

an ulcerated lesion; fissures, verrucous forms, and masses have been reported in fewer cases. In 2009, Antonello et al.⁶ described the case of a 40-year-old HIV-positive patient with perianal TB that presented as an ulcerating mass, a compound lesion very similar to the finding in our patient. The patient presented by Cheon et al.⁷ in 2013 was a 46 year-old man diagnosed with Crohn disease 30 years earlier and treated with mesalazine with no improvement of his rectal ulcers. Anal TB was diagnosed and the patient presented a marked improvement after 3 months of treatment. Another case of anal TB was reported in a 42-year-old patient on Adalimumab therapy for psoriatic arthritis.⁸

The treatment of anal TB is the same as for other forms of extrapulmonary TB. Patients should receive rifampicin, isoniazid, pyrazinamide, and ethambutol daily for 2 months, followed by rifampicin and isoniazid 3 times a week for 7 months (total treatment time, 9 months).⁹ In order to prevent the appearance of active tuberculosis, the Centers for Disease Control and Prevention advocates targeted screening and treatment of latent tuberculosis infection with 9 months of isoniazid. A newer regimen of weekly combined therapy with isoniazid and rifapentine for 12 weeks was cost-effective in directly observed therapy programs, particularly for populations that would not otherwise complete therapy and are at high risk for conversion to active disease, such as homeless patients.¹⁰

Conflict of interests

The authors declare no conflict of interest.

References

- Zumla A, George A, Sharma V, Herbert RHN, Oxley A, Oliver M. The WHO 2014 global tuberculosis report—further to go. *Lancet Glob Health*. 2015;3:e10–2.
 - Zumla A, Raviglione M, Hafner R, von Reyn CF. Tuberculosis. *N Engl J Med*. 2013;368:745–55.
 - Villa L, Trompa IM, Montes FN, Gómez JG, Restrepo CA. Analysis of mortality caused by tuberculosis in Medellín, Colombia, 2012. *Biomédica*. 2014;34:425–32.
 - Lee J, Lim JK, Seo H, Lee SYSY, Choi KJ, Yoo SS, et al. Clinical relevance of ground glass opacity in 105 patients with miliary tuberculosis. *Respir Med*. 2014;108:924–30.
 - Mathew S. Anal tuberculosis: report of a case and review of literature. *Int J Surg*. 2008;6:e36–9.
 - Antonello VS, Hoff LS, Kaercher D Jr, Santos BR. Anoperineal tuberculosis in an HIV patient. *Braz J Infect Dis*. 2009;13:246–7.
 - Cheon JH, Moon W, Park SJ, Park MI, Kim SE, Choi YJ, et al. A case of intestinal tuberculosis with perianal fistula diagnosed after 30 years. *Korean J Gastroenterol*. 2013;62:370–4.
 - Luquín N, Masiá M, Noguera R, Gutiérrez F. Anal tuberculosis complicating anti-TNF α therapy. *BMJ Case Rep*. 2014:2014.
 - World Health Organization. Treatment of extrapulmonary TB and of TB in special situations. In: *Treatment of tuberculosis guidelines*. Switzerland: World Health Organization; 2010. p. 95–7.
 - Gupta V, Sugg N, Butners M, Allen-White G, Molnar A. Tuberculosis among the homeless—preventing another outbreak through community action. *N Engl J Med*. 2015;372:1483–5.
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Cutaneous Sarcoid with Livedoid Changes in a Patient with Hashimoto's Thyroiditis



Sarcoidosis cutánea con cambios livedoides en un paciente con tiroiditis de Hashimoto

Dear Editor:

Association of sarcoidosis and autoimmune thyroiditis is rare. We report a case of cutaneous sarcoid surrounded by livedo on the lower extremities in a patient with Hashimoto's thyroiditis.

A 72-year-old female visited the Department of Dermatology of Hoshi General Hospital, complaining of asymptomatic reddish eruptions on the lower extremities which appeared six months previously. She had Hashimoto's thyroiditis for several years, but had been followed without medications. Physical examination showed multiple reddish, infiltrative round and irregular-shaped, up to 4-cm sized

