Case Report

Leukocytoclastic Vasculitis with Infective Endocarditis Mimicking Henoch-Schönlein Purpura

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ABSTRACT: Infective endocarditis (IE) is associated with bacteremia and vascular embolization by microorganisms. Characteristic dermatologic symptoms are Osler's node, Janeway spots, splinter hemorrhage, and petechial hemorrhage. In patients with IE, multiple palpable purpura can develop on the lower extremities in association with proteinuria, and differentiation from Henoch-Schönlein purpura (HSP) is often difficult when other symptoms of IE are absent or unapparent.

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KEYWORDS: leukocytoclastic vasculitis, infective endocarditis, Henoch-Schönlein purpura, direct immunofluorescence, IgA deposition

Leukocytoclastic vasculitis (LV) is caused by infectious diseases such as infective endocarditis (IE), hepatitis B, hepatitis C, and sepsis.[1] IE is associated with bacteremia and vascular embolization by microorganisms, including bacteria, fungi, and rickettsia.[1] IE has infectious symptoms (fever, anemia, and splenomegaly), cardiac symptoms (murmur and tachycardia), and symptoms of vascular embolization (bleeding in organs, infarctions, and thrombi).[2] Characteristic dermatologic symptoms are Osler's node, Janeway spots, splinter hemorrhage, and petechial hemorrhage.[3] Multiple palpable purpura may develop on the lower extremities in association with proteinuria in IE, and differentiation from Henoch-Schönlein purpura (HSP) is often difficult when palpable purpura developed on the lower extremities of IE are absent or unapparent.

We describe a patient who after initially receiving a diagnosis of HSP was subsequently found to have LV due to endocarditis after symptoms recurred during an interruption in treatment.

Case Report

In May 2010, a 43-year-old man presented to our hospital complaining of fever and fatigue. He had a past history of surgical treatment for tetralogy of Fallot at age 8 years and a family history of thrombocytopenia. He was examined in the internal and cardiovascular internal medicine clinic in our hospital in July 2010. α-*Streptococcus* was detected in a blood culture. Echocardiography was normal, and neither endocarditic vegetations nor prolapse of valves was detected. After a tentative diagnosis of sepsis of unknown cause, antibiotic therapy with penicillin was started and continued for 36 days. Fever and arthralgia were diminished but had not completely disappeared when medical treatment was interrupted due to the patient's work responsibilities. In November 2010, he visited our dermatology clinic with purpura on his lower extremities, low-grade fever, and arthralgia of his knees and feet.

Laboratory data were as follows-serum C-reactive protein concentration: 8.5 mg/dl, lactate dehydrogenase: 313

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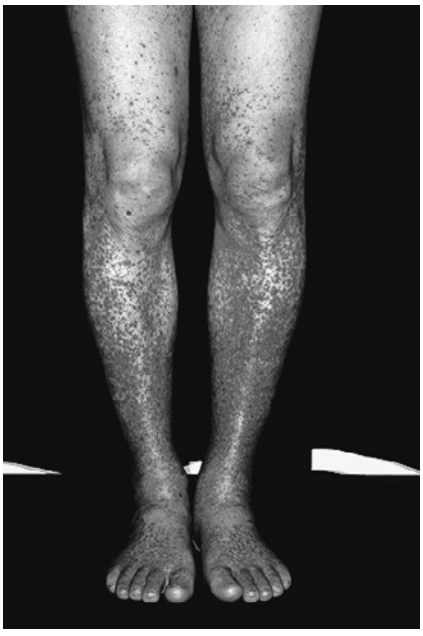

Fig. 1 Diffuse purpuric papules with multiple arthralgia of the knees and foot on both lower legs.

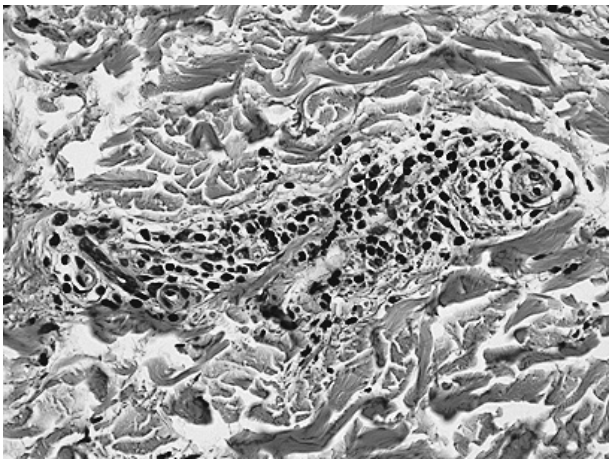

Fig. 2 Histopathologic findings from a purpuric papule on the left lower leg show infiltrations of neutrophils, monocytes, and nuclear dusts near the capillaries, and extravasated erythrocytes in the papillary dermis (HE stain, original magnification, ×400).
HE: hematoxylin and eosin

