultraviolet radiation (UVR) and visible light. Exposure to triggering wavelengths causes quick onset of clinical signs and symptoms. Solar urticaria was characterized by erythemal flares, burning, and itching, with less noticeable wheals in daily life. Positive wheal provocation on phototesting was required to diagnose the condition. Peak activation in most individuals was observed at longer ultraviolet-A (UVA) and/or Visible wavelengths.[1] Although the pathogenetic processes of SU remain unknown, it has been believed that photoallergen-induced IgE antibodies may bind mast cells, causing hives similar to type I acute allergies. Regarding treatment, it has been shown that even at higher dosages, half of chronic inducible urticaria (CINDU) patients remain resistant to antihistamines. The Urticaria Control Test (UCT) may indicate lower therapy response in chronic urticaria patients. Real-life data on the effectiveness of omalizumab in SU was inadequate, especially in long-term follow-up populations.[2] This study examined the clinical and therapeutic aspects of a long-term solar urticaria cohort, focusing on omalizumab management and outcomes. The response to omalizumab was characterized using the high-affinity immunoglobulin E (IgE) receptor (FcεRI) and the Urticaria Control Test.

Solar urticaria

Methods:

This observational, unicentric, ambispective study comprised adult patients diagnosed with SU. SU was identified in 41 people over this time period. Clinical and treatment characteristics were collected prospectively at first and follow-up visits and stored in an anonymised database. Each patient's basal UCT was gathered. The use of antihistamines at double and fourfold

dosages was investigated. To treat chronic urticaria, omalizumab was prescribed at 300 mg every 4 weeks if antihistamines were not effective after 4 weeks (per recommendations). A UCT score of 12 or higher indicated clinical control of the illness. Partial control was defined as UCT between 12 and 15, whereas total control was achieved at UCT 16. All patients underwent phototesting using the Spanish Photobiology Group's consensus standards. Readings were taken immediately, at 10, 30, and 60 minute intervals, as well as 24 hours later. If phototesting was negative, patients were advised to expose themselves briefly to natural light before the session to assess flare levels.

Results:

Overall, SU was found in 41 patients during this time. The cohort's median age of onset was 34.0 years, with females accounting for 63.4% of the total (n=26). Symptoms of SU include hives (n=41, 100%), itch (n=39, 95.1%), burning feeling (n=11, 26.8%), and angioedema (n=3, 7. 3%). The majority of patients (n=38, 92.7%) responded well to photoprovocation, with UVA and visible light being the most commonly used triggering waveband (n=11, 29. 7%). The median baseline IgE serum level was 136.5 UI/mL. Only 9.8% of patients tested positive for autoimmunity markers (ANA and anti-TPO). Thirteen individuals received omalizumab, with a median treatment duration of 48 months. Omalizumab treatment resulted in a substantial drop in FcεRI baseline levels and a subsequent increase in Urticaria Control Test in all patients. Drug survival rate at 48 months was 88.9%. The omalizumab stepping-down approach resulted in the discontinuation of the medication in only one patient. Patients receiving omalizumab had a reduced median baseline Urticaria Control Test ($p<0.01$) compared to those without

