Hyper Immunoglobulin E Syndrome with Concomitant Folliculotropic Mycosis Fungoides in a Filipino Child Treated with Narrowband UVB Phototherapy: A Case Report*

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Abstract

Hyper Immunoglobulin E Syndrome (HIES) is a primary immunodeficiency disorder characterized by the classic triad of recurrent staphylococcal abscesses, frequent airway infections, and increased serum immunoglobulin E. It is now widely accepted as a multisystem disorder with involvement of the skeletal, connective tissue, dental, and vascular systems. Lymphoma has been reported to occur at an increased frequency. Folliculotropic mycosis fungoides (FMF) is a rare variant of cutaneous T-cell lymphoma in which the neoplastic T lymphocytes display tropism for the follicular epithelium. We report a case of a 14-year old Filipino male with the classic type of HIES presenting with severe eczema associated with intractable pruritus, recurrent respiratory tract infections, cold abscesses, and a serum IgE of 9,350 IU/ml. Skin biopsy also revealed findings consistent with FMF. Narrowband UVB (NB-UVB) phototherapy was initiated three times a week with continuation of supportive medication. Patient reported significant relief of pruritus and gradual improvement of eczematous lesions after one month.

Keywords: Hyper IgE syndrome, Job's syndrome, Follliculotropic mycosis fungoides, narrowband UVB phototherapy

OBJECTIVES

To present the first documented case of Hyper Immunoglobulin E syndrome in Jose R. Reyes Memorial Medical Center

To present the first documented case of Hyper Immunoglobulin E syndrome with concomitant Folliculotropic Mycosis fungoides in the Philippines

To present the first case of Hyper Immunoglobulin E syndrome with concomitant Folliculotropic Mycosis fungoides treated with Narrowband UVB phototherapy

SIGNIFICANCE

Hyper Immunoglobulin E syndrome is a primary immunodeficiency disorder presenting with recurrent abscesses, pneumonia, and elevated serum IgE levels. In patients presenting with chronic relapsing eczema with recurrent skin infections, it is important that clinicians learn to recognize, or at least, think of HIES as a differential diagnosis. It is also imperative to recognize symptoms that may already be part of a syndrome. HIES is related to an increased risk of lymphoproliferative malignancies such as mycosis fungoides. Knowledge on the clinical spectrum of HIES will aid in the early diagnosis and prediction of the course and prognosis of this disease, thereby prolonging life.

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INTRODUCTION

Hyperimmunoglobulin E Syndrome (HIES) is a rare, complex primary immunodeficiency disorder with a worldwide prevalence of 1 in 1,000,000 persons with approximately 250 cases reported in literature.[1] Two distinct entities have been recognized – autosomal dominant HIES (AD-HIES) and autosomal recessive HIES (AR-HIES). However, most cases are considered sporadic.[2] Both types are characterized by the triad of recurrent staphylococcal abscesses, respiratory infections, and elevated serum IgE. In AD-HIES, there is also involvement of the skeletal, dental, connective tissue, and vascular systems, which is absent in AR-HIES. In patients with HIES, an increased incidence of lymphoproliferative disorders have been noted, particularly non-Hodgkin's lymphomas.[3] Cutaneous T-cell lymphomas are non-Hodgkin's lymphoma characterized by malignant T cells, with mycosis fungoides (MF) being the most common form. Folliculotropic mycosis fungoides (FMF) represents a distinct variant of MF that shows infiltrates of neoplastic T-helper cells that involve the follicular epithelium, with minimal or no involvement of the overlying epidermis. Patients present with alopecia and acneiform lesions such as pustules, milia, and clustered comedones involving most commonly the head and neck.[4] Only one case report of HIES with concomitant MF in literature exists. Narrowband UVB therapy is currently used for pruritic dermatoses such as atopic dermatitis and is the standard treatment in managing MF in children. No case reports have been presented in literature of HIES with MF treated with NB-UVB. This is a case of a 14-year-old Filipino male with HIES and concomitant FMF treated with NB-UVB for the relief of pruritus and improvement of lesions.

CASE REPORT

A 14-year-old male from Quezon City, Philippines, sought consult at the outpatient department due to generalized lichenified papules and pustules on severely dry skin.

Three years prior to consult, patient noted multiple skin-colored papules on the dorsa of both hands associated with intractable pruritus. Lesions gradually evolved into vesicles and pustules and later became lichenified. He sought consult at a dermatologist and was prescribed Cetirizine 10mg/tablet OD and emollient which gave temporary relief. Pruritus would abate but would recur, hence, oral antihistamine was shifted to Chlorphenamine maleate 4mg/tablet TID and then to Loratadine 10mg/tablet OD. Same lesions developed on the upper and lower extremities. Patient was then lost to follow-up.

Two years prior to consult, with the persistence of lesions and spread to the trunk, he was brought to a government pediatric hospital where an initial impression of lichen planus vs. acquired perforating disease was made. Clobetasol propionate 0.05% ointment BID was advised. A 4mm skin punch biopsy from the left elbow and leg revealed findings consistent with psoriasiform dermatitis. He was then referred to a dermatological institute where he was managed as a case of chronic eczema. Patient was subsequently treated with shifting topical corticosteroids, oral anti-histamines and emollients. Lesions and pruritus would be alleviated but would recur. Patient also reported developing multiple abscesses on the extremities with no associated tenderness, warmth, erythema, and fever. Due to financial constraints, patient was not able to come back for consult.

