Rheumatol Int (2006) 26:1154–1157
DOI 10.1007/s00296-006-0152-1

CASE REPORT

Cutaneous leukocytoclastic vasculitis with cervical tuberculous lymphadenitis: a case report and literature review

Hee Man Kim · Yong-Beom Park · Ho Young Maeng · Soo-Kon Lee

Received: 17 September 2005 / Accepted: 6 May 2006 / Published online: 8 July 2006

Abstract Cutaneous leukocytoclastic vasculitis (CLV) is a small-vessel vasculitis localized to the skin. Many possible causes exist for this pathological condition, including drugs, infection, collagen vascular disease, and malignancy. However, *Mycobacterium tuberculosis* is rarely reported to be associated with CLV. Here, we report a 49-year-old male patient that presented with fever, myalgia, and multiple palpable purpura on both of his legs. The biopsy from the purpura yielded a histologic diagnosis of leukocytoclastic vasculitis. The patient had several enlarged lymph nodes on his right neck, and the biopsy revealed tuberculous lymphadenitis. There were no signs of vasculitis present in the internal organs. After anti-tuberculosis treatment, his fever declined and the skin purpura were completely resolved. Although incidence is rare, tuberculosis should be considered as a possible cause of CLV.

Keywords Leukocytoclastic vasculitis · *Mycobacterium tuberculosis*

Introduction

Leukocytoclastic vasculitis is a small-vessel vasculitis and often involves systemic organs other than the skin, such as the joints, gastrointestinal tract, and kidney [1]. If it is confined to the dermal postcapillary venules, then it is designated as cutaneous leukocytoclastic vasculitis (CLV) [2]. The histopathology is characterized by fibrinoid necrosis of the vessel walls, extravasation of red blood cells, and the perivascular presence of polymorphonuclear leukocytes with fragmented nuclei [3]. In addition to the skin lesions, major clinical manifestations include palpable purpura and petechiae, fever, malaise, myalgias, and arthralgias [4]. There are many identifiable etiologic factors of CLV including: drugs, infection, collagen vascular disease, and malignancy [1, 5]. Among the infectious agents, bacteria and viruses are well recognized as causes of CLV, but *Mycobacterium tuberculosis* is rarely reported to be associated with CLV. In instances where *M. tuberculosis* is determined to be the cause, the exact pathogenesis of CLV due to *M. tuberculosis* remains unknown. Here, we report a case of tuberculous lymphadenitis presenting with CLV and a review of the literature.

Case report

A 49-year-old Korean man was admitted to our hospital presenting with a 1 week history of fever, myalgia, and arthralgia. He indicated a sensation of warmth and tenderness on the right side of his neck. He had no personal or family history of medical illness and had not taken any medications recently. Upon physical examination, his body temperature was 39.5°C, several lymph nodes were palpable on his right neck, and one small round purpura was discovered on his anterior lower right leg. On day 3 of his admission, multiple palpable purpura appeared on both lower legs and progressively spread to both thighs (Fig. 1).

H. M. Kim · Y.-B. Park · H. Y. Maeng · S.-K. Lee (✉)
Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, 134 Shinchon-dong, Seodaemun-ku, Seoul 120-752, Republic of Korea
e-mail: sookonlee@yumc.yonsei.ac.kr

