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Authors

Yeo, YW
Oon, HH
Lee, JS
et al.

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Case presentation

Papular angiolymphoid hyperplasia and lymphoplasmacytic plaque: a clinical and histological spectrum

YW Yeo¹, HH Oon², JS Lee², JY Pan², YJ Mok², SK Ng²

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¹Department of Dermatology, Singapore General Hospital, Singapore

²National Skin Centre, Singapore

Correspondence:

Yi Wei Yeo
Singapore General Hospital
Outram Road
Singapore 169608, Republic of Singapore
Tel: 65-63266866
Fax: 63214378
Email: kirstenyeo@gmail.com

Abstract

Acral pseudolymphomatous angiokeratoma of children (APACHE) is a rare form of cutaneous pseudolymphoma characterized by angiomatous papules with a predilection for the acral regions of children. Classically, a dense dermal lymphocytic infiltrate composed of both T and B cells is seen in histological specimens, together with prominent vessels lined by plump endothelial cells. Increasing evidence suggests that this condition is neither necessarily acral, pseudolymphomatous, nor angiokeratomatous. It may not always be a pediatric disease. Therefore, the correctness of its nomenclature has been questioned. Herein, we report three cases whose clinical and histological features were consistent with the diagnosis of APACHE. To our knowledge, this is the first report of APACHE from Southeast Asia. We also discuss why we believe “APACHE” to be a misnomer and support “papular angiolymphoid hyperplasia” as a more accurate and encompassing term. In addition, we illustrate a case with significant overlapping features with lymphoplasmacytic plaque in children, suggesting that both entities may exist on a clinical and histological spectrum.

Keywords: angiolymphoid hyperplasia, pseudolymphoma, angiokeratoma

Background

Acral pseudolymphomatous angiokeratoma of children (APACHE) is a rare clinical entity characterized by angiomatous papules with a predilection for the acral regions in children [1]. Histologically, a dense mixed dermal infiltrate is seen, together with prominent vessels lined by plump endothelial cells. There are at least 30 reported cases in the English literature to date, mostly arising from the Caucasian or Japanese population.

Herein we report three patients from Singapore in whom clinical and histological features were consistent with APACHE. To our knowledge, this is the first report of APACHE from Southeast Asia. We also discuss why we believe the name to be a misnomer and discuss its similarities to lymphoplasmacytic plaque in children.

Case synopsis

Case 1

A 22-year-old woman presented with a ten-year history of asymptomatic erythematous papules over the left forearm. There was no history of preceding trauma or insect bites and the lesions were non-progressive. She had been treated with topical and intralesional corticosteroids unsuccessfully.