One year prior to consult, pruritic papules and pustules were observed to be spreading to his face. He also noted gradual hair loss and excoriations starting from the parietal scalp. Due to the increase in the number of lesions and persistence of pruritus, patient came back to his previous doctor. Skin punch biopsy of the scalp showed scarring alopecia with eosinophilic spongiosis. He was then prescribed Minoxidil 5% lotion BID, Betamethasone dipropionate 0.05% ointment for the scalp and lichenified lesions, Prednisone 30mg/day, and oral anti-histamines. He was also instructed to apply Erythromycin 4% cream BID on infected lesions. Patient reported 50% improvement of his eczema and sparse growth of hair. However, symptoms persistently recurred. Total serum IgE was requested and was markedly elevated at 9,350 IU/ml. He was then advised referral to Allergology-Immunology service but was lost to follow-up. Persistence of symptoms subsequently prompted consult at our institution.

On systems review, patient reported recurrent cough and colds (around6-8 times a year), occasional ear discharge, and repeated episodes of pustules and abscesses observed not to be associated with cardinal signs of inflammations. Past medical history revealed an undocumented seizure disorder starting at 6 years old. He was maintained on Carbamazepine 200mg/tablet BID. Seizure episodes recurred until he was 9years old. Electroencephalogram done revealed multifocal epileptiform discharges from the left fronto-centro-parietal area. He had no history of other previous illnesses and hospitalizations. No similar illness and malignancies was reported in the family history.

On initial physical examination, patient had a blood pressure of 110/70, heart rate of 86 bpm, respiratory rate of 18 cpm, and temperature of 36.5^{0}C. Based on the Waterlow classification, patient had moderate wasting (70%) and stunting (86%). Interpupillary distance was increased at 60 mm (normal: 41-55 mm) denoting hypertelorism. Dental examination showed retention of primary 2 mandibular and 2 maxillary teeth (Figure 4). The neurologic, cardiovascular, respiratory, gastrointestinal, and musculoskeletal systems were unremarkable. On dermatological examination, he had generalized lichenified hyperpigmented papules and numerous pustules topped with excoriations over very dry skin with accentuated skin markings (Figure 1-2). There were also multiple well-defined alopetic patches topped with excoriations on the scalp (Figure 3.B.). There was absence of the eyebrows, eyelashes, and pubic hair. Multiple milia were noted to be distributed over the head and neck. Distinctive facial features such as a prominent forehead, deep-set eyes, broad nasal bridge, and rough skin with prominent pores were observed. (Figure 3.A.)

Laboratory work-up revealed leukocytosis (18.49 x 10^9 /L) with eosinophilia of 25% and total eosinophil count of 4,622 cells/µL. Serum IgE was elevated at 9,350 IU/ml, a 57-fold increase of the normal value. Urinalysis and fecalysis showed normal results ruling out parasitic infections. Thyroid stimulating hormone and FT_4 were normal, and rapid plasma reagin was non-reactive. Chest radiograph and head CT scan were likewise unremarkable. A 4 mm skin punch biopsy done at our institution showed findings consistent with mycosis fungoides. The epidermis showed some epidermotropism with parakeratotic invaginations in dilated follicular structures ("folliculotropism"). The papillary dermis was thickened with lichenoid infiltrates, lymphohistiocytic infiltrates and telangiectatic blood vessels (Figure 5. A-B). Immunohistochemical studies revealed the lymphocytes to be CD3-positive T cells. Rare CD20-positive B cells were identified. Alcian blue stain showed numerous mucin deposits surrounding follicular structures (Figure 6. A-D). A diagnosis of mycosis fungoides, folliculotropic variant, was then made. According to the International Society of Cutaneous Lymphoma (ISCL) and the European Organization of Research and Treatment of Cancer (EORTC), patient is stage IIB (T_3 N_0 M_0 B_0). (Table 1)

During regular consults, patient developed difficulty of breathing and cough. Chest xray was done which revealed pneumonia. He was then admitted at another government-owned hospital.

The National Institute of Health (NIH) Scoring System with Clinical and Laboratory Tests for Related Individuals with HIES (Table 2) was used to diagnose HIES, and revealed a total-point score of 51 (10 points for serum IgE >2,000 IU/ml, 8 points for skin abscesses, 2 points for pneumonia, 8 points for more than 3 retained primary teeth, 6 points for eosinophil count > 800 cells/µL, 5 points for characteristic face, 4 points for severe eczema, 4 points for > 6 upper respiratory infections per year, 4 points for the presence of lymphoma). However, his family does not have any history of HIES. Thus, our patient may be a sporadic case but may likely carry the HIES genotype.

Patient was then started with Prednisone 20 mg OD, Cetirizine 10 mg/tablet, Chlorphenamine maleate 4mg/tablet TID, and topical corticosteroids mixed with petroleum jelly (1:10) starting with Clobetasol propionate, Betamethasone dipropionate, Fluocinolone acetonide, and Mometasone furoate at 2-week intervals. He was also prescribed Ranitidine 150 mg/tablet OD, and Vitamin D and Calcium tablet BID. On subsequent follow-ups, Montelukast 10 mg/tablet and Cloxacillin 500mg/tablet QID for impetiginized lesions were added. Frequent application of emollient was strongly advised. He was also put on a hypoallergenic diet. After one month, patient reported diminished pruritus by approximately 50% and decrease in the number of lesions. However, he still complained of on and off stubborn pruritus.

Before initiating narrowband UVB phototherapy, liver and renal profiles were requested which were normal. He was also referred to Ophthalmology service for clearance. On examination, patient had punctate epithelial keratitis, OU. He was then prescribed Tobramycin eye ointment BID for 1 week. NB-UVB phototherapy for Fitzpatrick skin type III following Dr. Vichit's protocol was given 3 times a week beginning with 360 mJ/cm^2 with regimen following the standard treatment. He was advised to continue present medications and to apply sunblock with SPF > 50. Response to treatment with respect to pruritus was monitored every week. Patient is currently on the 12th session with current dose of 1130 mJ/cm^2 and a cumulative dose of 7,772 mJ/cm^2. He reported steady decrease in the pruritus of approximately 10% weekly. Photography was done every 2 weeks which showed lessening of the number of lesions especially at the back (Figure 7. A-B) and smoothening of the facial skin (Figure 8. A-B). During the course of therapy,

patient tolerated the procedure well with no episodes of erythema, burning, and nausea. However, he complained of a "cold" abscess described as localized thickening on the medial aspect of the right leg associated with pain. No erythema, discharge, and fever observed. After 2 days, he noted purulent discharge from the affected area.