Computerized tomography (CT) of his neck suggested probable cervical tuberculous lymphadenopathy. A biopsy of the cervical lymph nodes was performed, and the histology revealed chronic granulomatous inflammation with caseous necrosis (Fig. 2). Acid-fast bacilli were not found on Ziehl-Nielsen staining, but polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* was positive. The histology of the biopsy from the purpura on the skin revealed leukocytoclastic vasculitis without granuloma (Fig. 3). Initial laboratory findings were as follows: WBC: 3,500/mm^3 (neutrophil 84.4%, lymphocyte 11%, eosinophil 1%), Hb: 10.8 g/dl, platelets: 121,000/mm^3, erythrocyte sedimentation rate: 42 mm/h, C-reactive protein: 25.1 mg/dl, AST/ALT: 81/27 IU/L, and BUN/Cr: 5.1/0.9 mg/dl. Serological markers for HIV, cytomegalovirus, Epstein-Barr virus, Herpes simplex virus, Varicella-zoster virus, Hanta virus, leptospirosis, tsutsugamushi, hepatitis B and C, mycoplasma, and syphilis were all negative. Antinuclear antibody, anti-dsDNA antibody, anti-Ro antibody, anti-La antibody, and antineutrophil cytoplasmic antibody (ANCA) were also negative. Complement level was normal. Levels of serum IgG/A/M were 1,700/415/103 mg/dl, respectively (reference values: 700–1,600 mg/dl, 70–400 mg/dl, and 40–230 mg/dl, respectively). Urinalysis was within the normal range. The tuberculin test (2 TU) was positive (7×6 mm^2). Cultures of blood, stool, and urine were negative. Radiologic studies were performed to detect any underlying disease or evidence of vasculitis within the internal organs. The CT scans of the chest, abdomen and pelvis revealed no abnormalities. The angiography of the celiac artery, superior mesenteric artery, and both renal arteries revealed no stenosis or aneurysmal changes due to vasculitis. The patient received standard anti-tuberculosis therapy with isoniazid, rifampicin, ethambutol, and pyrazinamide. Over the next week his symptoms subsided, and the purpura on his legs gradually disappeared. During the 6-month course of treatment, there was no recurrence of purpura on the skin.

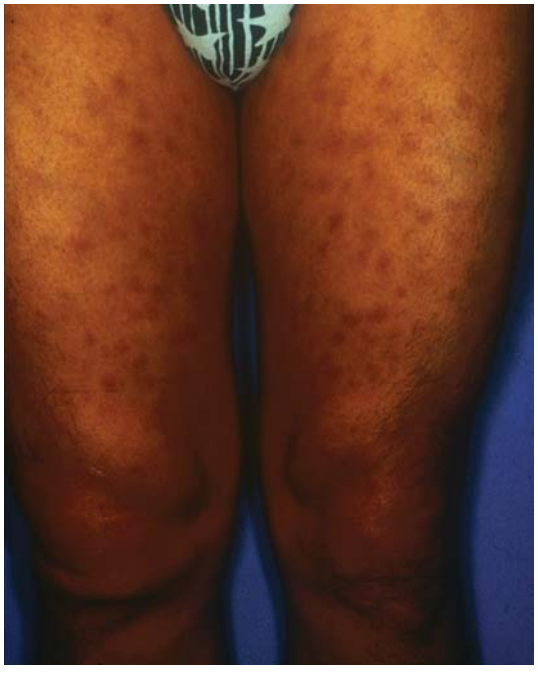

Fig. 1 Multiple palpable purpura were observed on both lower extremities

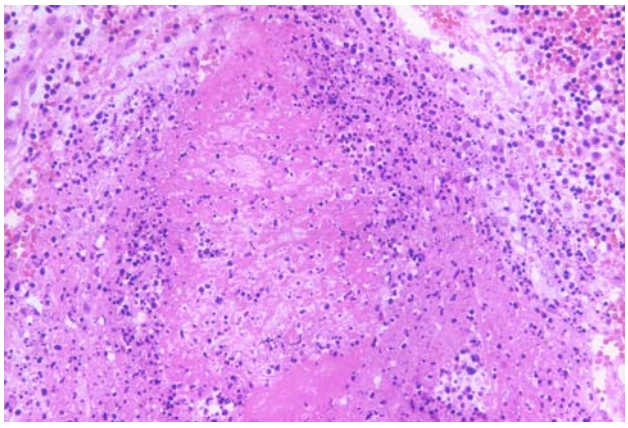

Fig. 2 Biopsy of a lymph node in the *right neck* shows chronic granulomatous inflammation with caseous necrosis