plaques on the anterior aspects of the bilateral thighs and lower legs (Fig. 1a). The erythematous plaques coalesced on the left thigh, and livedo was observed in the surroundings of the plaques on the thighs. Laboratory examination showed normal levels of angiotensin-converting enzyme (ACE) (13.6 U/L, normal: 7–25). Anti-thyroglobulin antibody showed high titers (86.8 IU/ml; normal <28), however, anti-thyroid peroxidase antibody, thyroid stimulating hormone, free T3 and T4 levels were within normal ranges. Chest X-ray did not reveal bilateral hilar lymphadenopathy. Computed tomography revealed a few lymph nodes within normal ranges and thyroid nodule. Ophthalmological examination denied uveitis. A tuberculin test revealed positive erythematous reaction sized 2-cm without induration. A skin biopsy taken from reddish plaque showed non-caseating granulomas with epithelioid cells throughout the dermis (Fig. 1b). Periodic acid-Schiff (PAS) and Ziehl-Neelsen staining did not detect bacilli. Immunohistochemistry revealed a number of CD68-positive macrophages in the lesional skin. Tumor necrosis factor- α (TNF- α) and interleukin-17 (IL-17) positive cells were also detected densely (Fig. 1c and d). Elastica

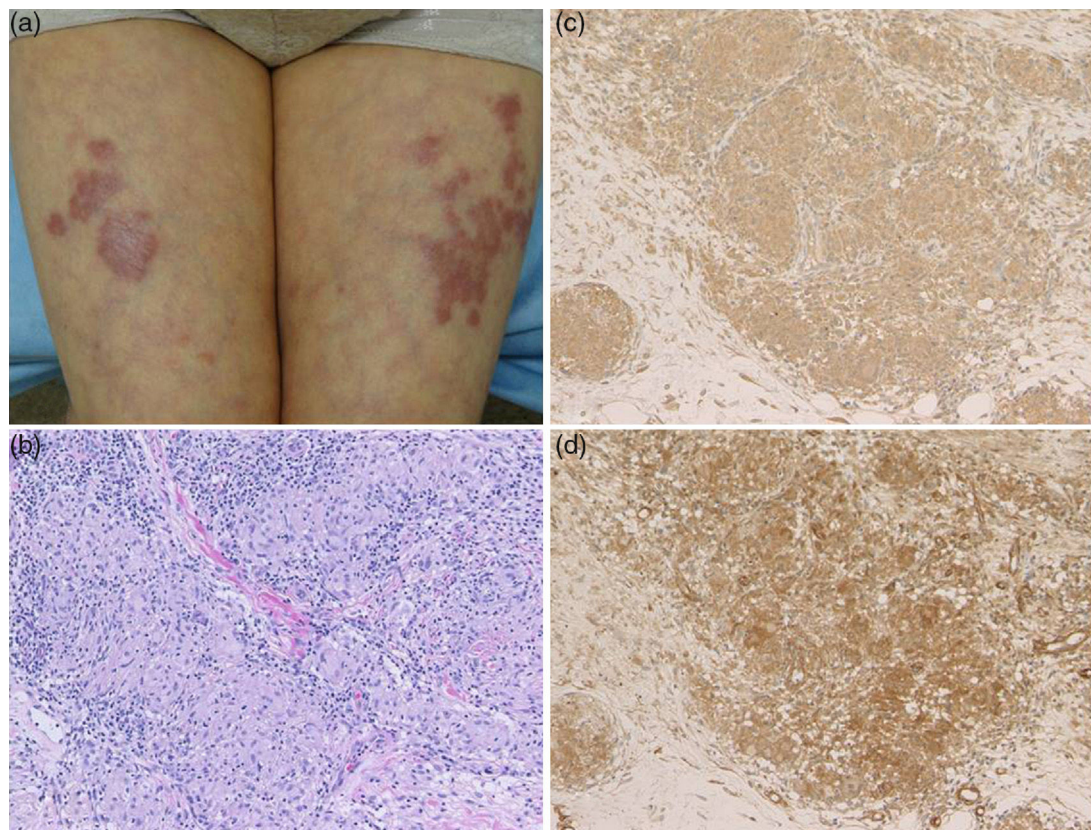


Figure 1 (a) Reddish plaques on the thigh along with livedoid changes. (b) Histological features showing sarcoidal granuloma, which are immunoreactive for TNF- α (c) and IL-17 (d) (original magnification: b; $\times 400$, c; $\times 200$, d; $\times 200$).

van Gieson stain showed that multiple sarcoidal granulomas were located around the vessels, but without fibrinoid degeneration.