DISCUSSION

HIES is a primary immunodeficiency disorder characterized by the triad of recurrent staphylococcal abscesses, frequent respiratory infections, and elevated serum IgE (serum IgE > 2,000 IU/ml). It was first described as Job's syndrome by Davis et al. in 1996 referring to the biblical character, Job, who was "smote with sore boils". They reported two girls suffering from recurrent eczema, pneumonia, and recurrent abscesses distinct for their lack of erythema, warmth, or tenderness. In 1972, Buckley et al. further described HIES in two boys who had the same symptoms but with characteristic facial appearance and extremely elevated serum IgE.[6] Since then, involvement of the skeletal, dental, connective tissue, and vascular system has been documented. It is an extremely rare condition with a worldwide prevalence of 1:100,000 with approximately 250 cases reported in literature.[1] It occurs in equal frequency among males and females.[3] Most cases are sporadic, but both AD-HIES and AR-HIES have been recognized.[5] In the Philippines, no case reports of HIES, more so HIES with MF, have been published from local journals, specifically from the Journal of Philippine Dermatological Society from 1990 to 2012. No cases have been reported from other dermatological institutions in our country. This is the first case of HIES documented in our institution.

AD-HIES or the classic type presents with the typical triad of symptoms but with a wide spectrum of clinical features divided into immunologic and somatic features. Immunologic features and their frequencies include peak serum IgE > 2,000 IU/ml (97%), moderate-severe eczema (95%), eosinophilia (90%), recurrent pneumonia (87%), abscesses (87%), mucocutaneous candidiasis (83%), newborn rash (80%), recurrent sinusitis or otitis (80%), bronchiectasis or pneumatoceles (70%), and lymphoma (5%).[6] The top 3 most prevalent features are present in our case. Eczema is often worsened by *Staphylococcus aureus* infection. Although frank pus is present on aspiration, cardinal features of inflammation, such as warmth, erythema, and tenderness, are often lacking. These are considered "cold" abscesses which occasionally occurred in our patient. Presence of cold abscess is pathognomonic for HIES but is not needed for a definitive diagnosis. Recurrent pyogenic pneumonia usually starts in early childhood. *S. aureus* is the most common pathogen, but *Streptococcus pneumonia* and *Haemophilus influenza* also frequently complicate respiratory infections. Healing of pneumonia often leads to subsequent formation of pneumatoceles and bronchiectasis – parenchymal abnormalities that may be sites of fungal infection caused by *Aspergillus sp.* or gram negative pathogens (*Pseudomonas aeruginosa*). Opportunistic infections are also seen in HIES. Pneumocystis jiroveci pneumonia, cryptococcosis, histoplasmosis, and mucocutaneous candidiasis have been reported.[3] Somatic features include characteristic face (85%), hyperextensibility (70%), retained primary teeth (70%), focal hyperintensities on brain MRI (75%), minimal trauma fractures (65%), scoliosis more than 10 degrees (60%), coronary vasculature anomalies (60%), and Arnold Chiari I malformations (40%).[7] Of these, distinctive facial features and dental abnormalities are observed in our patient.

The majority of cases of AD-HIES are caused by mutation in the signal transducer and activator of transcription 3 (STAT3). STAT3 is involved in the signal transduction of many cytokines and plays a role in wound healing, angiogenesis, cancer, and immunity. STAT3 is integral to Th17 cell differentiation and IL-17 production.[8] Th17 cells are thought to be important in the host defense through neutrophil recruitment, upregulation of antimicrobial peptides, and anti-fungal protection. Th17 cells are also essential for IL-22 secretion which is critical for beta-defensin production. Lack of beta-defensin is implicated in the susceptibility of HIES patient to *S. aureus* infection. HIES is also thought to result from Th1/Th2 cytokine production imbalance with Th2 predominance. Th1 cytokines activate cellular responses while those of Th2 induce the humoral immune system. A bias towards Th1 is associated with autoimmune diseases while Th2 predominance induces allergic reaction through hypereosinophilia and hyper IgE production. In STAT3 mutation, main Th1 cytokines such as IFN-γ and IL-2 are decreased whereas IL-4 and IL-10, primary Th2 cytokines, are increased.[9] Experimental studies have observed that decreased IFN-γ and increased IL-4 predispose to IgE production. However, the exact mechanism explaining the elevation of IgE remains poorly understood.[7] The chief concern of our case is severe pruritus. This is attributed to the increase in mast cells that goes with the elevation of IgE. Another feature of HIES is eosinophilia. Eosinophils play a role in allergic

conditions such as atopic dermatitis, helminthic infection, and drug hypersensitivity. IgE receptors are known to be expressed on eosinophils. Eosinophilia is then related to pronounced expression of IgE, thereby inducing pruritus as mediated by mast cells.[10]

Diagnosis of AD-HIES is based on the NIH Scoring System with Clinical and Laboratory Tests for Related Individuals with HIES.[3] A score of > 40 is suggestive of AD-HIES, 20-40 indeterminate, and < 20 is unlikely to indicate AD-HIES. The hallmark of this syndrome is an increased concentration of IgE, frequently higher than 5,000 IU/ml, and in some, reaching up to 100,000 IU/ml. A cut-off of 2,000 IU/ml is considered the cut-off point in establishing diagnosis. In adulthood, IgE level normalizes in 20% of cases. The severity of infectious complications do not correlate with serum IgE.[3] Eosinophilia is present in 90% of cases and values considered significant wavers within at least 2 SD above the normal range (usually higher than 700 cells/μL).

