

lymphomas which do not fit into the group of PCLBCL-LT or the group of PCFCL [1-3].

PCFCLs generally present as red-brown papules, plaques or nodules on the scalp, forehead or trunk. Presentation on the arm has been described before, associated with arm swelling but with normal looking epidermis [4]. Ulceration is very rarely observed in PCFCLs [3, 5]. There are a limited number of reported cases with impressive loco-regional aggressiveness, showing, however, a low tendency to systemic spread, even over a 20-year period [5].

PCFCLDT is characterized by a mixture of centrocytes and centroblasts with a follicular, follicular and diffuse, or diffuse pattern [1-3]. Large centrocytes are generally more plentiful in diffuse pattern [6]. Lesions presenting with a diffuse pattern of infiltration and consisting entirely of centroblasts should not be included in the PCFCLDT group. In this particular case, there was a diffuse infiltration of the subcutis, composed mainly of large centrocytes and a relatively small number of centroblasts, which were not confluent. In addition, the immunophenotype, as described above, does not allow us to classify this lymphoma otherwise. MUM1 positivity was observed in a few cells but it has been reported to be expressed by a small minority of PCFCL [7, 8]. However, it has been suggested that strong MUM-1 expression may point to a more aggressive behavior of PCFCL [8]. The observed high Ki67/MIB1 positive fraction also advocated an aggressive course, which was evident from the rapid evolution of the lesion.

Additionally, irregular networks of CD21-positive follicular dendritic cells are typically observed in PCFCL [6, 9], especially in the nodular pattern, whereas FDCs are usually absent in the diffuse pattern [10]. The absence of FDCs in this particular case demonstrates the diffuse pattern of this lymphoma.

PCFCLs rarely spread to lymph nodes, spleen or bone marrow and have an excellent prognosis in the majority of cases. Excision and radiation therapy are effective for localized lesions. In unusual circumstances, systemic therapy with a combination of rituximab and chemotherapy is recommended [3, 5, 6].

Our case indicates that there may be a subgroup of PCFCLs which present with a rapid clinical evolution, diffuse pattern of infiltration, high Ki67/MIB1 index and need to be treated as high grade lymphomas, due to the high tumor burden. Nevertheless, despite the aggressive local behavior, there was an excellent response to treatment, confirming the overall, well-documented, good prognosis of primary cutaneous follicle center lymphomas. ■

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Treatment of non-episodic angioedema associated with eosinophilia with suplatast tosilate, an anti-allergic selective Th2 cytokine inhibitor

Angioedema associated with eosinophilia (AE) is characterized by angioedema and urticaria, eosinophilia, increased body weight and a benign course without involvement of the internal organs [1, 2]. More than 60 cases of the non-episodic (N) type of AE have been reported, mostly in Asian countries; systemic administration of corticosteroids or anti-histamines was empirically chosen in most of these cases [2, 3]. We present the first published case in the English literature of successful treatment of NAE with oral suplatast tosilate, an anti-allergic selective Th2 cytokine inhibitor.

A 24-year-old Japanese woman was referred to us after developing urticarial eruptions with edema of both hands and legs. She had noticed these symptoms after being bitten by insects on both legs during a trip to Okinawa, the most southerly region of Japan. The symptoms had persisted for more than 2 weeks despite treatment with topical corticosteroids and oral fexofenadine hydrochloride (60 mg twice daily). She had previously had atopic dermatitis, which had been treated with topical steroids. During the presenting

