Granulomatous pigmented purpuric dermatosis with localization of *Propionibacterium acnes* in granulomas

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Granulomatous pigmented purpuric dermatosis (GPPD) is a rare variant of pigmented purpuric dermatoses [1]. Herein, we report a case of GPPD with localization of *Propionibacterium acnes* (*P. acnes*) in the granuloma, suggesting a sarcoidosis-like aetiology of GPPD.

A 60-year-old woman consulted our hospital for a rash on her extremities. Purpura had appeared on her lower legs two years before her initial visit to a previous hospital. The lesions were refractory to topical steroids, and she was referred to our hospital. A physical examination revealed purpuric plaques on her extremities (Fig. 1 a). Biopsy specimens from the purpuric lesions on her leg and arm showed epithelioid granuloma with extravasation of red blood cells in the superficial dermis (Fig. 1 c). Red blood cell extravasation was particularly apparent surrounding granulomas involving capillaries (Fig. 1 d). Biopsy specimens were negative for Fite's acid-fast stain, Grocott stain and periodic acid-Schiff (PAS) stain. The granulomas did not appear to be associated with the hair follicles histopathologically. No necrobiosis was found in the skin lesion. No apparent abnormality was found on a chest X-ray or on head, neck, chest and abdominal CT scan images. The acetylcholine esterase test and beta-D glucan assay using the patient's serum and the interferon-gamma release assay using the patient's blood were negative. We suspected cutaneous sarcoidosis, and we performed photodynamic therapy on the eruption. The rash resolved after treatment.

Five years later, exanthemas recurred on the patient's extremities (Fig. 1 b). Skin biopsy specimens from exanthemas on both the upper and lower limbs showed the same findings that were observed in previous biopsies (Fig. 1 e, f). Immunohistochemistry analysis with *P. acnes*-specific monoclonal antibodies (PAB antibodies), which specifically react with the *P. acnes* cell membrane [2], revealed small round bodies within the granulomas, which were assumed to be *P. acnes* (Fig. 1 g, h). The PAB antibody used in the present study was previously proven to react with the *P. acnes*-specific epitope of lipoteichoic acid. [2] In addition, the specificity and sensitivity of the antibody were confirmed previously. [2, 3] The patient refused our proposal of oral antibiotics, and topical clindamycin gel was not effective for the exanthema.

To our knowledge, this is the first case report of GPPD with localization of *P. acnes* in the granuloma. In 2011, Bachmeyer et al. reported a case of systemic sarcoidosis with a purpuric skin manifestation that mimicked GPPD [4]. It is difficult to distinguish cutaneous sarcoidosis with pigmented purpuric lesions from GPPD based on clinical and pathological features, and no clear criteria exist that can distinguish GPPD from cutaneous sarcoidosis with purpuric manifestations if the patient lacks other organ involvement [5]. Furthermore, systemic sarcoidosis with asymptomatic lesions of other organs could be misdiagnosed as GPPD.

P. acnes localization in granulomas is known to participate in the pathogenesis of

sarcoidosis [2, 6]. A recent meta-analysis of 11 studies revealed a significant association between sarcoidosis and the presence of *P. acnes*, and the detection of *P. acnes* by immunohistochemistry and Western blotting analysis was remarkably specific for sarcoidosis [7]. Therefore, in this case, the localization of *P. acnes* in granulomas suggests a role of sarcoid reactions in the development of GPPD lesions.

To the best of our knowledge, positive cultures of *P. acnes* from skin lesions of cutaneous sarcoidosis have never reported in the literature. Thus, to date, there is only indirect evidence of the pathogenic role of *P. acnes* infection in cutaneous sarcoidosis. There is only one case report of cutaneous sarcoidosis associated with *P. acnes*. The previous case was a 25-year-old woman with livedoid sarcoidosis on her back and lower legs, and the authors considered that specific staining for *P. acnes* within granulomas around the vessels might suggest haematogenous dissemination of *P. acnes*. Because our case had marked vascular involvement and was resistant to topical clindamycin gel, the *P. acnes* in the granuloma of our case was also presumed to be disseminated haematogenously rather than transcutaneously.

To detect the localization of *P. acnes* in GPPD lesions, immunohistochemistry analysis with PAB antibodies may be a powerful tool. Further research including more GPPD patients and sarcoidosis patients is needed to clarify the association of *P. acnes* with GPPD and cutaneous sarcoidosis with pigmented purpuric lesions.

References

1. Battle LR, Shalin SC, Gao L. Granulomatous pigmented purpuric dermatosis. *Clin Exp Dermatol* 2015; 40: 387–90.

2. Negi M, Takemura T, Guzman J, et al. Localization of Propionibacterium acnes in granulomas supports a possible etiologic link between sarcoidosis and the bacterium. *Mod Pathol* 2012; 25: 1284–97.

3. Suzuki Y, Uchida K, Takemura T, et al. Propionibacterium acnes-derived insoluble immune complexes in sinus macrophages of lymph nodes affected by sarcoidosis. *PLoS One* 2018; 13: e0192408.

4. Bachmeyer C, Eguia B, Callard P, Moguelet P. Purpuric papulonodular sarcoidosis mimicking granulomatous pigmented purpura. *Eur J Dermatol* 2011; 21: 110–1.

