CASE REPORT

Nodular granulomatous phlebitis: An uncommon tuberculid

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INTRODUCTION

Nodular granulomatous phlebitis is a rare tuberculid. Patients present with tender subcutaneous nonulcerated nodules on the lower limbs along the distribution of superficial veins. Typical histologic findings include granulomatous phlebitis with epitheloid granulomas and Langhans giant cells within the vessel wall. We describe a case of nodular granulomatous phlebitis and its diagnostic challenges.

CASE REPORT

A 17-year-old Chinese girl presented with a 1-year history of recurrent bilateral tender nonulcerating plaques and nodules on the dorsum of her feet and shins. A short course of oral corticosteroids and nonsteroidal anti-inflammatory drug helped relieve the discomfort from the lesions. She was otherwise asymptomatic, denied any chronic cough, hemoptysis, fever, or night sweats. She was healthy with no regular medications. She denied any personal history of tuberculosis or contact history. She received Bacille Calmette-Guérin vaccination as a child.

On examination, she had violaceous indurated plaques and nodules over the dorsolateral aspects of both feet (Fig 1). Examinations of her other systems were unremarkable, with no palpable lymphadenopathy. The initial differential diagnoses were erythema nodosum, erythema induratum, or medium-vessel vasculitis.

Laboratory investigations including a full blood count, liver function, and renal function tests were normal. Erythrocyte sedimentation rate was elevated at 32 mm/h. Chest radiograph was normal.

Antinuclear antibody, anti–double-stranded DNA antibody, and antineutrophil cytoplasmic antibodies were negative. Urinalysis was unremarkable.

The first skin biopsy performed on a nodule from the right foot showed a mixed septal-lobular paniculitis without any granuloma formation. A second skin biopsy performed 9 months later from a nodule on the left foot showed granulomatous inflammation affecting a medium-sized vessel within the lower reticular dermis (Fig 2). There was caseous necrosis filling the vessel lumen surrounded by epitheloid histiocytes, Langhans-type giant cells, and lymphocytes that had infiltrated and destroyed the vessel wall (Fig 3, A). There was absence of a well-formed internal elastic lamina on Verhoeff Van Gieson stain, confirming that the vessel was a vein (Fig 3, B). Direct immunofluorescence was negative. Periodic acid–Schiff and Gomori methenamine silver stains were negative for fungal organisms. Ziehl-Neelsen (ZN) stain and Wade-Fite stain were both negative for acid-fast bacilli. Tissue culture was negative for mycobacterium.

Three months later, the patient reported submandibular lymphadenopathy. However, the lymphadenopathy had resolved by the time she was seen by an otolaryngologist. A biopsy of her posterior nasal space found necrotizing granulomatous

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inflammation. Special stains for mycobacterium and fungi were negative. Tissue culture and polymerase chain reaction (PCR) were negative for mycobacterium. T-SPOT tuberculosis test was notably reactive. Repeat chest radiograph showed a 1.2-cm pulmonary nodule in the right mid-zone. Sputum cultures grew Mycobacterium tuberculosis (MTB). There were no other symptoms. She was treated for pulmonary tuberculosis and was started on a 6-month course of rifampicin, isoniazid, pyrazinamide, and ethambutol. Two months after starting antituberculous therapy, the cutaneous lesions resolved with postinflammatory hyperpigmentation, with resolution of the lung nodule.

DISCUSSION

Tuberculids represent delayed hypersensitivity reactions to MTB in individuals with moderate to high levels of immunity against MTB. The 3 main types of tuberculids are papulonecrotic tuberculid, lichen scrofulosorum, and erythema induratum of Bazin.