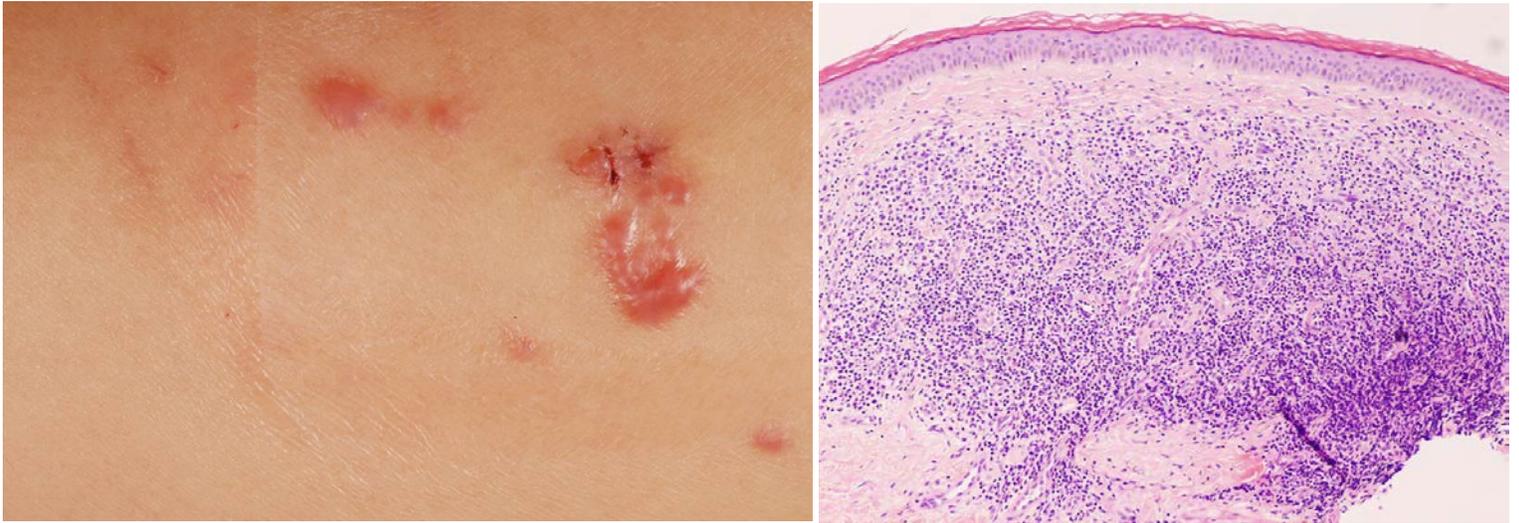


Figure 1. Coalescing erythematous papules seen on the lateral aspect of the left forearm. **Figure 2.** There is a dense upper dermal infiltrate of mainly lymphocytes, some plasma cells and occasional eosinophils. Dilated dermal blood vessels with prominent endothelial cells are present within. There is a grenz zone. (haematoxylin and eosin, original magnification x 40)