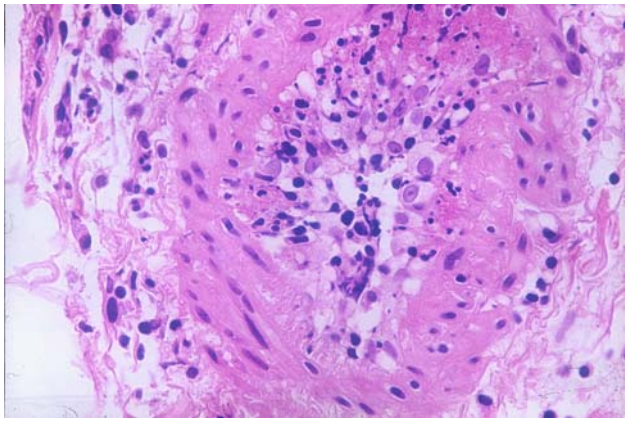

Fig. 3 Biopsy of a skin lesion shows vascular damage with perivascular neutrophilic infiltrate, eosinophilic fibrinoid changes in vessel walls, and nuclear debris, which is comparable to pathology seen in leukocytoclastic vasculitis

Discussion

The CLV is identical to dermal lesions that occur as a component of systemic small-vessel vasculitis [2].

Table 1 Cases of cutaneous leukocytoclastic vasculitis (CLV) associated with *Mycobacterium tuberculosis*

Reference	Year of publication	Age	Sex	Site of *M. tuberculosis* infection	Diagnostic method of tuberculosis	Location of purpura	Presenting symptoms	Recurrence of purpura
[9]	1987	U	U	Pulmonary tuberculosis	Sputum AFB smear	U	U	No
[10]	1990	24	M	Tuberculous lymphadenitis	Lymph node biopsy	Four extremities	Neck swelling	No
[11]	1993	U	U	Tuberculous lymphadenitis	Lymph node biopsy	Legs	Purpura	No
[12]	1996	61	F	Tuberculous lymphadenitis	Lymph node biopsy	Lower legs	Purpura	No
[13]	1998	15	F	Pulmonary tuberculosis	Sputum PCR	Lower legs	Purpura	No
[13]	1998	13	F	No infected organ	Blood mononuclear cell PCR	Four extremities	Purpura	No
[14]	2000	U	U	Pulmonary tuberculosis	Sputum AFB smear	U	U	No
[15]	2000	36	M	Pulmonary tuberculosis	Sputum culture	Lower legs	Fever, cough	No

AFB acid-fast bacilli, *U* unidentified in the report, *PCR* polymerase chain reaction

Twenty percent of leukocytoclastic vasculitis cases involve a systemic organ [4]. The exact pathogenesis of CLV remains uncertain, but it appears to be mediated by the deposition of circulating immune complexes within specific vessels. The deposits subsequently activate the complement cascade and release vasoactive substances and chemotactic factors that cause the accumulation of polymorphonuclear cells and release of lysosomal enzymes [6, 7], which leads to vessel wall injury. However, other autoantibodies such as ANCA, inflammatory mediators, and adhesion molecules may be involved in the pathogenesis of CLV. In addition, various conditions and diseases can cause CLV; drugs and infection cause approximately 10% of vasculitic skin lesions [1]. Malignancy is associated with less than 1% of cases of CLV [8]. According to previous studies, up to 61% of cases of CLV are idiopathic, depending on the degree of investigation and the duration of follow up [1].

Various infectious agents, such as bacteria, viruses, fungi, protozoa and helminthes, are associated with vasculitis. However, *M. tuberculosis* is rarely reported to be associated with CLV, and we found only 8 cases reported in the English literature (Table 1). Four patients (50%) had pulmonary tuberculosis, and three patients (37.5%) had tuberculous lymphadenitis. Acid-fast bacilli were found within sputum in four patients, and within tissue from lymph nodes in three patients. Lee et al. used PCR with blood mononuclear cells in order to diagnose tuberculosis, although this is not a standard test [13]. Four patients (50%) presented with purpura on the skin prior to their diagnosis of tuberculosis. The purpura in all eight patients subsided completely after anti-tuberculosis treatment, and did not recur.