Nodular granulomatous phlebitis was proposed as a tuberculid after reports of patients with subcutaneous nonulcerating nodules on the anteromedial aspect of lower limbs, with epitheloid granulomas within cutaneous veins on histology.1,2 These lesions resolved without scarring upon completion of antituberculous therapy.1,2 Patients either had active pulmonary or extrapulmonary tuberculosis or had contact history, although not all reported patients had an identifiable focus of tuberculosis or relevant contact history at the time of diagnosis despite positive Mantoux tests.1,3

The hematogenous dissemination of mycobacterial antigens was proposed as a potential mechanism in the pathogenesis of nodular granulomatous phlebitis and other tuberculids. Tissue cultures were rarely positive for MTB in tuberculids. Hara et al2 described 5 patients with granulomatous phlebitis. MTB DNA was identified by PCR in skin biopsy specimens in all patients, whereas tissue cultures and ZN stain were negative for mycobacterium. Other studies found that MTB DNA may be detectable by PCR in 25% to 71% of cases of erythema induratum of Bazin, and 50% of cases of papulonecrotic tuberculid.4,5

Granulomatous phlebitis is also seen in miliary tuberculosis and was reported in a patient with systemic lupus erythematous on long-term prednisolone who had subcutaneous nodules on the lower legs.5 Skin biopsy found granulomatous phlebitis and caseation necrosis with epithelioid granulomas and Langhans giant cells.2 ZN stains also showed MTB within the necrotic areas.2 MTB was cultured from the patient’s cerebrospinal fluid.2

We believe our patient had nodular granulomatous phlebitis as a tuberculid given the clinical appearance of her lesions, the presence of granulomatous phlebitis with negative stains and tissue culture for mycobacterium, the presence of culture-proven pulmonary tuberculosis, and the resolution of her lesions while on antituberculous therapy. Her lesions did not ulcerate, unlike erythema induratum of Bazin. Tissue stains were negative for bacterial or fungal elements, whereas her autoimmune workup was negative. She was clinically well, with no risk factors for miliary tuberculosis. Negative ZN stain and tissue cultures indicated her lesions to be a tuberculid rather than a result of hematologic dissemination of MTB. It is likely that this patient had latent tuberculosis that reacti-

Fig 1. Nodular tuberculid. Violaceous dermal plaques on dorsolateral surface of left foot admixed with postinflammatory hyperpigmentation.

Fig 2. Skin biopsy shows vasculitis of a medium-sized vessel within the lower reticular dermis. (Hematoxylin-eosin stain; original magnification: ×40.)
management strategies. Other differential diagnoses for granulomatous vasculitis include granulomatosis with polyangiitis, Churg-Strauss syndrome, vasculitis secondary to autoimmune or inflammatory diseases, lymphoproliferative disorders, and other infections such as fungal infections or syphilis. Starting immunosuppressive treatment in a patient in whom infective causes are inadequately ruled out may lead to worsening of the underlying infection, with increased morbidity and mortality.

CONCLUSION

Nodular granulomatous phlebitis is a tuberculid that should be considered in patients with tender subcutaneous nodules, granulomatous phlebitis on histology, and resolution of lesions when starting antituberculous therapy. The presence of a granulomatous vasculitis or phlebitis should prompt a thorough search for tuberculosis and exclude other causes of granulomatous vasculitis.

REFERENCES

1. Parker SC, McGibbon DH. A new tuberculid? J Cut Pathol. 1989;16:319 (abstract).
2. Hara K, Tsuzuki T, Takagi N, Shimokata K. Nodular granulomatous phlebitis of the skin: a fourth type of tuberculid. Histopathology. 1997;30(2):129-134.
3. McHugh A, Siller G, Williamson R, Faulkner C. Nodular granulomatous phlebitis: a phlebitic tuberculid. Australas J Dermatol. 2008;49(4):220-222.
4. Schneider JW, Jordaan HF, Geiger DH, et al. Erythema induratum of Bazin. A clinicopathological study of 20 cases and detection of Mycobacterium tuberculosis DNA in skin lesions by polymerase chain reaction. Am J Dermatopathol. 1995;17:350-356.
5. Victor T, Jordaan HF, Van Niekerk DJT, et al. Papulonecrotic tuberculid. Identification of Mycobacterium tuberculosis DNA by polymerase chain reaction. Am J Dermatopathol. 1992;14:491-495.

Fig 3. A, Caseous necrosis within the center of the vessel lumen surrounded by a dense granulomatous infiltrate of epithelioid histiocytes and Langhans-type giant cells admixed with lymphocytes (Hematoxylin-eosin stain). B, The lack of an internal elastic lamina confirms that the vessel is a vein (Verhoeff Van Gieson elastic stain).