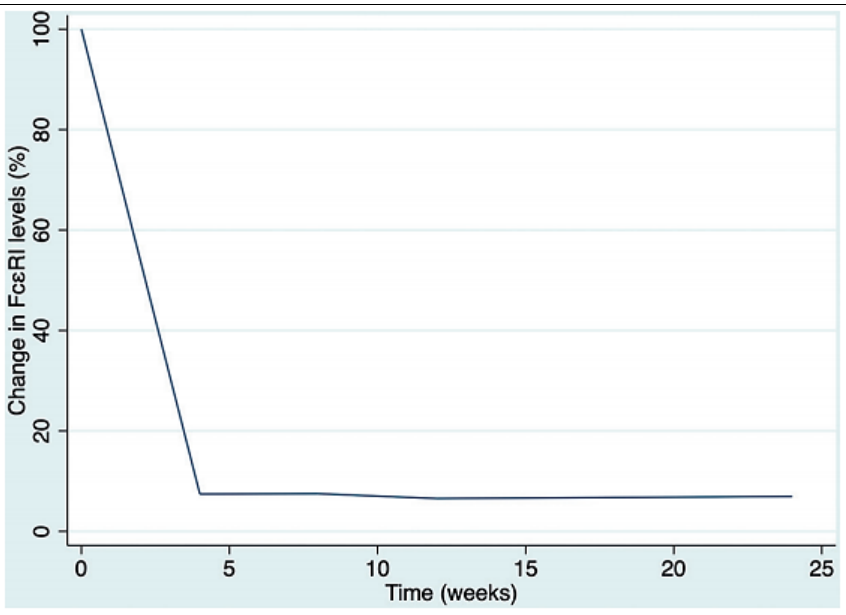

Figure 1. Percentage drop in high-affinity immunoglobulin E (IgE) receptor (FcεRI) baseline levels in individuals following omalizumab initiation at weeks 0, 4, 8, 12, and 24

remission. At week 24, 7/11 patients had a UCT of 16, suggesting total control. Initiating omalizumab resulted in a significant reduction in FcεRI expression in basophils from baseline at week 4 and remained consistent until week 24 (Fig 1).

Discussion:

The correlation between a reduction in FcεRI and improved clinical outcomes in omalizumab responders might highlight the significance of an IgE type 1 hypersensitivity in SU pathogenesis in actual clinical settings. Patients experience a quick response to omalizumab in real-life settings, as evidenced by UCT readings. This study highlighted the need of using omalizumab when antihistamines fail.[2] These findings were parallel with earlier research by Morgado-Carrasco D et al. indicating that omalizumab may achieve partial/total control quickly after starting treatment.[3]

Conclusion:

This study expanded the understanding of the effects of Omalizumab in actual clinical settings and emphasized the pathogenic significance of IgE-mediated pathways in solar urticaria, where FcεRI appeared as a potential biomarker of Omalizumab response.

Initiating omalizumab resulted in a quick clinical response and a considerable drop in baseline FcεRI levels. This highlights the pathogenic significance of IgE-mediated pathways through therapeutic response.

Reference:

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3. Morgado-Carrasco D, Giácaman-Von der Weth M, FustáNovell X, Podlipnik S, Pérez-Ferriols A, Aguilera P. Clinical response and long-term follow-up of 20 patients with refractory solar urticaria under treatment with omalizumab. J Am Acad Dermatol. 2023;88:1110–1111.

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.SPSS version 27 was used for data analysis in this study.

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.

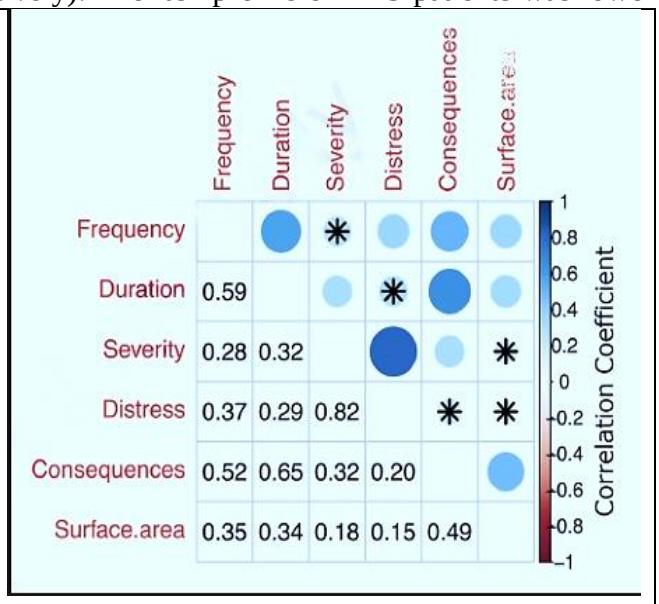

Figure 1: The correlation matrix of the itching dimensions indicates the strength of the relationship between two variables.

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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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 analyze 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. All statistical analyses were conducted using SPSS 23.0.

Results:

This study examined 38 males and 45 women, 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 nonuniform 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 nonuniform patterns. The pigment granules' size, color, and distribution are all uniform when there is a uniform pattern. A thorough investigation is required because uniform granular pigmentation during dermoscopy is a unique sign of drug response.

