

Case 4

A 12 year-old Thai girl from Bangkok

Chief complaint: A 4-year history of multiple confluent erythematous papules and plaques on right arm



Present illness:

She presented with a 4-year history of pruritic erythematous papules and on right arm which was diagnosed as chronic eczema but the lesion was not relieved by topical corticosteroids. Skin biopsied was done and showed dense lichenoid infiltration with lymphocyte exocytosis. Immunohistochemistry showed positivity of CD3, CD7, CD4, CD8, and Ki-67. She was provisional diagnosed as solitary mycosis fungoides and treated with 29 sessions of local NBUVB phototherapy and topical 0.25% desoximetasone. The lesion was flatten but 3 months after cessation of phototherapy, the rash was relapsed.

Past history:

She has no underlying disease.

Family history:

There was no family history of cancer or similar lesion.

Physical examination:

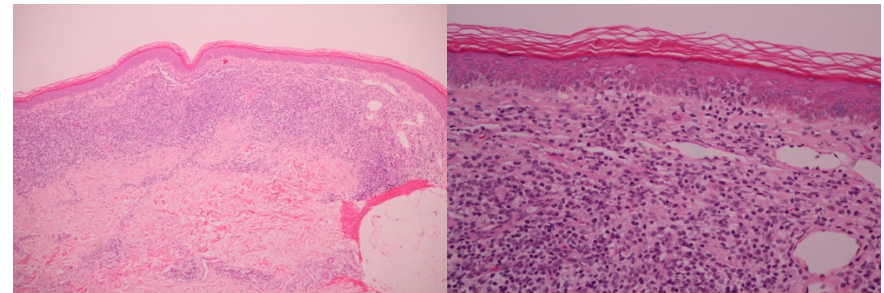
Other systemic examination revealed no abnormality.

Dermatological examination:

Multiple confluent non-blanchable erythematous papules and plaques on posterior aspect of right arm, 3 cm above elbow

Histopathology: (S16-31866, S17-35099, Right arm)

- Dense diffuse inflammatory cells infiltration in the upper dermis
- The inflammatory cells infiltration composed of lymphocytes admixed with some plasma cells and prominent thick-walled blood vessels
- Exocytosis of some lymphocytes within lower epidermis



Immunohistochemistry: (S18-024773, Right arm)

- Positive: CD3, CD7, CD4, CD8, CD20 of lymphocytes
- Positive: D2-40 and CD34 at vascular channels
- Positive: Ki-67 (20%-30%)

TCRG gene clonality assay:

- Presence of polyclonal TCRG gene rearrangements

Laboratory investigations:

- CBC: Hb 12 g/dL, Hct 37%, Plt 413,000 /mm³, WBC 11,670 /mm³ (N 69%, L 24%, M 4%, E 2%, B 1%)
- LDH: 185 U/L (125-220 U/L)
- AST/ALT: 18/14 U/L

- BUN/Cr: 10/0.55 mg/dl

Diagnosis: Acral pseudolymphomatous angiokeratoma of children

Treatment:

- Intralesional triamcinolone 10 mg/ml
- Local UVA phototherapy once weekly start dose 10 J/cm², increment 5J/treatment, fixed dose 50 J/cm²

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Discussion:

Acral Pseudolymphomatous Angiokeratoma of Children or APACHE was first described in 1988 by Ramsay, et al.¹⁻³ It is a rare, benign cutaneous disease with unknown etiology, characterized by multiple, asymptomatic erythematous-violaceous papules and nodules, usually located unilaterally on the acral distribution, mostly affecting children aged between 2 to 13 years.²⁻⁴ However, cases with non-acral areas, solitary or linear lesion⁵, and also cases occurring in adults has been reported, leading to different terms of the disease such as papular angiolympoid hyperplasia, acral angiokeratoma-like pseudolymphoma, pseudolymphomatous angiokeratoma.^{3,4} Nowadays approximately 25 cases has been reported in the literature.²

In the past, APACHE was described as a vascular malformation or tumor of vascular nature.³ In present, histopathological study, including immunohistochemistry reveals a dense subepidermal lymphocytic infiltration admixed with numerous histiocytes, plasma cells and eosinophils in some cases.^{6,7} Prominent blood vessels with plump endothelium was also seen, included forming of lymphoid follicles in some cases.^{1,3,5} As the feature of dense lymphocytic infiltration, it could be a sign of pseudolymphoma while others support the lymphoid hyperplasia entity.³ Immunohistochemistry demonstrated the admixture of B- (CD20+) and T- (CD3+) lymphocytes with variety in proportion.^{1,3} CD8+ and CD4+ T-cell also have been report with variety in proportion, even equal in number.^{3,6,7} Antibodies against kappa or lambda light chains of B cells showed equal in number.⁷