episode she had gained 3.5 kg in weight (+8.8% of her body weight), but experienced no other symptoms. On clinical examination, we found marked edema of both hands and legs. Echocardiography showed normal cardiac function. Laboratory examinations revealed leukocytosis with massive eosinophilia (white blood cell count, $22.0 \times 10^9/L$; eosinophil count, $12.7 \times 10^9/L$) and increased serum concentrations of lactate dehydrogenase (384 IU/L (normal range, 100-210 IU/L)). No coagulation abnormalities were identified. Serum concentrations of IgG, IgM and IgA were normal. No anti-nuclear antibodies were found. She had an extraordinarily high serum concentration of chemokine (c-C motif) ligand 17 (CCL17)/thymus and activation-regulated chemokine (TARC) (53,830 pg/mL (normal range, <700 pg/mL)). We made a diagnosis of NAE and decided to start oral suplatast tosilate (100mg three times a day) and continue oral fexofenadine hydrochloride (60mg twice a day) for 152 days because the former inhibits Th2 cells [4, 5], a possible crucial player in this pathogenesis. After this change in treatment, her hand and leg edema disappeared 16 days and 23 days after visit, respectively, and her body weight returned to baseline value within 5 weeks. Her eosinophil counts returned to normal within one month, these changes correlating with a remarkable decrease in serum TARC concentrations (figure 1). The serum IgE level did not change during the course of the episode.

AE is classified into two clinical subtypes: an episodic type with recurrent episodes of fever and increased serum IgM concentrations, reported originally by Gleich [1], and a milder N type, without fever or increased serum IgM, which has largely been reported in Asian countries [2]. Since NAE reportedly abates spontaneously in most cases, whether

specific treatment is required remains controversial. Two studies have shown that various treatments, including corticosteroids and antihistamines and a wait-and-see policy make no significant difference to disease duration [3, 6]. Conversely, several recent reports have described occasional systemic involvement in patients with NAE [7, 8] that has necessitated treatment to prevent the progression of eosinophilic infiltrations. Suplatast tosilate is a selective Th2 cytokine inhibitor developed in Japan, which suppresses production of interleukin (IL)-4, IL-5 [6] and CCL17/TARC [4] through its inhibitory effect on Th2 cells, eosinophils and dendritic cells, although the details of action remain not fully elucidated. It is now widely used for the treatment of bronchial asthma, allergic rhinitis and atopic dermatitis. Because Th2 cells are believed to contribute to the pathogenesis of NAE [3, 9], this agent is a possible candidate for treating this condition as previously described in Japan [10]. In the present case, the eosinophil count increased during treatment with fexofenadine hydrochloride alone, whereas it decreased shortly after the initiation of suplatast tosilate therapy, suggesting that this combination is more effective than fexofenadine hydrochloride alone. Our case suggests that suplatast tosilate may be an effective therapeutic option for the treatment of NAE, although evaluation in case-controlled studies is required to confirm this. ■

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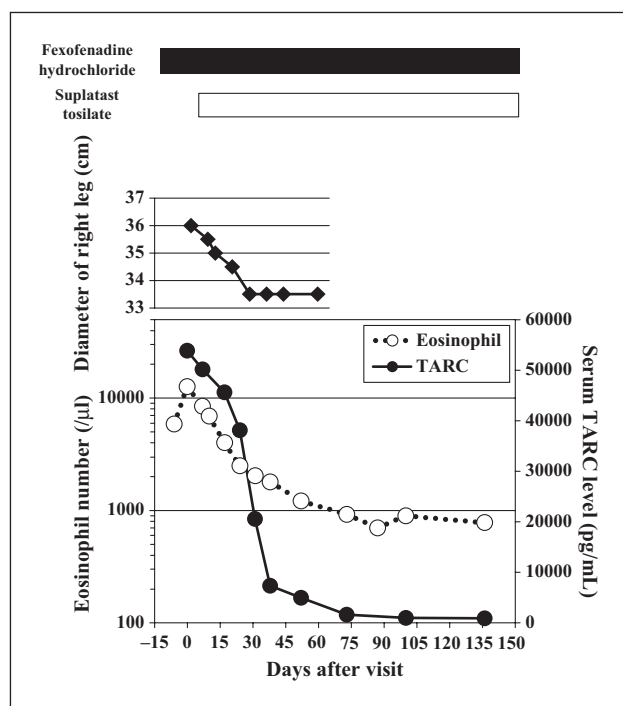


Figure 1. Evolution of the diameter of the right leg, eosinophil count and serum TARC concentrations, before and after treatment.

