Cutaneous lesions as a clue for diagnosing systemic sarcoidosis.

Atchareeya Sujichanthararat MD,

Padcha Pongcharoen MD.

ABSTRACT:

SUJICHANTHARARAT A, PONGCHAROEN P. CUTANEOUS LESIONS AS A CLUE FOR DIAGNOSING SYSTEMIC SARCOIDOSIS. THAI J DERMATOL 2019; 35: 206-211.

DIVISION OF DERMATOLOGY, DEPARTMENT OF INTERNAL MEDICINE, FACULTY OF MEDICINE, THAMMASAT UNIVERSITY, PATHUMTHANI, THAILAND.

Sarcoidosis is a granulomatous disorder of unknown cause that usually involves multiple organs in which skin lesion could be one of the manifestations and may be the first clinical sign of the disease. Diagnosing sarcoidosis is quite challenging in Thailand due to our unfamiliarity with it.

We reported a male patient with asymptomatic rash in which skin biopsy revealed naked granuloma with no evidence of infection. After reviewing his previous history of asymptomatic abnormal chest radiograph which was diagnosed smear-negative pulmonary tuberculosis with complete nine-month course of anti-tuberculosis medications. He was performed bronchoscopy with tissue biopsy and revealed non-caseating granuloma with no evidence of infection. All of these had led to the diagnosis of systemic sarcoidosis.

Key words: sarcoidosis, granulomatous disorder

From: Division of dermatology, Department of Medicine, Faculty of Medicine, Thammasat University, Pathumthani, Thailand

Corresponding author: Padcha Pongcharoen MD, email: padchapong@hotmail.com

Received: 2 April 2019 Revised: 23 September 2019 Accepted: 6 November 2019

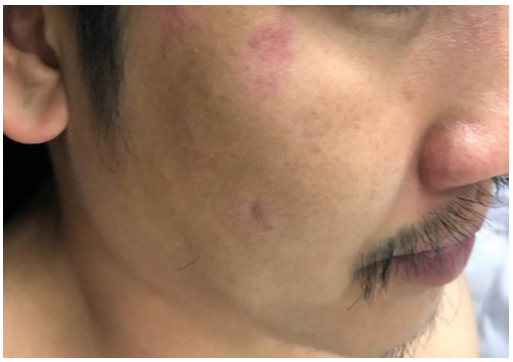
Introduction

Sarcoidosis is a granulomatous disorder that involves multiple organs, including skin[1]. The etiology is unclear, but it is likely that a heterogenous set of triggers leads to the formation of non-caseating granulomas in genetically susceptible individuals[2]. Cutaneous sarcoidosis occurs in up to one third of patients with systemic sarcoidosis. Recognition of cutaneous lesion is important because it provides a visible clue to the diagnosis.

Sarcoidosis is considered to be rare in Southeast Asia but may be underestimated because of the lack of awareness of its existence[3]. Diagnosis of sarcoidosis is based on compatible clinical, radiographic and histological findings[2,4]. A lot of investigations need to be performed to rule excluded other possible causes that can mimic sarcoidosis, especially in endemic area of tuberculosis like Thailand.

Case report

A 35-year-old man who was otherwise healthy presented to the dermatology clinic with a three-year history of asymptomatic erythematous rashes over his face and body. He denied history of prolonged fever, night sweat or weight loss. Six years ago, he was diagnosed with smear-negative pulmonary tuberculosis from abnormal chest radiograph and chest computed tomography without any chest symptom. Bronchial biopsy revealed non-caseating granulomas with negative for Acid Fast bacilli (AFB), Gomori Methenamine-Silver (GMS) and Periodic Acid Schiff (PAS) stains. He completed a nine-month course of anti-tuberculosis medications (2IRZE+7IR). No family members experienced similar skin lesions.