IU/l, alkaline phosphatase: 356 IU/l, white blood cell count: 15.2×10^3 /μl, red blood cell count: 3.68×10^6 /μl, hemoglobin: 9.3 g/dl, platelet: 100×10^3 /μl, urine proteins: 3+, and hematuria: 3+, D-dimer: 16.2 μg/ml, fibrin degradation product: 26.3 μg/ml, immunoglobulin (Ig) G: 2299 mg/dl, IgE: 242 IU/ml, complement component 3 (C3): 62 mg/dl, and complement component 1q (C1q): 17.7 μg/ml.

On physical examination, purpura with various signs was seen on his thighs and lower extremities (Fig. 1), and joint pain was present in his knees and feet. There were no symptoms of tonsillopharyngitis or cervical lymphadenopathy and no unusual findings in the chest or abdomen. A skin biopsy specimen from a purpuric papule on his left lower leg showed infiltrations of neutrophils, monocytes, and nuclear dust near capillaries, and extravasated erythrocytes in the papillary dermis (Fig. 2). Direct immunofluorescence (DIF) revealed deposits of C3 and fibrinogen in the small vessel wall of the papillary dermis (Fig. 3), but IgG, IgA, and IgM were not detected. These histologic findings were consistent with LV.

We tentatively diagnosed HSP based on the patient's clinical and laboratory findings and recommended that he be admitted to hospital, which he declined due to his work responsibilities. We began daily treatment with 30 mg of oral prednisolone, penicillin, an anti-allergy drug (Allegra®: Sanofi-Aventis SA, Paris, France), and styptics (Adona®: Mitsubishi Tanabe Pharma Corp., Osaka, Japan; Transamin®: Daiichi Sankyo Co. Ltd., Tokyo, Japan). One week later, he was admitted and treated with 30 mg of prednisolone for 4 days and 20 mg of prednisolone for 2 weeks. After the purpura disappeared and his fever abated, he was discharged from hospital. However, proteinuria and hematuria did not improve during hospitalization. A needle biopsy of the kidney was not possible because the patient had horseshoe kidneys. Serum creatinine (1.87 mg/dl) and urinary protein were elevated, and he again developed purpura on his lower extremities. Therefore, we began pulse therapy at the nephrology clinic with 500 mg of methylprednisolone and 40 mg of oral prednisolone daily. During methylprednisolone pulse therapy (with continuation of prednisolone), the purpura and arthralgia improved, but low-grade fever and renal dysfunction persisted. Plasma exchange and open renal biopsy were scheduled. Unlike the previous examination, echocardiography showed typical endocarditic vegetations and prolapse of valves in the pulmonary artery and aorta. α-*Streptococcus* was again detected in a blood culture. Computed tomography (CT) scanning showed a pulmonary embolism and embolic splenic infarction. Roth spots and macular bleeding were observed on fundus examination. IE was diagnosed, and he was readmitted to the department of cardiovascular internal medicine. During prednisolone tapering, antibiotic therapy with aminobenzyl penicillin, gentamicin, penicillin G, and ceftriaxone was initi-

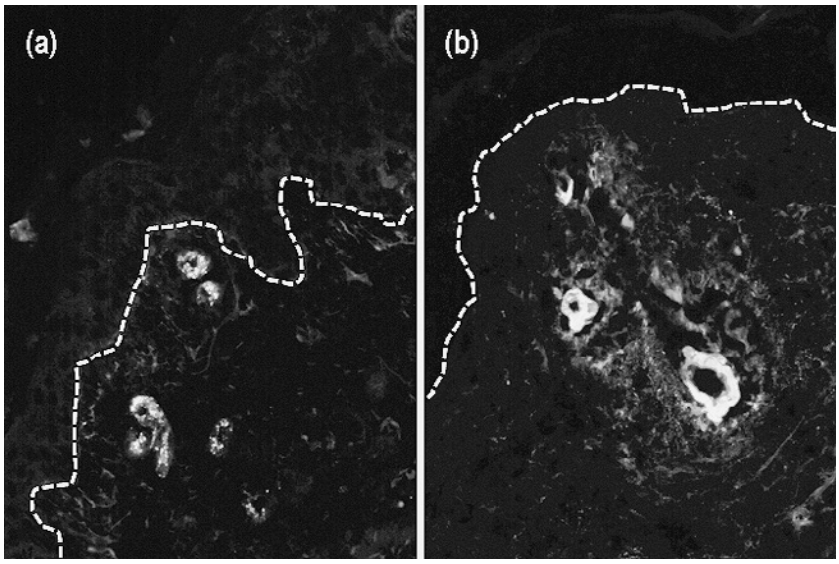

Fig. 3 Direct immunofluorescence shows deposits in the small vessel wall in the papillary dermis. (a) C3 deposit in the upper dermis (original magnification, ×200); (b) fibrinogen deposit in the upper dermis (original magnification, ×100). C3: complement component 3