APACHE also shows a vascular component, immunohistochemistry has shown the expression of CD34 and podoplanin (D2-40) suggested a vascular malformation in nature.^{3,8} However, there was a literature reported the expression of Wilms tumor-1 (WT-1) with lack of D2-40 by the vascular component of the case, explained a proliferative endothelial nature rather than malformation.³ By the way, APACHE is classified as a distinct type of pseudolymphoma at present.^{2,3,9} However, the exact nature of this disease remains undetermined.⁷

The differentiation of cutaneous pseudolymphoma from malignant lymphoma is the one of the most challenging problems in dermatopathology.⁹ The band-like cell infiltration pattern was similar to histopathology of mycosis fungoides (MF), the lack of or minimal epidermotrophism could differentiate cutaneous lymphoma from MF.^{9,10} Moreover, the immunohistochemical study and demonstration of clonal T-cell rearrangements and aberrant T-cell phenotype can be used to distinguish APACHE from MF and also cutaneous lymphoma.⁹ So, further investigations should be performed to exclude malignant cell populations.^{2,9}

Many modalities were reported as a treatment of APACHE, included surgical excision, curettage, shave excision followed by electrocautery, intralesional triamcinolone, cryotherapy, and radiotherapy.^{2,4} However, only surgical excision, curettage, and shave excision followed by electrocautery have been performed with resulting in disappearance of the lesion without recurrence.⁴

Our patient is a 2 year-old girl presented with 4 years history of multiple confluent non-blanchable erythematous papules and plaques on posterior aspect of right arm, previously diagnosed as chronic eczema and then solitary mycosis fungoides after skin biopsied. The lesion recurred after cessation of local NBUBV phototherapy. Skin biopsy was done again and showed lichenoid infiltration in the upper dermis, exocytosis of lymphocytes and atypical cells with immunohistochemistry staining positivity of CD20, CD34, and D2-40. APACHE was diagnosed. She has been treated with local UVA

phototherapy, one of the first line therapy of pseudomycosis fungoides¹¹, and intralesional corticosteroids. After 31 sessions of local UVA phototherapy and 3 treatments of intralesional corticosteroids the lesion was significantly flatten but not completely cured. The phototherapy was continued and 3-month follow-up was scheduled.

References:

1. Ramsay B, Dahl MC, Malcolm AJ, Wilson-Jones E. Acral pseudolymphomatous angiokeratoma of children. *Arch Dermatol.* 1990;126:1524-5.
2. Lessa PP, Jorge JC, Ferreira FR, Lira ML, Mandelbaum SH. Acral pseudolymphomatous angiokeratoma: case report and literature review. *An Bras Dermatol.* 2013;88:39-43.
3. Fernandez-Flores A, Fierro S, Larralde M. Expression of WT-1 by the vascular component of acral pseudolymphomatous angiokeratoma of children. *J Cutan Pathol.* 2015;42:50-5.
4. Kim Y, Dawes-Higgs E, Mann S, Cook DK. Acral pseudolymphomatous angiokeratoma of children (APACHE). *Australas J Dermatol.* 2005;46:177-80.
5. Kiyohara T, Kumakiri M, Kawasaki T, Takeuchi A, Kuwahara H, Ueda T. Linear acral pseudolymphomatous angiokeratoma of children (APACHE): further evidence that APACHE is a cutaneous pseudolymphoma. *J Am Acad Dermatol.* 2003;48:S15-7.
6. Okuyama R, Masu T, Mizuashi M, Watanabe M, Tagami H, Aiba S. Pseudolymphomatous angiokeratoma: report of three cases and an immunohistological study. *Clin Exp Dermatol.* 2009;34:161-5.
7. Hagari Y, Hagari S, Kambe N, Kawaguchi T, Nakamoto S, Mihara M. Acral pseudolymphomatous angiokeratoma of children: immunohistochemical and clonal analyses of the infiltrating cells. *J Cutan Pathol.* 2002;29:313-8.
8. Tokuda Y, Arakura F, Murata H, Koga H, Kawachi S, Nakazawa K. Acral pseudolymphomatous angiokeratoma of children: a case report with immunohistochemical study of antipodoplanin antigen. *Am J Dermatopathol.* 2012;34:e128-32.
9. Lee MW, Lee DK, Choi JH, Moon KC, Koh JK. Clinicopathologic study of cutaneous pseudolymphomas. *J Dermatol.* 2005;32:594-601.
10. Heng YK, Koh MJ, Giam YC, Tang MB, Chong WS, Tan SH. Pediatric mycosis fungoides in Singapore: a series of 46 children. *Pediatr Dermatol.* 2014;31:477-82.
11. Woos GS. 146: Inflammatory diseases that simulate lymphomas: Cutaneous pseudolymphomas. In: Goldsmith LA, Katz SI, Gilchrist BA, Paller AS, Leffell DJ, Wolff K, editors. *Fitzpatrick's dermatology in general medicine*, vol. 2, 8th edition. Philadelphia: The McGraw-Hill companies; 2012. p. 1777-8.