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

Reference:

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Case report on Eosinophilic Pustular Folliculitis Misidentified as Eczema

Introduction:

Eosinophilic pustular folliculitis (EPF) is an uncommon persistent itching aseptic condition. This condition is characterized by clustered or restricted follicular papules and pustules on an erythematous base, with a central pattern of self-healing and persistent hyperpigmentation.[1] EPF mostly affects the face, trunk, and extremities, but can also occur in seborrheic skin regions and palmoplantar region. Despite the lack of hair follicles in the palmoplantar area, EPF can still occur. When pustules appear on the palmoplantar area, it's important to examine the possibility of EPF with palmoplantar pustulosis. However, there are very few reports in the literature of EPF that just affect the palmoplantar region.[2] This study described a case where eosinophilic pustular folliculitis first appeared on the palms of both hands. Initially, the lesions were misdiagnosed as "eczema".

Case Presentation:

A 35-year-old male patient has been experiencing with recurring erythematous patches with bumps and itching on his face, trunk, hands, and feet for the past 10 years and having a recent onset of one month. The patient first presented ten years ago with exudation, crusted scabs, pustules, erythematous plaques, and crusted erosions on the hands and feet, along with minor itching. The patient was diagnosed with eczema and skin infection at an external clinic. Treatment included oral prednisone 30mg/day, cefradine, and topical corticosteroid cream, which improved symptoms. After resolving the hand and foot rash, the patient continued to have recurring erythematous patches, plaques, and bumps on their face, neck, back, hands, and feet, along with slight itching. After several visits to external clinics, the patient was diagnosed with "generalized eczema" and treated with topical corticosteroids, oral doxycycline, and topical corticosteroid ointment. Although these treatments gave temporary relief, they relapsed quickly after termination. The symptoms, which included severe erythematous patches, plaques, and bumps on the face, neck, back, hands, and feet, as well as slight facial swelling and itching, reappeared a month ago. There was no fever, joint discomfort, coughing up phlegm, diarrhoea, or abdominal pain. The patient came to hospital for additional care after not receiving any therapy, and a preliminary diagnosis of global eczema was made. Treatment included Tripterygium wilfordii glycosides 20mg three times a day, levocetirizine pills 5mg

once a day, ketotifen tablets 1mg every evening, and compound glycyrrhizin tablets 50mg three times a day. After one week of taking oral medicine, the patient was admitted to the hospital due to no improvement. A dermatologic examination revealed pinhead-sized pimples on the back, some of which were semi-annular in shape, large infiltrative erythema and swollen plaques with indistinct margins on both cheeks of the face, and irregular erythema with scattered pinhead-sized bumps on the neck. The hands and feet show diffuse erythematous desquamation with pinpoint-sized pustules (Figure 1).

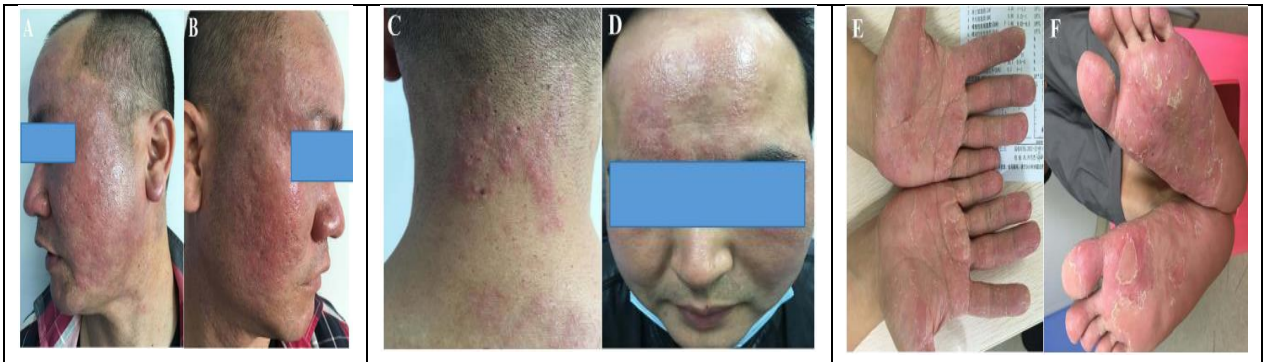

Figure 1. The face displays (A and B) large infiltrative erythematous and swollen plaques with indistinct margins; the neck displays (C) irregular erythematous plaques with scattered pustules the size of a pinhead; and the back displays (D) indistinct erythematous plaques with pustules the size of pinheads on some of the erythematous plaques, some of which are semi-annular in shape; Hands and feet (E and F) covered in sporadic pustules the size of a pinhead and diffuse erythematous desquamation.