5. Sezer E, Yalçın Ö, Erkek E, Şahin S. Pigmented purpuric dermatosis-like sarcoidosis. *J Dermatol* 2015; 42: 629–31.

6. Asahina A, Miura K, Saito I, Oshikata C, Ishii N, Eishi Y. Cutaneous sarcoidosis with livedoid lesions: evidence of the involvement of Propionibacterium acnes. *J Dermatol* 2013; 40: 501–2.

7. Zhou Y, Hu Y, Li H. Role of propionibacterium acnes in sarcoidosis: a meta-analysis. *Sarcoidosis Vasc Diffuse Lung Dis* 2013; 30: 262-7.

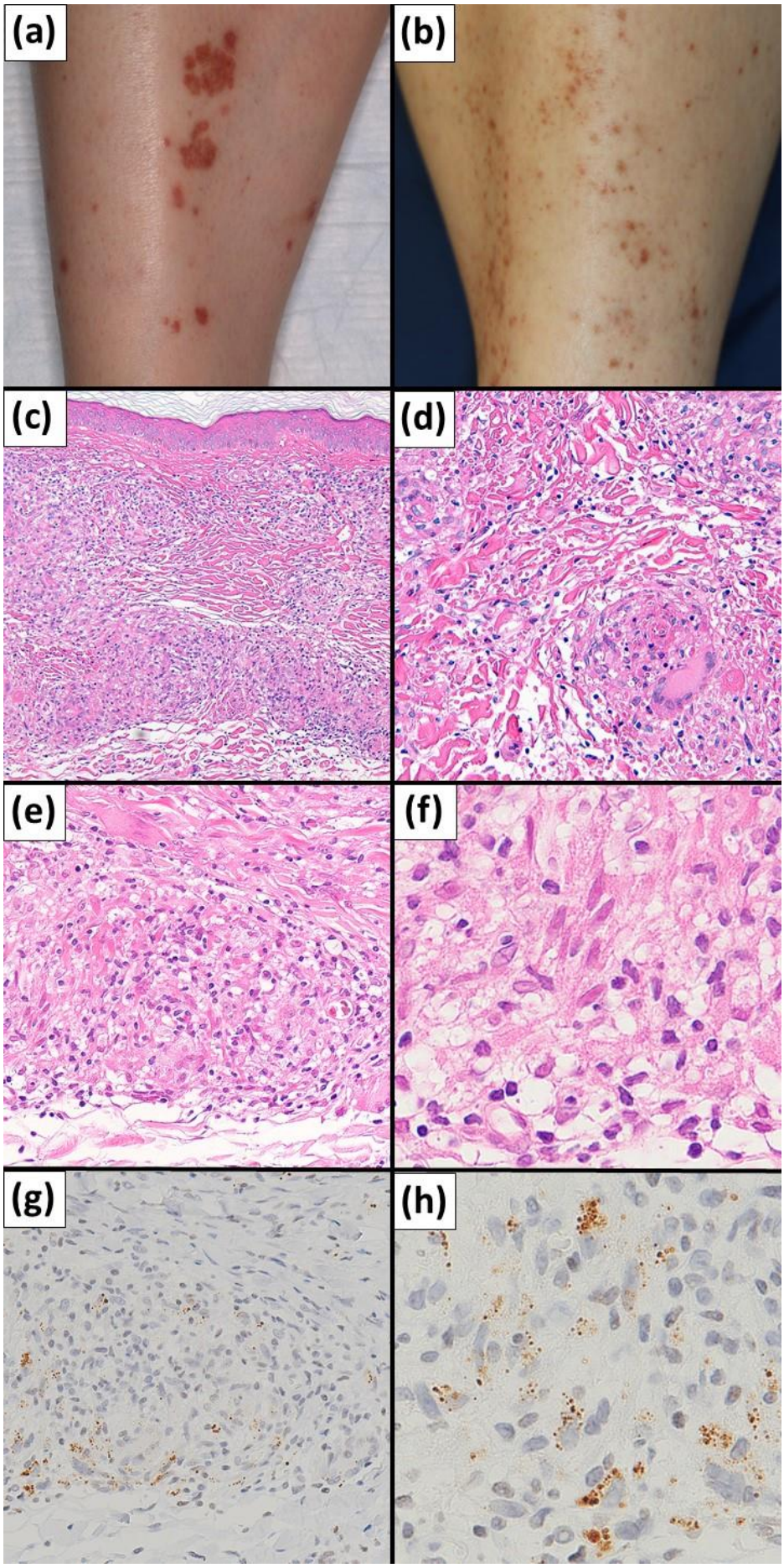
(a)
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Figure legend

Figure 1

(a) Purpuric plaques on the lower leg at the initial hospital visit.

(b) Recurrent punctate purpura on the lower leg.

(c, d) Pathological findings from an exanthema on the leg at the initial hospital visit. (c) A biopsy specimen taken from a recurrent exanthema on the arm showed epithelioid granuloma in the superficial dermis. (d) Involvement of the dermal capillaries and extravasation of red blood cells are also demonstrated (haematoxylin-eosin, original magnification ×100 (c) and ×200 (d)).

(e, f) Pathological findings from a recurrent exanthema on the arm showed an epithelioid granuloma with giant cells (haematoxylin-eosin, original magnification 400× (e) and 1000× (f)).

(g, h) Immunohistochemistry of the biopsy specimen performed using PAB antibodies. Small, round bodies within the sarcoid granuloma were assumed to represent *P. acnes* (original magnification 400× (g) and 1000× (h)).