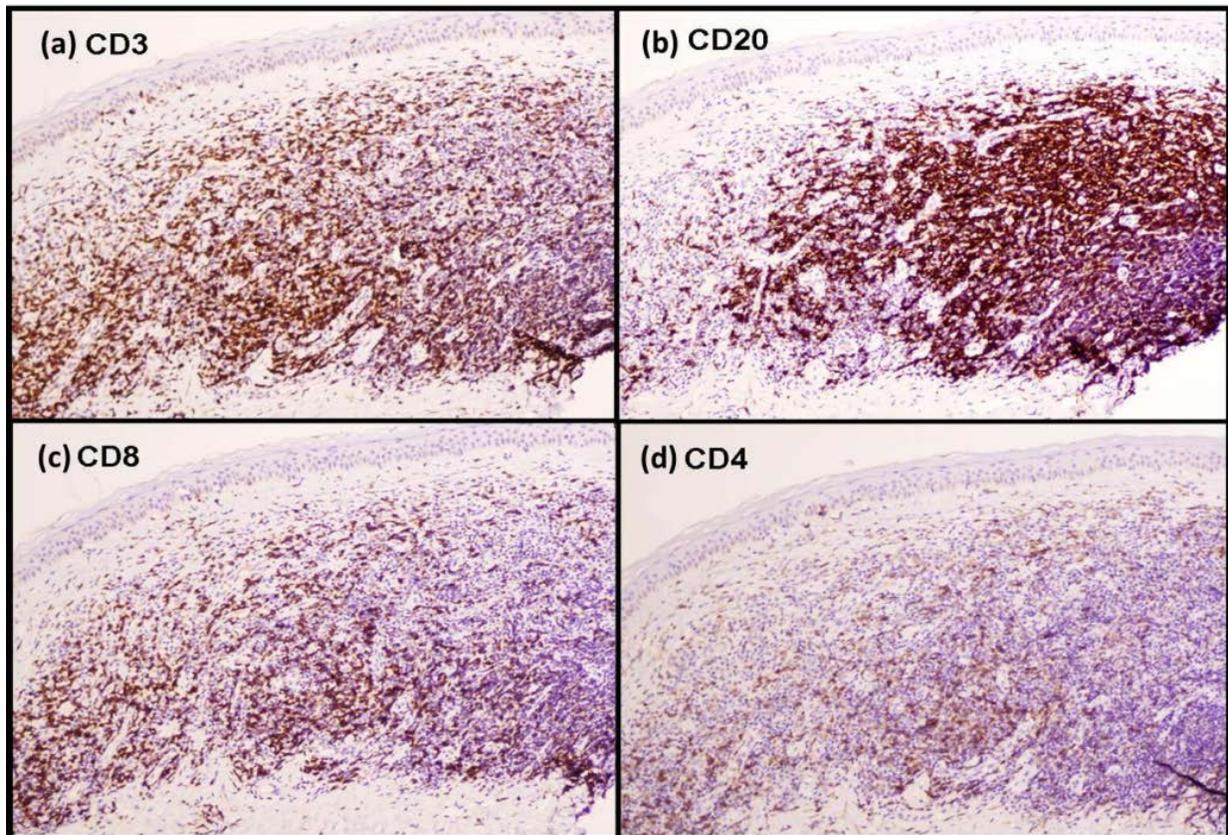


Figure 3. There is a mixture of T cells (a, CD3), and B cells (b, CD20) within the infiltrate. CD8 (c) and CD4 T cells (d) are found in relatively equal proportions. (Immunoperoxidase stain, original magnification x 100)

Examination revealed coalescing erythematous papules over the left lateral forearm. Biopsy revealed a dome-shaped lesion with loss of rete ridges and an underlying Grenz zone. There was a dense upper dermal infiltrate of lymphocytes and plasma cells, associated with a proliferation of capillaries with prominent endothelial cells. The lymphocytes were typical, with small

hyperchromatic nuclei and minimal cytoplasm. Immunohistochemistry showed a mixed infiltrate of T and B cells. CD8 and CD4 T cells were found in relatively equal proportions. There was no light chain restriction.

The clinical and histological findings were consistent with a diagnosis of APACHE. Its benign nature was communicated to the patient but she was keen for excision of the lesion.

Case 2

A 10-year-old woman presented with an asymptomatic plaque over the left elbow for five years, with no preceding history of trauma or insect bites. Clinically, there were hyperpigmented papules coalescing into a well-defined plaque with an erythematous center.

Biopsy showed a dense nodular infiltrate in the upper to mid dermis composed of lymphocytes, histiocytes, and plasma cells admixed with prominent blood vessels. Basal vacuolar alteration with some apoptotic keratinocytes was seen at the dermo-epidermal junction. Immunohistochemistry revealed a mixture of T cells (70%) and B cells (30%). There was no light chain restriction.

A diagnosis of APACHE was made. She was treated with topical and intralesional corticosteroids with initial improvement, but the plaque recurred and was subsequently excised.

Case 3



Figure 4. An erythematous plaque with a keratotic surface in a linear configuration flanked by one papule on either side