Fungal microscopy of face erythema shows few spores, but negative results for buttocks, hands, and feet. A skin biopsy of the back erythema shows that there is mild epidermal keratinocyte edema, abundant eosinophilic infiltration, a small amount of inflammatory cell infiltration around the superficial dermal blood vessels, and a small number of neutrophils and lymphocytes surrounding the hair follicles and sebaceous glands in the dermis. Acid-fast staining was negative. Based on the results, the diagnosis was eosinophilic pustular folliculitis (classic type). After discharge, the patient was given 75mg of oral indomethacin every day. After ten days of therapy, the erythematous spots on the face, neck, and trunk gradually disappeared, pustules dried up, and a few adhering scales formed (Figure 2). Upon follow-up, the peripheral blood eosinophil count returned to normal. The patient continued to take 75mg of oral indomethacin daily, and after one month of therapy, the symptoms disappear. Medication was discontinued, and no recurrences were noted during a three-month follow-up.

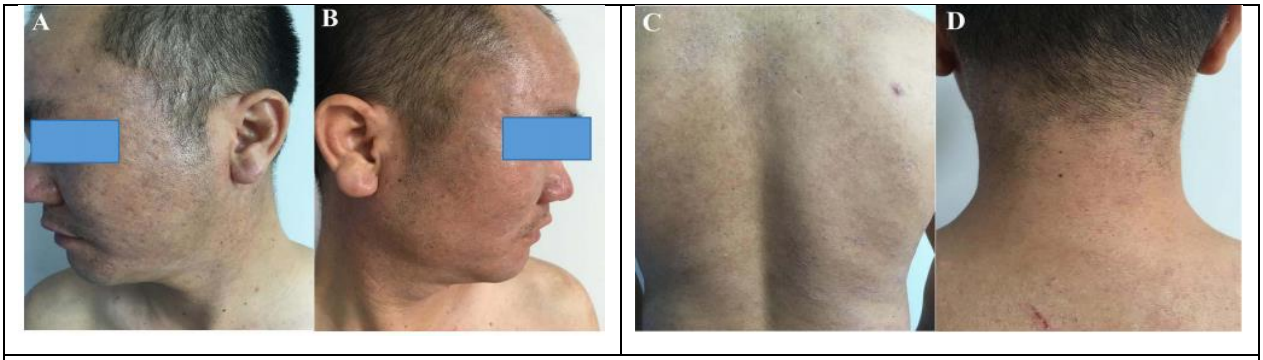

Figure 2. Vanished skin lesions on the back of the face and neck

Discussion:

Eosinophilic pustular folliculitis (EPF) was categorized into three types: infantile, immunosuppression-related, and classic. With a male-to-female ratio of 2.64:1 and an average onset age of 35–40 years, the classic type was most frequently observed in Japanese people. There were several treatments to treat this illness. Indomethacin was the first-line therapy; corticosteroids, tetracycline, colchicine, retinoids (including isotretinoin), tacrolimus, salicylic acid, and UV radiation were the second-line therapies.[2] Gulcan Saylam Kurtipek et al. showed that topical corticosteroids, calcineurin inhibitors, dapsone, antihistamines, and systemic antibacterial and anti-inflammatory medications were among the available treatment options for infantile eosinophilic pustular folliculitis.[3]

Conclusion:

Eosinophilic folliculitis's cause was yet unknown, however it might be related to anomalies in the immune system. Tetracycline-class medications, such as minocycline or doxycycline were used as second-line therapies for classical EPF.

Tetracycline-class medicines, such as minocycline and doxycycline, are used as second-line treatments for classical Eosinophilic pustular folliculitis (EPF).

Reference:

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