Table 1 Summary of patients who developed purpura associated with infective endocariditis

Author	Year	Isolated bacterium	Renal dysfunction	Histopathology
Horwits et al.[4]	1967	*Streptococcus viridans*	(+)	ND
Horwits et al.[4]	1967	*Streptococcus viridans*	(+)	ND
Rubenfeld et al.[5]	1977	*Lactobacillus*	(+)	LV
Spach et al.[6]	1991	*Corynebacterium jeikeium*	ND	ND
Orfila et al.[7]	1993	*Streptococcus mitis*	(+)	LV
Soto et al.[8]	1994	*Streptococcus bovis*	(+)	ND
Toyohara et al.[2]	1997	*Streptococcus mitis*	(+)	LV
Iwasaki et al.[9]	1997	*Streptococcus viridans*	(−)	LV
Masuzawa et al.[10]	2002	*Streptococcus intermedius*	(−)	LV
Masu et al.[11]	2005	Methicillin-sensitive *Staphylococcus aureus*	(−)	LV
Fujisawa et al.[12]	2005	Methicillin-sensitive *Staphylococcus aureus*	(−)	LV
Uchihira et al.[13]	2006	*Streptococcus mitis*	ND	LV
Suzuki et al.[14]	2006	*Streptococcus*	(+)	LV
Baba et al.[15]	2006	*Staphylococcus aureus*	(−)	ND
Kato et al.[16]	2009	*Streptococcus oralis*	(+)	LV
Kondo et al.[17]	2010	*Staphylococcus sanguinis*	(−)	LV

ND: not described, LV: leukocytoclastic vasculitis

ated, and replacement of the aortic and pulmonary valves was scheduled. However, the patient developed lower back pain, vomited large amounts of blood, and died of blood loss on day 25 of hospital readmission. The suspected cause of death was superior mesenteric arterial embolism.

Discussion

A review of the relevant literature showed 16 cases of purpura with IE (Table 1).[2,4–17] Among these 16 cases, streptococcus was detected in 10 and renal dysfunction was noted in 8. Petechial hemorrhage can be detected in 20% to 40% of IE cases, but purpura is very rare in IE.[18] Histopathologic examination showed LV in 11 of 16 cases;

IgA deposition to capillaries was detected by DIF in only 1 case.

IE can be fatal, and early identification and management are thus important for improving prognosis. In patients with LV presenting with purpura, IE should be included in the differential diagnosis, particularly in those with a past history of cardiac valvulopathy or cardiac surgery such as valve replacement. In our patient, clinical symptoms of purpura, proteinuria, hematuria, and arthralgia mimicked HSP. IE skin histopathologic findings, namely, deposition of fibrinogen and complement in the capillaries of the papillary dermis, were also compatible with HSP. In addition, a previous cardiac echogram did not suggest IE, although the patient did have a fever of unknown origin. Therefore, we were unable to diagnose his condition until purpura and fever recurred. In HSP, deposition of IgA in the blood vessels of the superficial dermis is a characteristic finding. However, among reported cases with LV and IE, deposition of IgG or IgM is often detected,[1] but only 1 had IgA deposition.[2] Most reported cases of purpura with IE were associated with renal involvement,[4,5,7,8] and deposit of IgG or IgM is detected in the glomus.[1] In our case, we could not do a renal biopsy of a horseshoe kidney. Weakened bacterium like *Streptococcus viridans* and *Streptococcus mitis* can be the primary causative organism.[1] In some cases, antineutrophil cytoplasmic antibody[19] or cryoglobulin[20] were detected, which indicates that infection itself is involved with the appearance of abnormal antibodies. However, the extent of abnormal antibody involvement in the mechanisms of vasculitis development is unknown. The presence of complement and the lack of IgA in DIF might indicate the presence of LV rather than HSP, and careful systemic examination should thus be performed in such cases.

Conclusions

Skin manifestations and renal symptoms (proteinuria and hematuria) of LV with IE can mimic HSP, as was the case in our patient. DIF should be performed at initial skin biopsy to examine IgA deposition in such cases. Immunofluorescence with HSP[21] is more likely to show granular IgA in the superficial dermal blood vessels, and DIF did indeed show that our patient had LV with IE. Patients without IgA deposition should be carefully investigated for evidence of IE, using established criteria for clinical, microbiologic, and echocardiographic findings.