In 2004, Renner et al. reported an autosomal recessive form of HIES, sharing the same triad of recurrent staphylococcal abscesses, recurrent respiratory infections, and elevated IgE, but with the following differences: 1.) increased incidence of neurologic abnormalities, 2.) increased susceptibility to viral infections such as herpes simplex virus and molluscum contagiosum, 3.) absence of somatic features of AD-HIES, 4.) increased risk for malignancy, 5.) extremely elevated eosinophils and IgE, and 6) inability to form pneumatoceles. It is caused by dedicator of cytokinesis 8 gene (DOCK8) mutation which also causes Th17 deficiency.[12] Autosomal recessive pattern is assumed because of consanguinity and multiple affected siblings. This form is more lethal in childhood because of early-onset neurologic complication such as ischemic infarctions, hemiplegia, and subarachnoid hemorrhage.

The mainstay of treatment is prevention and control of infection. Antibiotics directed against *Staphyloccoccus aureus, Haemophilus influenzae,* and *Streptococcus pneumoniae* are recommended. The use of long-term antibacterial chemotherapy, including trimethoprime/sulfamethoxazole, semisynthetic penicillin, or cephalosporins significantly reduces skin abscesses and staphylococcal pneumonia. Sequelae of pneumonia, such as pneumatocele, lung abscess, and bronchiectasis may require surgical intervention. Patients are advised to apply topical antibacterials on localized infected lesions. Patients are advised oral anti-histamines and liberal use of emollients for pruritus. Experimental studies about the use of IFN-γ to improve neutrophil chemotactic functions have been undertaken. However, a case of autoimmune thrombocytopenia in one patient has been reported. Monitoring of complications must be undertaken closely by periodic imaging of the bones, chest, and heart. Referral to ophthalmology and dental services are advised.

Prognosis with AD-HIES is good with patients reaching adulthood. However, lifespan is relatively shortened compared to the healthy population. Fatal hemorrrhage due to cystic lung disease infected with opportunistic agents, metastatic fungal disease to the brain, and lymphoma are the most common causes of mortality.[13]

Patients with HIES are seen to have 5% increased risk for lymphoma.[7] Although HIES is a T cell-mediated disorder, the lymphoid malignancies reported in literature are mostly B cell in origin with few reports of cutaneous T cell lymphomas. Mycosis fungoides is the most common type of cutaneous T cell lymphoma in adults with a prevalence of 0.36 per 100,000 persons.[21] Although, it is rare in children, it happens to be the most common variant of cutaneous T-cell lymphoma in children and adolescents as well. Mycosis fungoides has been reported to start in childhood in around 4% of all MF cases. Limited (involving less than 10% of the total skin surface) or generalized (involving more than 10% of the total skin surface) patch-stage disease without lymph node involvement or with histologically negative nodes are the most common clinical presentations of childhood MF.[22] In literature, a single case report exists linking MF and HIES. [19] The association between HIES and, specifically, MF has yet to be elucidated and the mechanism underlying susceptibility to lymphoma remains unclear.

Folliculotropic mycosis fungoides is a rare clinical variant of MF characterized by follicular cysts, or comedo-like lesions with preferential involvement of the head and neck (80%).[20] The extremities and trunk can also be involved. Infiltrated plaques (55%), acneiform lesions (comedo-like and epidermal cysts) (45%), and follicular keratosis-pilaris–like lesions (45%) are the more prominent features. These lesions are often accompanied by alopecia and moderate-to-severe pruritus. Our patient presented with multiple alopetic patches topped with excoriations on the scalp, numerous milia on the face and neck, and loss of eyebrows, eyelashes, and pubic hair. Little is known

about the etiology of FMF, although it has been suggested that the epithelium of the hair follicle might express higher levels of skin-selective homing receptors and adhesion molecules than the epidermis leading to preferential tropism of the neoplastic lymphocytes towards the follicle.[23] Diagnosis is made clinically and histopathologically. In addition to the classical findings of MF, emphasis was laid on the following histological features: degree and density of folliculotropism of lymphocytes, presence of follicular mucin (confirmed by Alcian blue - PAS stain), presence and number of eosinophils (< 5, 5–20, > 20 per section), location of folliculotropism (infundibular / isthmic / bulbar), presence of granulomas, and presence of conventional epidermotropism outside the follicles.[24] Histopathological findings in our patient's biopsy were consistent with findings in FMF that include selective infiltration of the follicular epithelium by atypical lymphocytes and mucinous degeneration of the follicular epithelium.

Staging of MF is based on skin manifestations, nodal, visceral, and blood involvement. (Table 1) Our patient presented with skin manifestations of more than 10% of body surface area. However, FMF has been shown to be associated with a worse prognosis than expected for clinical stage and is considered equivalent to T_3 tumors.[25]

Classic MF in children with no extracutaneous involvement has a good prognosis. However, the course of FMF with concurrent HIES is unknown. In the case report of Miyayama et al.[19], the patient died 2 years after the findings of lymph node involvement and extremely elevated serum IgE (536,640 IU/ml).