Tuberculosis can manifest itself in two types of skin lesions: direct lesions and hypersensitivity vasculitis [15]. The major difference between these lesions is whether or not mycobacteria exist within the lesion. Hypersensitivity vasculitis can be caused by the deposition of immune complexes formed by antibodies against *M. tuberculosis* proteins in the small-vessel walls, and therefore the organism is absent in the lesion [15]. The existence of circulating immune complexes has been demonstrated in 56% of patients with active tuberculosis, and it has been suggested that the sequential measurement of these complexes could be useful as a guide to successful treatment of tuberculosis [16]. However, not all immune complexes in tuberculosis cause vasculitis, and the prevalence of vasculitis in tuberculosis seems to be very low. In a study by Visser and Heyl [11], there was only one CLV case among 92 patients with cutaneous tuberculosis.

In conclusion, although incidence is rare, tuberculosis should be considered as a possible cause of CLV. In all previous cases of CLV with tuberculosis, anti-tuberculosis treatment completely resolved the skin lesions.

References

1. Ekenstam E, Callen JP (1984) Cutaneous leukocytoclastic vasculitis. Clinical and laboratory features of 82 patients seen in private practice. Arch Dermatol 120:484–489
2. Charles J, Ronald JF (1997) Small vessel vasculitis. N Engl J Med 20:1512–1523
3. Lacour JP, Castanet J, Perrin C, Vitetta A, Ortone J-P (1993) Cutaneous leukocytoclastic vasculitis and renal cancer: two cases. Am J Med 94:104–108
4. Sais G, Vidaller A, Jucgla A, Servitje O, Condom E, Peyri J (1998) Prognostic factors in leukocytoclastic vasculitis. Arch Dermatol 134:309–315
5. Bonnefoy M, Claudy AL (1988) Etude prostpective de facteurs associes aux vascularites leucocytoclasiques. Ann Dermatol Venereol 115:27–32
6. Mackel SE, Jordon RE (1982) Leukocytoclastic vasculitis. A cutaneous expression of immune complex disease. Arch Dermatol 118:296–301
7. Sams WM Jr (1985) Human hypersensitivity angiitis, an immune complex disease. J Invest Dermatol 85:114s-148s
8. Mertz LE, Conn DL (1992) Vasculitis associated with malignancy. Curr Opin Rheumatol 4:39–46

9. Pacheco A, Mateos P, Medina J, Guisasola L, Garrillo F, Perez-Oteiza J (1987) Pulmonary tuberculosis and Schoenlein-Henoch purpura. Rev Clin Esp 180:515–517
10. Chan CHS, Chong YW, Sun AJM, Hoheisel GB (1990) Cutaneous vasculitis associated with tuberculosis and its treatment. Tubercle 71:297–300
11. Visser AJ. Heyl T (1993) Skin tuberculosis as seen at Ga-Rankuwa hospital. Clin Exp Dermatol 18:507–515
12. Sais G, Vidaller A, Jucgla A, Peyri J (1996) Tuberculous lymphadenitis presenting with cutaneous leukocytoclastic vasculitis. Clin Exp Dermatol 21:65–66
13. Lee AY, Jang JH, Lee KH (1998) Two cases of leukocytoclastic vasculitis with tuberculosis. Clin Exp Dermatol 23:225–226
14. Martinez V, Zeller V, Caumes E, Katlama C, Bricaire F (2000) Cutaneous vascultitis disclosing pulmonary tuberculosis. Ann Med Intern 151:664–666
15. Minguez P, Pintor E, Buron R, Diaz-Pollan B, Puche JJ, Pontes JC (2000) Pulmonary tuberculosis presenting with cutaneous leukocytoclastic vasculitis. Infection 28:55–57
16. Johnson NMcl, McNicol MW, Burton Kee EJ, Mowbray JF (1981) Circulating immune complexes in tuberculosis. Thorax 36:610–617