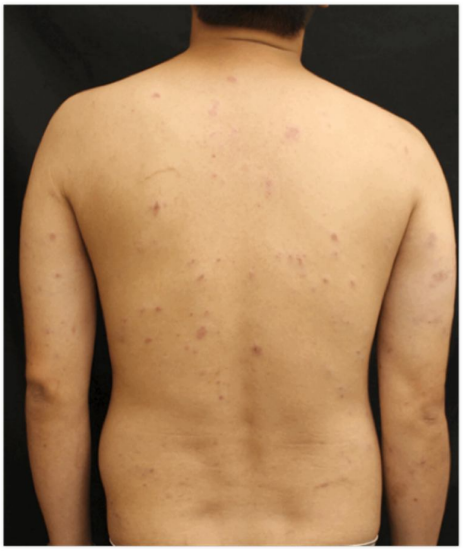


Figure 1 Multiple erythematous patches and plaques with telangiectasia over face and body.

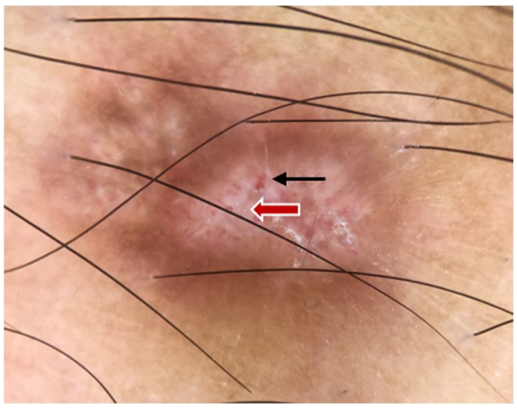


Figure 2 Dermoscopy revealed scar-like hypopigmentation (red arrow) and telangiectasias (black arrow).

Physical examination revealed clubbing of all finger and toe nails and increased splenic dullness. Ophthalmologic examination revealed normal. Skin examination found multiple erythematous patches and plaques with prominent telangiectasia on face, trunk and all extremities (Figure 1). Dermoscopy revealed scar-like hypopigmentation with telangiectasias on each lesion (Figure 2). A skin biopsy was performed which tissue section revealed non-necrotizing granulomatous dermatitis in upper and lower dermis with no nerve and appendages involvement (Figure 3). The granulomatous infections were excluded by negative for AFB, modified-AFB, Wade-fite and GMS stainings, and also negative for fungal culture, mycobacterial culture and polymerase chain reaction (PCR) for mycobacterium. No polarizable material was seen. Tuberculin skin test was negative.

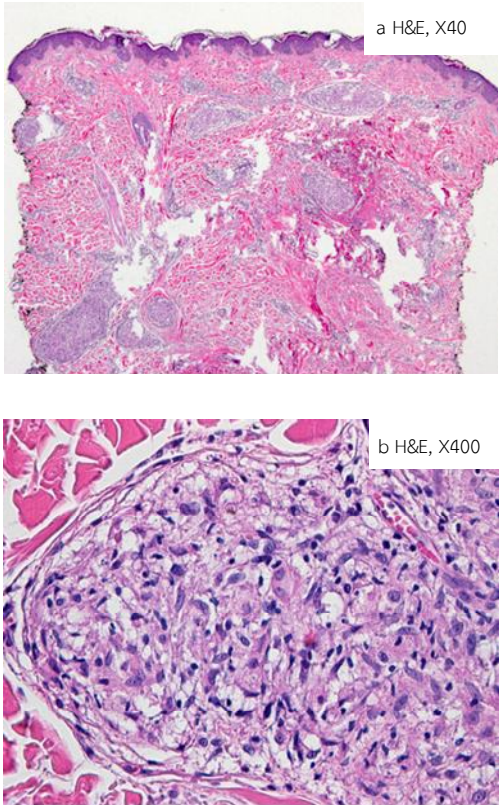


Figure 3 Skin histopathology revealed granulomatous inflammation in upper and lower dermis with few surrounding lymphocytes which compatible with “naked granuloma”.
(a) H&E, X40, (b) H&E, X400

The complete blood count, biochemical blood tests and electrolytes including calcium were within normal range. Chest radiograph showed reticulonodular opacity in both lungs,

more pronounced on right upper lung (RUL) zone and increased opacity of bilateral perihilar regions. High-resolution computed tomography (HRCT) found conglomerated masses at right hilar and right upper lung with multiple scattering nodules at both lungs, size up to 1.2 cm and multiple calcified nodes at para-aortic, bilateral paratracheal and bilateral hilar nodes size up to 1.1x1.3 cm. Pulmonary function test was compatible with mild restrictive pattern.