Recurrent and intractable pruritus is one of the complaints of our patient, hence, addressing it will bring considerable relief and improvement of the quality of life. HIES and atopic dermatitis share common features being both Th2-mediated, with increased IgE levels, and eosinophilia. A recent systematic review concluded that in view of its efficacy, benefit–risk profile, and costs, NB-UVB should be considered as the first-line phototherapeutic option for moderate to severe AD.[14] NB-UVB reduces the production of Th2 chemokines without excess production of proinflammatory cytokines, suggesting its therapeutic effectiveness on Th2-mediated skin disorders such as atopic dermatitis, subacute prurigo, and eosinophilic pustular folliculitis.[15] NB-UVB phototherapy has also been used in the treatment of childhood MF especially for early stages (I-II). However, MF is rarely cured. Instead, most treatments are aimed at controlling the symptoms, improving the quality of life, and preventing the disease from progressing into later stages. Because of the perifollicular localization of the dermal infiltrates, patients with follicular MF should always be considered to have tumor-stage disease, regardless of the clinical appearance of the skin lesions. UVB irradiation is thought to be therapeutic by suppressing the function of the neoplastic population of clonal T-cells in the skin and around hair follicles, and by serving as an upregulator of the immune system.[26] Following this line of thought, the rationale for performing NB-UVB on a patient with HIES and MF is acceptable. NB-UVB was also initiated on a 56-year-old Japanese female with FMF. After 24 (total 12.3 J/cm2) exposures, all of the lesions had completely disappeared.[26] On follow-up 3 years after her presentation, there were no new skin lesions. In a case report by Hinrichs et al[16], a patient with HIES was successfully treated with a 4-month course of UVA irradiation 5 times a week. However, we decided to give NB-UVB because of shorter exposure time, shorter course of therapy, longer periods of remission, and less side effects, making it safer to use in children.[17] The most common adverse effect is erythema followed by a case of painful erythema and reactivation of herpes simplex virus.[14]

Patient was put on NB-UVB 3 times a week and was advised to continue other present medications. As relief of pruritus denotes a better prognosis in MF, grading of the severity of pruritus was done weekly. Patient reported 10% improvement each week. Photography was done every 2 weeks and after 1 month of treatment, smoothening of the facial skin and decrease in the number of lesions especially at the back were observed. However, after the 12th session, patient complained of thickening of the skin over the medial aspect of the right leg associated with pain. No fever, erythema, and warmth noted. Purulent discharge was expressed from the area 2 days after. He was then advised to start Cefalexin 500mg/tablet QID for 7 days and to apply cool compress which gave prompt relief.

Aside from the clinical improvement, it is advised that periodic monitoring of the CBC, liver and renal profiles, and chest imaging be done to watch out for complications and to assess for adverse effects of phototherapy.

CONCLUSION

Hyperimmunoglobulin E Syndrome is a rare primary immunodeficiency disorder classically characterized by the triad of recurrent staphylococcal abscesses, frequent respiratory tract infections, and elevated serum IgE. With continuing research, it is now widely accepted as a multisystem disorder involving the skeletal, dental, connective tissue, and vascular systems. Diagnosis is mainly clinical in addition to the hallmark of increased serum IgE and eosinophilia. In patients presenting with chronic relapsing eczema with recurrent skin infections, it is important that clinicians learn to recognize, or at least, think of HIES as a differential diagnosis.

Increased risk of lymphoma such as mycosis fungoides has been reported in HIES which further complicates management of this disorder. However, strength of association and mechanism of susceptibility has yet to be determined.

Confronted with a patient with HIES and MF, narrowband UVB phototherapy may be appropriate for the management of these two disorders. NB-UVB phototherapy acts by reversing Th2 response predominance, subsequently leading to decreased IgE and eosinophils, and restraining the function of neoplastic population of clonal T cells in the skin. Based on the response of our patient to the irradiation, NB-UVB is suggested for the management of pruritus, improvement of skin lesions, and suppression of malignant cells. Close monitoring and early recognition of complications is imperative in order to prolong life.

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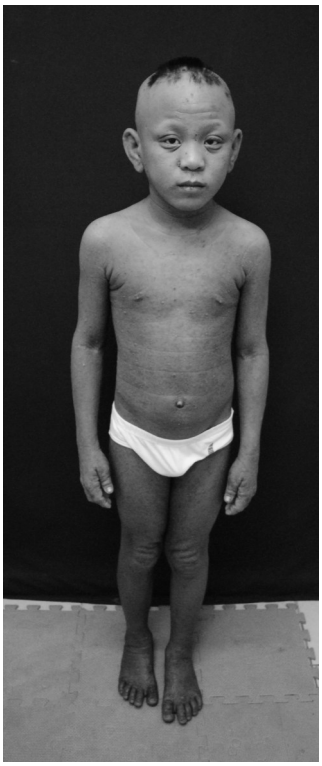

Figure 1.Generalized lichenified hyperpigmented papules and some pustules topped with excoriations over very dry skin with accentuated skin markings. Note moderate wasting and stunting.

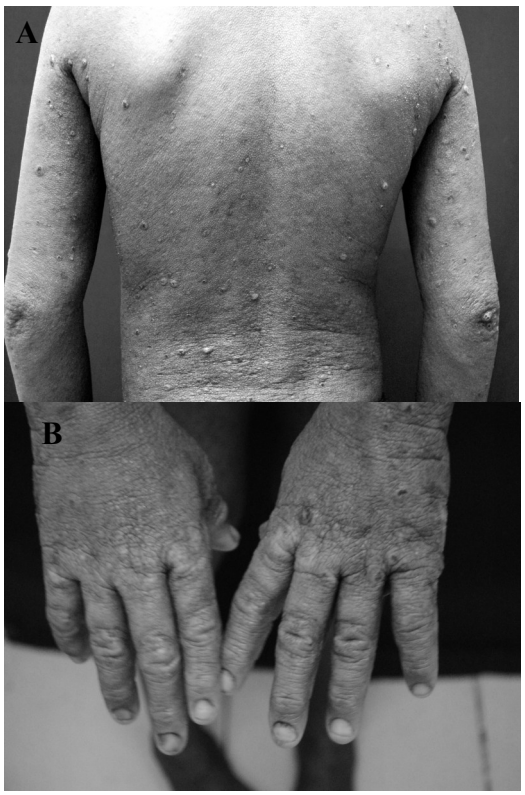

Figure 2. A. Multiple ill-defined hyperpigmented papules topped with excoriations over the back
B. Lichenified papules and plaques with some pustules on both hands.