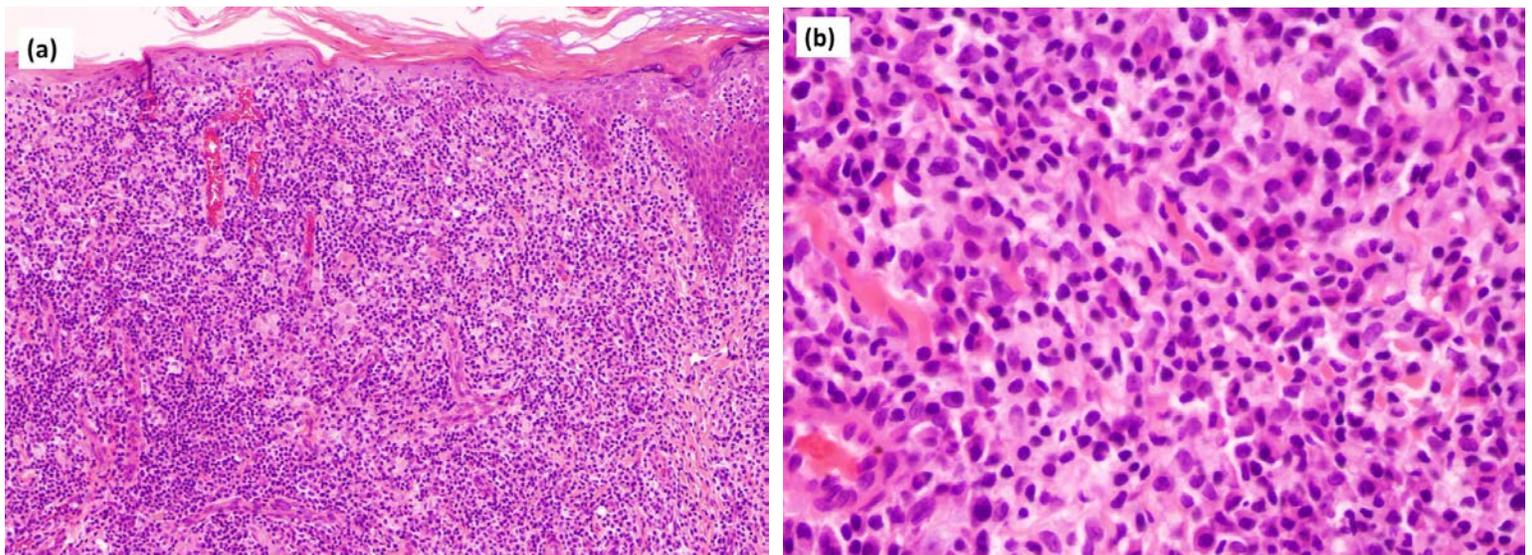


Figure 5. (a): A dense upper to mid-dermal diffuse infiltrate of lymphocytes, histiocytes and plasma cells with increased numbers of small dermal blood vessels. (haematoxylin and eosin, original magnification x 100); (b) A significant number of plasma cells was noted in the infiltrate (haematoxylin and eosin, original magnification x 200)

A 6-year-old boy presented with an asymptomatic right ankle rash for eighteen months without prior trauma. Examination showed an erythematous plaque with a keratotic surface in a linear configuration flanked by one papule on either side over the right medial ankle.

Biopsy showed lymphocytes effacing the dermoepidermal junction and a dense upper to mid-dermal diffuse infiltrate of lymphocytes, histiocytes, and plasma cells admixed with increased numbers of small dermal blood vessels. A mid and deep perivascular infiltrate of mainly plasma cells and some lymphocytes was also seen. Immunohistochemistry showed equal numbers of T and B cells with a CD4:CD8 ratio of 1:1. A germinal center featuring a follicular dendritic meshwork on the CD21 stain was noted. No light chain restriction was seen.

A diagnosis of APACHE was made and he opted for treatment with clobetasol cream in view of its benign nature.

Discussion

APACHE was first reported by Ramsay [1] in 1983 as a unilateral eruption of angiomatous papules on acral areas of young children, resembling angiokeratomas clinically. Histopathologically, there was a striking upper dermal lymphohistiocytic infiltrate simulating a pseudolymphoma, together with prominent thickened capillaries. Running a benign course, he suggested that they may represent a vascular nevus. APACHE was subsequently classified as a pseudolymphoma by Kaddu [2] in 1994 based on a dense mixed T and B cell infiltrate and he proposed the term “small papular pseudolymphoma”.

Indeed, recent evidence has shown that this entity is neither necessarily acral, pseudolymphomatous, angiokeratomatous nor confined to children. As such, there has been controversy over the nomenclature.

In terms of location, reports have confirmed lesions at non-acral sites including the back [2,3], shin [10], arm [11], thigh [13,14], and even the genitals [3]. Although classically multiple and papular, alternative morphologies including a single plaque have been described [8,10].

Although termed pseudolymphomatous, APACHE differs from conventional pseudolymphomas. Clinically, cutaneous pseudolymphomas commonly occur on the face and acral lesions are infrequent. They are also mostly seen in adults rather than children. Histologically, there are also subtle differences. A superficial and deep infiltrate is seen in typical B cell pseudolymphomas, whereas the infiltrate in APACHE is predominantly upper dermal.

Although APACHE may bear clinical resemblance to angiokeratomas, its histology does not, as angiokeratomas are characterized by dilated vascular channels lined by a layer of flattened endothelial cells within an expanded papillary dermis; they lack the dense inflammatory infiltrate seen in APACHE.

Finally, there are at least nine reports of APACHE arising in adults [2,5,7,9,12-14,16], suggesting that this disease is not confined to children.

Interestingly, APACHE shares some histological features of angiolymphoid hyperplasia with eosinophilia (ALHE). Both show a mixed cellular infiltrate with thickened vessels lined by plump endothelial cells. However, APACHE may contain other cell types such as plasma cells and multinucleated giant cells; eosinophils may not be present. The infiltrate in APACHE tends to be upper dermal whereas deeper dermal involvement is seen in ALHE. Although both have prominent dermal blood vessels, endothelial cells in ALHE are comparatively plumper and often exhibit “hobnailing”. Clinically, ALHE is also seen in adults with a head and neck predilection [14].