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Jacquet erosive diaper dermatitis: a not-so-rare syndrome

Jacquet erosive diaper dermatitis (JED), also called dermatitis syphiloides posterosiva, is typically described as a severe irritant dermatitis affecting the genital and/or the perianal region. JED usually affects infants aged >6 months but can also arise in adults with urinary and/or fecal incontinence [1, 2]. Usually JED is characterized by 2-5 mm, well-demarcated, red-purple papules with central umbilication, which can evolve into punched-out erosions and ulcers. This form of dermatitis has become relatively rare. We present another case of JED in a child affected by spina bifida. A 6-year-old male was affected by spina bifida and he was operated on at birth for spinal cord untethering. The spinal defect led to urinary and fecal incontinence. About a month before, he had developed multiple papular-erosive itchy lesions, in some cases umbilicated, localized on the glans and on the foreskin (*figures 1A-C*). The child had no other symptoms or lymphadenopathy. Skin swabs were positive for *E. coli*. A diagnosis of JED was made. Response to topical treatment with zinc oxide cream and aqueous solution of eosin 2% was poor; also treatment with topical sucralfate 4% cream three times daily for 2 months led to only partial improvement. Thus, we suggested performing a surgical circumcision of the penis. The histology of the skin showed a non-specific inflammatory infiltrate and mild epidermal hyperplasia (*figure 1D*). Two months

after the surgery a complete resolution of the lesions was obtained. We report a case of JED treated with topical zinc oxide cream, aqueous solution of eosin 2% and topical sucralfate cream which achieved only little improvement, while removing the urinary stagnation by circumcision and using proper sanitary nappy rules led to a complete healing. JED is a form of diaper dermatitis usually characterized by 2-5 mm, umbilicated or eroded papules and nodules in the genital and perianal areas. Nevertheless, JED may occur with a heterogeneous pattern, some authors suggested that JED, perianal pseudoverrucous papules and nodules (PPPN) and granuloma gluteale infantum (GGI) could be all part of the same clinical spectrum, representing the result of chronic irritant contact dermatitis [3]. Probably all three diseases represent the same entity with different names, depending on the predominance of the clinical lesion: papules/erosions (JED), papules (PPPN) and nodules (GGI). One or another of these lesions may dominate at different times in the evolution of dermatitis or may be different inflammatory responses to various stimuli [4]. Some authors have performed many biopsies of these diseases and shown a histological overlap among JED, PPPN and GGI [5]. The differential diagnosis of JED includes: fungal and bacterial infections, cutaneous Crohn's disease, Langerhans cell histiocytosis and acrodermatitis enteropathica. The pathogenesis involves several factors: urinary and fecal incontinence, infrequent diaper changing, persistence of detergent residues and use of rough toilet paper/diapers. The continued contact with urine increases the skin pH and makes it more susceptible to irritants [6], such as the fecal enzymes (proteases and lipases), which are activated by the alkaline pH [7]. The occlusion of the diaper and the friction of baby's movements perpetuate the irritation process. Some authors attribute the increase of this disease to the growing use of reusable diapers, as they are considered more natural, ecologic and economic [8]. The diagnosis of JED is based on clinical features because histology shows only a non-specific polymorphous inflammatory infiltrate and sometimes mild epidermal hyperplasia. JED is not so uncommon but its recognition is important in order to avoid inappropriate treatment. The literature documents a poor efficacy of topical treatment with antibiotics, miconazole, zinc oxide and non-steroidal anti-inflammatory drugs, while some reports described successful treatment with topical sucralfate [9, 10]. However, full recovery is achieved only by removing the main irritating factors, as our case, in which topical treatment was ineffective and a surgical therapy was necessary. In our patient the spinal defect led to chronic urinary and fecal incontinence but the circumcision reduced the amount of urinary stagnation and we obtained the complete healing of the disease. ■

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Figure 1. A-C) Multiple papular-erosive lesions, in some cases umbilicated, localized on the glans and on the foreskin; D) Histology of our case showed hyper-parakeratosis and a non-specific polymorphous inflammatory infiltrate in the interstitium.

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