Once sarcoidosis was suspected, the patient was performed re-bronchoscopy. Transbronchial biopsy of right upper lung tissue revealed non-caseating granuloma with negative for AFB, GMS, PAS stains. Fungal and mycobacterial cultures were negative. Polymerase chain reaction (PCR) for tuberculosis was undetectable. The CD4/CD8 ratio in bronchoalveolar lavage fluid was 9.5.

The patient was performed 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) to look for active organ involvement and it showed increased uptake in lymph nodes at cervical, thoracic, intraabdominal, and inguinal lymph nodes, both lungs, skin at back and lower calves, and mildly increased uptake at posterolateral wall of left ventricle. Transthoracic echocardiography (TTE) revealed no abnormalities. Cardiac MRI showed evidence of mid wall delayed enhancement suggestive of prior interstitial fibrosis involving left ventricular myocardium at septal and inferior walls.

All of the above had eventually led us to the diagnosis of systemic sarcoidosis with skin, lung, and possible cardiac involvements. The patient received prednisolone 60 mg/day (1mg/kg/day) and tapered gradually to the present dose of 10 mg on alternate days. After three months of treatment, the following CXR, CT-chest and pulmonary function test had showed significant improvement, while the skin lesions were complete remission. He is still under regular follow up.

Discussion

Sarcoidosis is a multisystem disorder of unknown etiology. Exposure to extrinsic triggers in people with a genetic risk and inappropriate immune responses is believed to play a role in sarcoidosis pathogenesis. Upregulation of CD4+ T helper cells result in formation of epithelioid granuloma[1]. One of the major features of the disease is the occurrence of non-caseating granulomatous inflammatory reaction[5]. The most frequently affected organs are the lung and mediastinal lymph nodes, followed by the eyes and skin[6]. At present, there is no well-defined diagnostic criteria for sarcoidosis[2]. Making the diagnosis of sarcoidosis is based on compatible clinical and radiographic features with evidence of non-caseating granulomas and evidence of no alternative diseases[2,4].

There are some recommendations for approaching to diagnose thoracic sarcoidosis in tuberculosis-endemic regions. Chest radiograph is recommended in all patients. Bilateral symmetric hilar lymphadenopathy in an asymptomatic patient is highly suggestive for active sarcoidosis. High-resolution computed tomography (HRCT) of chest has been proven to have better efficacy in assessing subtle parenchymal changes. The author also suggested to do contrast-enhanced computed tomography in all suspected cases of sarcoidosis in endemic regions with nodal involvement on CXR to exclude tuberculosis[8].

Cutaneous involvement in sarcoidosis is about 20-35%[1,5,6]. One series in Spain reported systemic involvement present in 82.5% of patients with cutaneous sarcoidosis and systemic involvement was detected after follow up four to nine years with a mean time of six years[7]. Cutaneous sarcoidosis can be classified as specific and non-specific lesions[6]. Specific cutaneous sarcoidosis is the rash that demonstrate evidence of granuloma on biopsy[1]. Specific skin lesion can present with any pattern, so it was called "great imitators"[5]. Our patient had specific skin lesions which compatible with angiolupoid sarcoidosis. This type of skin lesion is a variant of lupus pernio with more prominent telangiectasia[1]. It is an infrequent variant, affecting 8% of patients with specific cutaneous sarcoidosis and rarely reported in Western countries but have a higher prevalence in Asian series[9,10]. It had been reported in 38% of patients in a series from Taiwan; associated with eye involvement (67%)[9]. It usually manifests as single plaque, preferentially located on the face, ears or scalp[10]. However, some authors mentioned that angiolupoid is a loosely used term for any sarcoidosis lesions with telangiectasia, or may cause by telangiectatic formation induced by high-potency topical steroid use.[1]

When sarcoidosis is diagnosed, we have to find other possible involved organs[4]. Routine ophthalmologic examinations should be performed in all cases even if they have no ocular symptoms[4]. Because ocular sarcoidosis should always be treated to prevent permanent vision impairment[4]. Eye examination of our patient was normal.