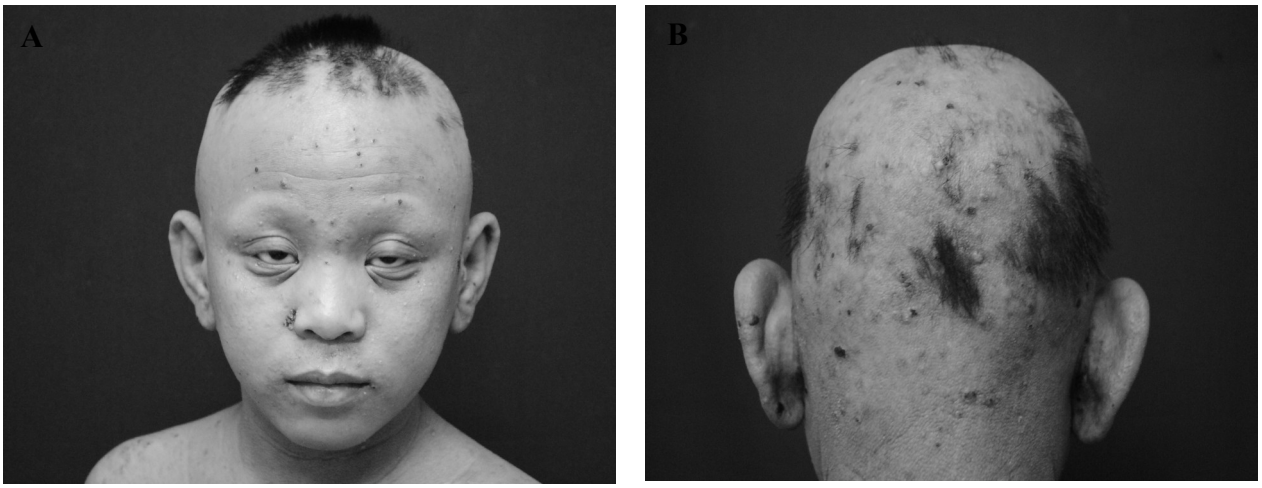

Figure 3. A. Distinctive facial features are observed such as prominent forehead, deep-set eyes, broad nasal bridge, and wide and fleshy nasal tip. Facial skin was also noted to be rough with excoriations and prominent pores. There is loss of eyebrows and eyelashes. **B**. Multiple well-defined alopetic patches topped with excoriations.

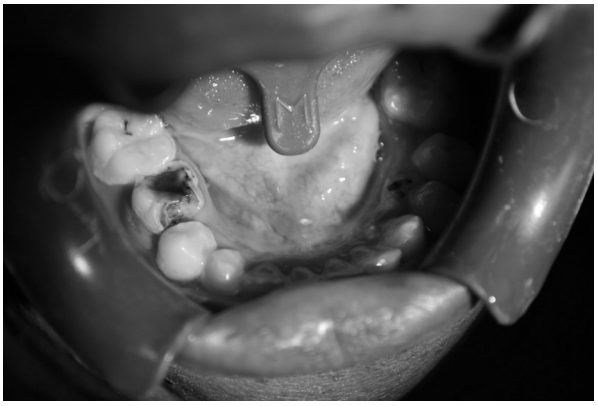

Figure 4. Retained primary lower maxillary teeth

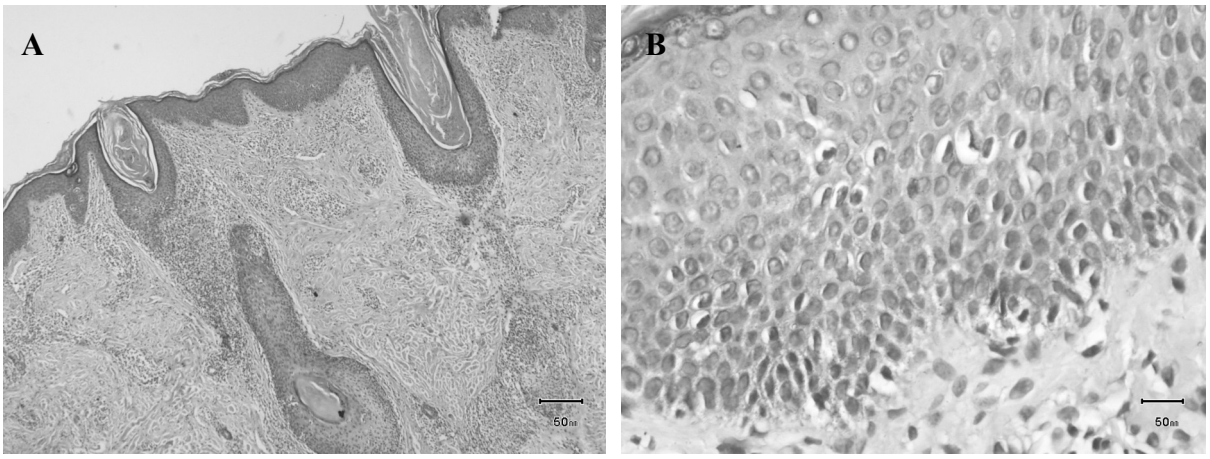

Figure 5. A. Hyperplastic epidermis with parakeratotic invagination in dilated follicular structures. Papillary dermis is thickened with lichenoid infiltrates, patchy dense perifollicular infiltrate of lymphohistiocyte, and telangiectatic blood vessels. **B.** Some epidermotropism.