Having considered the above reasons why ‘APACHE’ may not be an accurate description of the condition, as well as the prominent histological similarities it shares with ALHE, we support the proposition by Chedraoui [14] that ‘papular angiolymphoid hyperplasia’ would be a more appropriate term. This overlap in clinical features was also previously recognized by Burrall and Barr [17] who reported three unusual cases of ALHE with its characteristic vascular proliferation of plump endothelial cells but an without its typical infiltrate and suggested that the common denominator of these “inflammatory angiomatoses” is that of the plump “histiocytoid” endothelial cell.

Immunohistochemical analyses have been used to better characterize the precise nature of the lymphocytic infiltrate in APACHE. Studies have consistently shown a mixture of T and B cells [1, 4-16], with the former usually being the dominant cell type. This would comprise near equal numbers of CD4+ and CD8+ cells. However, a case reported by Okuyama [13], observed a B cell dominant infiltrate, which may point to a spectrum, rather than a single pathology.

Clonality studies are also important in excluding cutaneous lymphoma. These studies have repeatedly demonstrated polyclonality in APACHE [4-9,12-13]. However, a case reported by Lee [10] demonstrated a positive immunoglobulin heavy chain assay on duplex polymerase chain reaction. The authors therefore highlighted that the generally held belief of APACHE's benign nature could be premature. Nevertheless, there have been no reports of malignant transformation in the literature.

Recently, entities such as "lymphoplasmacytic plaque in children"[21] and "T-cell rich angiomatoid polypoid pseudolymphoma" (TRAPP) [22] have been described, which bear similar clinical and histological features with APACHE.

"Isolated benign cutaneous plasmacytosis in children" was first described by Gilliam in 2009 [18] based on two children with localized erythematous papules on the legs resembling APACHE. However, histology showed a dermal infiltrate composed predominantly of polyclonal plasma cells. A similarly benign course was noted. It was renamed "pretibial lymphoplasmacytic plaque in children" by Fried [19], but subsequent reports revealed that lesions were not necessarily pretibial and the term "lymphoplasmacytic plaque in children" [21] was proposed. Proponents of this entity suggest that there are sufficient clinicopathological features to differentiate this from APACHE. Moulouquet, however, reported a case with significantly overlapping features [20]. He suggested that APACHE and lymphoplasmacytic plaque may be part of a spectrum of pseudolymphomas.

Indeed, considerable numbers of plasma cells are not infrequently described in APACHE [6,10,11,15]. Furthermore, although lymphoplasmacytic plaque is described as a solitary plaque compared to multiple papules in APACHE, the reported morphology in APACHE is also variable.

Our third case illustrates that distinction between these two entities can be difficult. He presented with an erythematous linear plaque resembling lymphoplasmacytic plaque. However, two flanking papules were noted. Histologically, numerous plasma cells were seen, together with increased numbers of small blood vessels. This considerable clinicopathological overlap further suggests that APACHE and lymphoplasmacytic plaque in children could well be a spectrum of a single entity.

The etiology of APACHE has remained elusive. Postulated etiologies include mechanical trauma or a hypersensitivity to insect bites, in view of its acral location and reports of a linear configuration. It has been suggested that this initial insult results in a reactive angiolymphoid proliferation which self-perpetuates [3].

Definitive treatment appears to be that of complete excision with no recurrence at up to 15 years of follow up [1, 3]. Topical and intralesional steroids have yielded only temporary improvement [4,5,10,12-14], whereas recurrence was noted after carbon dioxide laser [10]. Left untouched, the lesions generally persist but remain non-progressive [1].

In conclusion, APACHE, more appropriately termed "papular angiolymphoid hyperplasia" is a form of pseudolymphoma, which appears to take a benign course. The significant clinical and histological overlap illustrated in our third case, and that by Moulouquet [20], suggest that both conditions could well be part of a spectrum. However, further reports of newer entities such as "lymphoplasmacytic plaque in children" are needed to clarify this.

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