Treatment was dictated by vital organ involvements such as pulmonary or ocular sarcoidosis. Corticosteroids were the mainstay of treatment[5]. Topical or intralesional corticosteroids may be used in sarcoidosis with only skin involvement[5]. Systemic treatment of the skin is reserved for symptomatic, widespread, disfiguring, and/or quality of life-altering disease[1].

Conclusion

Diagnosing sarcoidosis in tuberculosis-endemic areas are quite challenging because

tuberculosis can share many clinical features. Required combination of clinical and radiographic features with biopsy specimen demonstrating non-caseating granulomas and excluding other multisystem granulomatous diseases. Our patient presented with asymptomatic rashes with skin histopathology showed naked granuloma without evidence of infection, therefore sarcoidosis was suspected that led to more investigations to confirm the diagnosis. Nevertheless, when we establish the diagnosis of cutaneous sarcoidosis, it is essential to assess for potential extracutaneous involvement that may be affect the treatment.

Acknowledgements

The authors are very grateful to Asst. Prof. Narongkorn Saiphoklang, MD from the Division of Pulmonology, Faculty of Medicine, Thammasart University for his consultation and performing bronchoscopy, and to Asst. Prof. Ing-orn Arunakul, MD and Kid Bhumimuang, MD from the Division of Cardiology for cardiac evaluation.

References

1. Sanchez M, Haimovic A, Prystowsky S. Sarcoidosis. Dermatol Clin 2015; 33: 389-416.
2. Heinle R, Chang C. Diagnostic criteria for sarcoidosis. Autoimmun Rev 2014; 13: 383-7.
3. Dacosta JL. Geographic epidemiology of sarcoidosis in southeast asia. Am Rev Respir Dis 1973; 108: 1269-72.
4. Haimovic A, Sanchez M, Judson MA, Prystowsky S. Sarcoidosis: A comprehensive review and update for the dermatologist. J Am Acad Dermatol 2012; 66: 699.e1-e18.
5. Tchernev G. Cutaneous sarcoidosis: the "great imitator": etiopathogenesis, morphology, differential diagnosis, and clinical management. Am J Clin Dermatol 2006; 7: 375-82.
6. Liu KL, Tsai WC, Lee CH. Cutaneous sarcoidosis A retrospective case series and a hospital-based case-control study in Taiwan. Medicine (Baltimore) 2017; 96: e8158.
7. García-Colmenero L, Sánchez-Schmidt JM, Barranco C, Pujol RM. The natural history of cutaneous sarcoidosis. Clinical spectrum and histological analysis of 40 cases. Int J Dermatol 2019; 58: 178-84.
8. Goyal A, Khilnani G, Das A, Naranje P, Bhalla A, Guleria R. Dilemma of diagnosing thoracic sarcoidosis in tuberculosis-endemic regions: An imaging-based approach. Part 2. Indian J Radiol Imaging 2017; 27: 380-8.
9. Wu MC, Lee JY. Cutaneous sarcoidosis in southern Taiwan: Clinicopathologic study of a series with high proportions of lesions confined to the face and angiolupoid variant. J Eur Acad Dermatology Venereol 2013; 27: 499-505.
10. Arias-Santiago S, Fernández-Pugnaire MA, Aneiros-Fernández J, et al. Recurrent Telangiectasias on the Cheek: Angiolupoid Sarcoidosis. Am J Med 2010; 123: e7-e8.