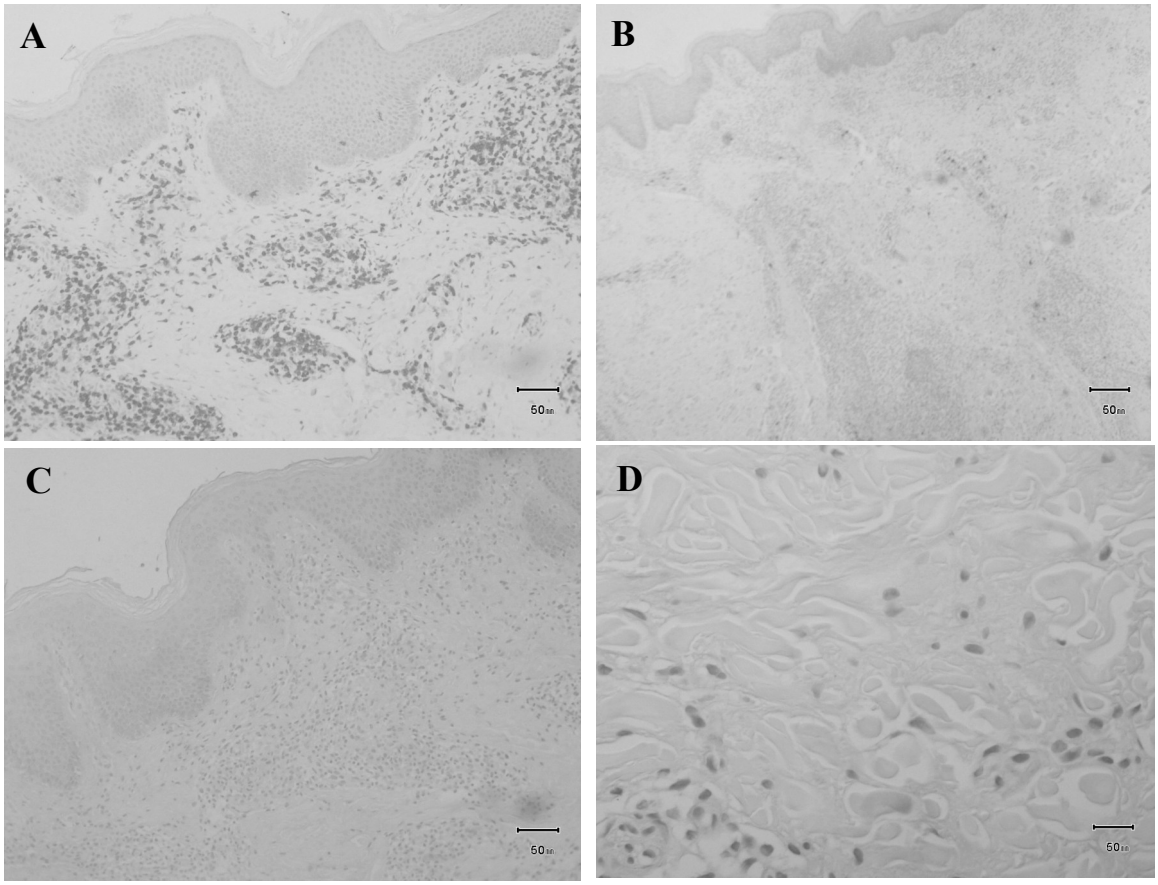

Figure 6. A. Immunohistochemical studies revealed the lymphocytes to be CD3-positive T cells. **B.** Rare CD20-positive B cells were identified. **C.** Alcian blue stain showed numerous mucin deposits surrounding follicular structures **D.** Closer look at the mucin deposits.

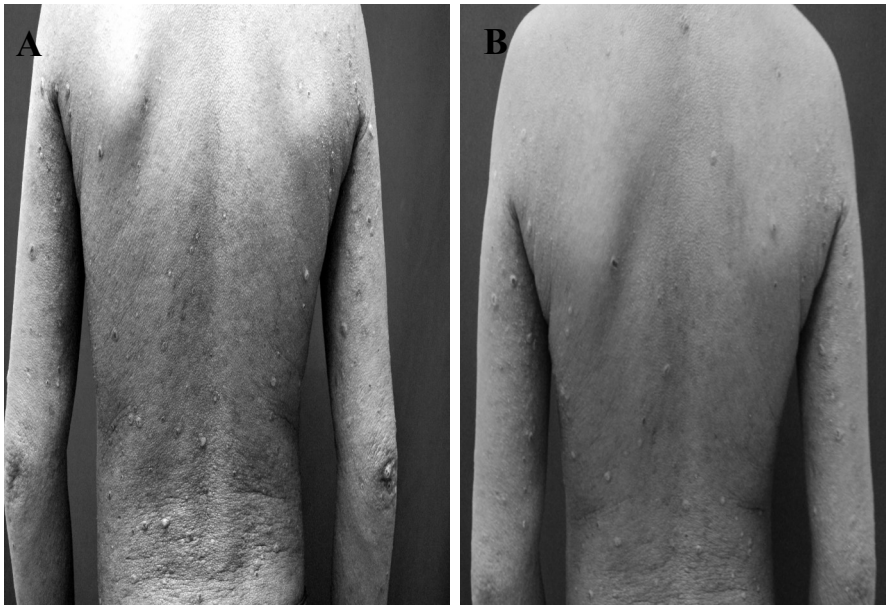

Figure 7. A. Photograph of the back at baseline. **B.** Photography taken at the same area after 12 sessions of NB-UVB phototherapy. Note decrease in the number of lesions.