Autoimmune thyroiditis is sometimes seen in association with sarcoidosis,¹ and to date, several cases of co-occurrence of sarcoidosis and Hashimoto's thyroiditis have been reported. Isernet et al.² reported that 10 out of 348 patients with sarcoidosis had autoimmune thyroiditis, and sarcoidosis preceded autoimmune thyroiditis in 9 cases. The diagnosis of autoimmune thyroiditis was made when sarcoidosis was in remission. Papadopoulos et al.³ reported that 13 patients had thyroid autoimmunity (6 with Hashimoto's thyroiditis, 2 with Graves' disease and 5 with isolated positive thyroid serology) among a series of 78 patients with sarcoidosis. Nakamura et al.⁴ found 7 cases of Hashimoto's thyroiditis in a series of 62 patients with pulmonary sarcoidosis. Unfortunately, an open biopsy of thyroid nodule was not carried out to differentiate thyroid sarcoidosis in the present case. At present, sarcoidal lesions were not detected in other organs, *i.e.* lung or eyes. Moreover, a tuberculin test revealed positive reaction. Therefore, we consider that the patient developed cutaneous sarcoid only; however, we will carefully follow-up this patient whether symptoms of systemic sarcoidosis will appear in the future.

Macrophages play an important role in sarcoidal granuloma formation *via* several cytokines such as TNF- α and IL-1 β . Several recent studies have reported the effectiveness of TNF- α inhibition for sarcoidosis. Our studies showed a number of CD163-positive macrophages surrounding the

degenerated collagen in the dermis. In addition, strong expression of IL-17 and TNF- α was detected in the lesional skin of sarcoidosis. TNF- α activates Th17 cells leading IL-17 production, and recent studies have shown that IL-17 was abundantly detected in sarcoidal lesions, suggesting that Th17 cells induce granuloma formation by suppressing regulatory T-cells.⁵ Recent findings suggest an important etiologic role of *Propionibacterium acnes* (*P. acnes*) in sarcoidosis. *P. acnes* induces IL-17 and interferon- γ ,⁶ and is thus implicated to play a pathogenic role in sarcoidosis *via* Th1/Th17 cytokines.

Finally, livedo was seen around sarcoidal plaques on the bilateral thigh. To date, only a few cases have been presented with livedo in association with sarcoidosis.⁷⁻⁹ A biopsy was taken from the sarcoidal plaque, but not from the surrounding livedo. However, histological examination showed granulomas around the vessels, which may induce livedo.

Ethical disclosures

Protection of human subjects and animals in research.

The authors declare that no experiments were performed on humans or animals for this investigation.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Conflict of interest

The authors declare no conflict of interest.

References

1. Antonelli A, Ferrari SM, Corrado A, Di Domenicantonio A, Fallahi P. Autoimmune thyroid disorders. *Autoimmun Rev.* 2015;14:174–80.
2. Isern V, Lora-Tamayo J, Capdevila O, Villabona C, Mañá J. Sarcoidosis and autoimmune thyroid disease: a case series of ten patients. *Sarcoidosis Vasc Diffuse Lung Dis.* 2007;24:148–52.
3. Papadopoulos KI, Hörnblad Y, Liljebadh H, Hallengren B. High frequency of endocrine autoimmunity in patients with sarcoidosis. *Eur J Endocrinol.* 1996;134:331–6.
4. Nakamura H, Genma R, Mikami T, Kitahara A, Natsume H, Andoh S, et al. High incidence of positive autoantibodies against thyroid peroxidase and thyroglobulin in patients with sarcoidosis. *Clin Endocrinol (Oxf).* 1997;46:467–72.
5. Ten Berge B, Paats MS, Bergen IM, van den Blink B, Hoogsteden HC, Lambrecht BN, et al. Increased IL-17A expression in granulomas and in circulating memory T cells in sarcoidosis. *Rheumatology.* 2012;51:37–46.
6. Agak GW, Qin M, Nobe J, Kim MH, Krutzik SR, Tristan GR, et al. *Propionibacterium acnes* induces an IL-17 response in acne vulgaris that is regulated by vitamin A and vitamin D. *J Invest Dermatol.* 2014;134:366–73.
7. Hayashi S, Hatamochi A, Hamasaki Y, Kitamura Y, Ishii Y, Fukuda T, et al. A case of sarcoidosis with livedo. *Int J Dermatol.* 2009;48:1217–21.
8. Takenoshita H, Yamamoto T. Erythema nodosum-like cutaneous lesions of sarcoidosis showing livedoid changes in a patient with sarcoidosis and Sjögren's syndrome. *Eur J Dermatol.* 2010;20:640–1.
9. Shibama S, Igawa K, Munetsugu T, Fukuyama K, Nishizawa A, Takayama K, et al. A case of sarcoidosis presenting as livedo. *Ann Dermatol.* 2014;26:773–4.

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