References

1) Ishiko A: Vasculitis with an infection. *Derma* (156): 62–66, 2009 (J)
2) Toyohara A, Chen KR, Miyakawa S, et al.: A case of infective endocariditis with leukocytoclastic vasculitis. *Rinsho Hifuka* **51**: 225–227, 1997 (J)
3) Franks AG Jr: Dermatology in General Medicine vol.2 (4th ed) p2068. Fitzpatrick TB, Eisen AZ, Wolff K, et al. (Eds) McGran-Hill, New York, 1993
4) Horwitz LD, Silber R: Subacute bacterial endocarditis presenting as purpura. *Arch Intern Med* **120**: 483–486, 1967
5) Rubenfeld S, Min KW: Leukocytoclastic angiitis in subacute bacterial endocarditis. *Arch Dermatol* **113**: 1073–1074, 1977
6) Spach DH, Celum CL, Collier AC, et al.: Palpable purpura associated with Corynebacterium jeikeium endocarditis. *Arch Dermatol* **127**: 1071–1072, 1991
7) Orfila C, Lepert JC, Modesto A, et al.: Rapidly progressive glomerulonephritis associated with bacterial endocarditis: Efficacy of antibiotic therapy alone. *Am J Nephrol* **13**: 218–222, 1993
8) Soto A, Jorgensen C, Oksman F, et al.: Endocarditis associated with ANCA. *Clin Exp Rheumatol* **12**: 203–204, 1994
9) Iwasaki T, Kubota Y, Manita M, et al.: A case of infective endocariditis with bacterial rupture of a cerebral aneurysm after allergic vasculitis on the lower legs. *Shindan-to-Chiryo* **85**: 2077–2079, 1997 (J)
10) Masuzawa M, Murano K, Koyano T: Osler's nodule. *Hifubyo Shinryo* **24**: 951–954, 2002 (J)
11) Masu A, Atsumi M, Adachi T, et al.: A case of infective endocariditis taking opportunity of detection with atopic dermatitis. *Hifuka no Rinsho* **47**: 766–767, 2005 (J)
12) Fujisawa T, Yamanaka S, Kawai S, et al.: A case of petechial hemorrhagic lesion with infective endocariditis. *Hifubyo Shinryo* **27**: 1407–1410, 2005 (J)
13) Uchihira M, Takahata Y, Hamamoto Y, et al.: A case of infective endocariditis with purpura on ventral toes as a clue to the diagnosis. *Nishi Nihon Hifuka* **68**: 500–503, 2006 (J)
14) Suzuki T, Minami H: A case of purpura on the arms and legs associated with infective endocariditis. *Rinsho Hifuka* **60**: 565–567, 2006 (J)
15) Baba S, Ohhara H, Akasaka T: A case of Janeway spots associated with infective endocariditis. *Rinsho Hifuka* **62**: 74–77, 2008 (J)
16) Kato A, Morita A: A case of anaphylactoid purpura complicated with infectious endocariditis. *Rinsho Hifuka* **63**: 640–644, 2009 (J)
17) Kondo M, Nishii M, Mizutani H: Osler's node happened to infective endocarditis following brain abscess. *Hifuka no Rinsho* **52**: 75–77, 2010 (J)
18) Pankey GA: Acute bacterial endocarditis at the University of Minnesota Hospitals, 1939-1959. *Am Heart J* **64**: 583–591, 1962
19) Kodo K, Hida M, Omori S, et al.: Vasculitis associated with septicemia: Case report and review of the literature. *Pediatr Nephrol* **16**: 1089–1092, 2001
20) Hellmich B, Ehren M, Lindstaedt M, et al.: Anti-MPO-ANCA-positive microscopic polyangiitis following subacute bacterial endocarditis. *Clin Rheumatol* **20**: 441–443, 2001
21) Rapini RP: Vasculitis and other purpuric diseases. *Practical Dermatopathology* p71–72. Elsevier Mosby, Philadelphia, 2005

(J): in Japanese

ヘノッホ・シェーンライン紫斑病に類似した感染性心内膜炎に合併した白血球破砕性血管炎の１例

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要約：白血球性破砕性血管炎は感染性心内膜炎，B 型肝炎，C 型肝炎，敗血症などの感染症により発症する疾患である．感染性心内膜炎は細菌，真菌，リケッチアを含めた微生物による菌血症や血管塞栓と関連し，感染徴候（発熱，貧血，脾腫），心症状（心雑音や頻脈），血管塞栓徴候（臓器出血，梗塞，塞栓）を認める．特徴的な皮膚所見は，Osler 結節，Janeway 斑，下腿の点状出血である．さらに感染性心内膜炎における尿蛋白と相関して下腿に触知可能な紫斑が多発するが，下腿の紫斑以外の典型的な症状がない場合や明白でない場合にはヘノッホ・シェーンライン紫斑病との鑑別がしばしば困難である．

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