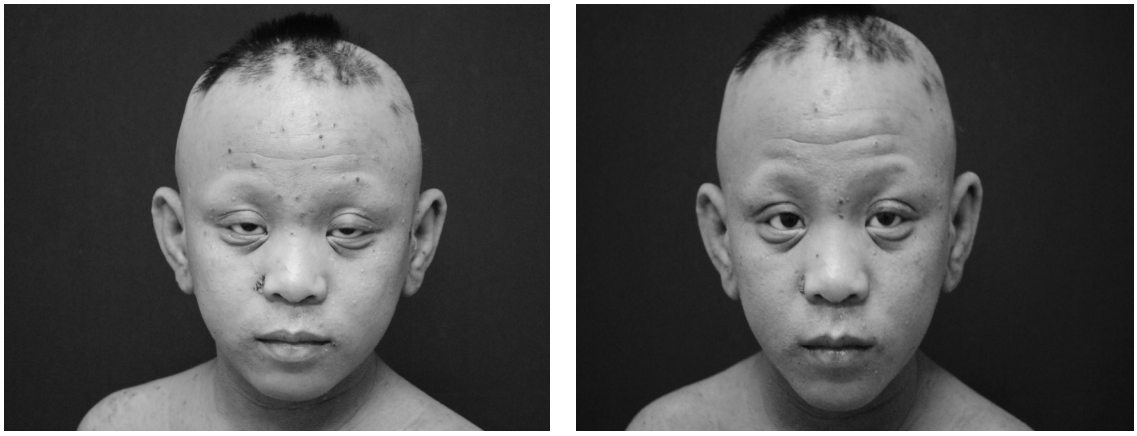

Figure 8. A. Photograph of the face at baseline. **B.** Photograph taken of the face after 12 session of NB-UVB. Note smoothening of the facial skin and decrease in excoriations.

Table 1 International Society of Cutaneous Lymphoma (ISCL) and the European Organization of Research and Treatment of Cancer (EORTC) Staging of Mycosis

TNMB stages

Skin	
T_1	Limited patches,* papules, and/or plaques† covering < 10% of the skin surface. May further stratify into T_{1a} (patch only) vs T_{1b} (plaque ± patch).
T_2	Patches, papules or plaques covering ≥10% of the skin surface. May further stratify into T_{2a} (patch only) vs T_{2b} (plaque ± patch).
T_3	One or more tumors‡ (≥ 1-cm diameter)
T_4	Confluence of erythema covering ≥80% body surface area
Node	
N_0	No clinically abnormal peripheral lymph nodes§; biopsy not required
N_1	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 1 or NCI LN_{0-2}
N_{1a}	Clone negative*
N_{1b}	Clone positive*
N_2	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 2 or NCI LN_3
N_{2a}	Clone negative*
N_{2b}	Clone positive*
N_3	Clinically abnormal peripheral lymph nodes; histopathology Dutch grades 3-4 or NCI LN_4; clone positive or negative
N_x	Clinically abnormal peripheral lymph nodes; no histologic confirmation
Visceral	
M_0	No visceral organ involvement
M_1	Visceral involvement (must have pathology confirmation¶ and organ involved should be specified)
Blood	
B0	Absence of significant blood involvement: ≤5% of peripheral blood lymphocytes are atypical (Sézary) cells‖
B_{0a}	Clone negative*
B_{0b}	Clone positive*
B1	Low blood tumor burden: > 5% of peripheral blood lymphocytes are atypical (Sézary) cells but does not meet the criteria of B_2
B_{1a}	Clone negative*
B_{1b}	Clone positive*
B2	High blood tumor burden: ≥1000/μL Sézary cells‖ with positive clone*

Table 2. Scoring System with Clinical and Laboratory Tests for Related Individuals with HIES

Clinical Finding	Points [1]									
	0	1	2	3	4	5	6	7	8	10
Highest serum-IgE level (IU/mL) [2]	<200	200-500			501-1,000				1,001–2,000	>2,000
Skin abscesses	None		1–2		3-4				>4	
Pneumonia (episodes over lifetime)	None		1		2		3		>3	
Parenchymal lung anomalies	Absent						Bron-chiectasis		Pneumato-coele	
Retained primary teeth	None	1	2		3				>3	
Scoliosis, maxi-mum curvature	<10°		10°-14°		15°-20°				>20°	
Fractures with minor trauma	None				1-2				>2	
Highest eosino-phil count (cells/ µL) 3	<700			700-800			>800			
Characteristic face	Absent		Mildly pre-sent			Present				
Midline anomaly [4]	Absent					Present				
Newborn rash	Absent				Present					
Eczema (worst stage)	Absent	Mild	Moderate		Severe					
Upper-respiratory infections per year	1-2	3	4-6		>6					
Candidiasis	None	Oral	Fingernails		Systemic					
Other serious infections	None				Severe					
Fatal infection	Absent				Present					
Hyperextensibility	Absent				Present					
Lymphoma	Absent				Present					
Increased nasal width [5]	<1 SD	1-2 SD		>2 SD						
High palate	Absent		Present							
Young-age cor-rection	>5 years			2-5 years		1-2 years		≤1 year		

Scoring:
> 40 Suggestive of AD-HIES
20-40 Indederminate
< 20 Unlikely to indicate AD-HIES

From Grimbacher et al (1999b)
1. The entry in the furthest-right column is assigned the maximum points allowed for each finding.
2. Normal <130 IU/mL
3. 700/µL = 1 standard deviation (SD), 800/µL = 2 SD above the mean value for normal individuals.
4. For example, cleft palate, cleft tongue, hemivertebrae, other vertebral anomaly, etc.
5. Compared with age- and sex-matched controls