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Original

# Antiphospholipid Antibodies in Patients with Cutaneous Polyarteritis Nodosa and Livedo Vasculopathy: An Initial Report

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Recently, it has been reported that the presence of anti-phosphatidylserine-prothrombin complex (anti-PS/PT) antibodies can serve as markers in cutaneous polyarteritis nodosa (CPN) patients.

We examined antiphospholipid antibodies (aPL) in 24 patients with CPN and 11 with livedo vasculopathy (LV). Furthermore, we investigated β-thromboglobulin, platelet factor 4, thrombin anti-thrombin III complex, D-dimer, protein C, protein S and thrombomodulin.

As a result, we detected several kinds of aPL in 10 CPN and 5 LV patients. Among them, IgM anti-PS/PT antibodies were detected more frequently than other aPL in CPN and levels of the antibodies in CPN had a tendency to be high, compared with healthy controls, although no significant differences were found ($p = 0.06$). Those antibodies were also detected in about 27% of LV patients. In addition, the titer of one case was much higher.

In conclusion, it can be suggested that IgM anti-PS/PT antibodies might act as a pathogenic factor for CPN, and that there may be a common pathogenic mechanism between CPN and some cases of LV, thereby indicating that CPN might have another pathogenesis and is a distinct entity from systemic polyarteritis nodosa.

**Key Words**: cutaneous polyarteritis nodosa, livedo vasculopathy, antiphospholipid syndrome, antiphospholipid antibody, anti-phosphatidylserine-prothrombin complex antibody

## Introduction

Cutaneous polyarteritis nodosa (CPN), initially described in 1931 by Lindberg[1], is benign in many cases, although the histological features of the skin lesions are common with those of systemic polyarteritis nodosa (PAN). It has been controversial whether CPN is a skin feature of PAN or a distinct clinical entity.

In 2007, Kawakami et al[2] reported a high titer of anti-phosphatidylserine-prothrombin complex (anti-PS/PT) antibodies in patients with CPN. They suggested that the thrombotic process may trigger the development of CPN and that those antibodies will become widely recognized as new factors for CPN.

On the other hand, CPN, livedo vasculopathy (LV) and antiphospholipid syndrome (APS) present similar skin symptoms such as livedo reticularis clinically, although they are not always the same histologically. CPN shows necrotizing vasculitis of small muscular arteries in subcutaneous tissues, and LV and APS show vascular thrombosis in the dermis and/or subcutaneous tissues. It has been reported that antiphospholipid antibodies (aPL), including IgM anti-PS/PT antibodies[3], are also detected in some cases of LV.

We examined aPL, platelet activity and coagulation to investigate their relationship in CPN and LV, and to determine whether there is a common factor in these diseases.

## Materials and methods

**1. Clinical investigation** (Table 1)

Subjects were 24 patients with CPN (1 man, 23

**Table 1** Clinical characteristics of the patients.

| | | CPN | LV |
|---|---|---|---|
| Number of patient | | 24 | 11 |
| Age | Mean ± SD | 42.6 ± 16.9 | 44.3 ± 21.7 |
| | Range | 18-77 | 18-77 |
| Sex | Male | 1 | 2 |
| | Female | 23 | 9 |

CPN: cutaneous polyarteritis nodosa, LV: livedo vasculopathy

women; mean age 42.6 ± 16.9 years; mean ± SD; range 18–77) and 11 patients with LV (2 men, 9 women; mean age 44.3 ± 21.7 years; mean ± SD; range 18–77) who visited our department between February, 2007 and June, 2012.

The diagnoses of these patients were based on clinical features and examinations of internal organs including the following tests: chest x-ray, electrocardiogram, computed tomography of the brain, neck, chest and abdomen, magnetic resonance imaging or magnetic resonance angiography of the brain, abdomen and lower limbs, ultrasonography of the abdomen, heart and carotid artery, abdominal arterography, neurological examination, and ophthalmologic examination, and we attempted to confirm all results histologically.

**2. Histological investigation**

Skin biopsy specimens were obtained from lesional skin of the lower extremities in all patients, fixed in 10% formalin, and stained with hematoxylin and eosin. All samples, except for 4 CPN cases which were examined at a previous hospital, were also used for direct immunofluorescence staining and incubated with commercially prepared fluoresceinated antisera specific to human immunoglobulin (Ig) G, IgM, IgA, $C_1$, $C_3$ and fibrinogen. All CPN samples except for 2, which were examined at a previous hospital, were also used for Elastica-van Gieson stain. Informed consent was obtained from all patients.

**3. Laboratory investigation**

We examined aPL including IgG and IgM anticardiolipin (aCL) antibodies, IgG anti-$\beta_2$-glycoprotein I-dependent cardiolipin (anti-$\beta_2$GP I/CL) antibodies, lupus anticoagulant (LAC) and IgG and IgM anti-PS/PT antibodies. IgG and IgM aCL, IgG anti-$\beta_2$GP I/CL antibodies and IgG anti-PS/PT antibodies were measured using specific enzyme-linked immunosorbent assays (ELISA), LAC was examined by measuring dilute Russell's viper venom time (dRVVT) in 34 cases, activated partial thromboplastin time (APTT) was measured in 22 cases, and mixing studies and demonstration of phospholipid dependence (PL) was determined in 22 cases. All tests were performed by SRL, Inc. (Tokyo, Japan). The normal range was determined based on the data provided by SRL, Inc.

IgM anti-PS/PT antibodies were measured using an ELISA method according to the manufacturer's protocol (Medical & Biological Laboratories Co., Ltd., Nagoya, Japan). Briefly, serum samples diluted to 1 : 100 were added to 96-well plates coated with PS/PT and were incubated for 1 hour at 25℃. After washing, peroxidase-conjugated anti-human IgM antibodies were added to each well. After incubation and washing, substrate (3,3',5,5'-tetramethylbenzidine and $H_2O_2$) was added, which was acted upon by the bound enzyme to produce color. The absorbance of the solution in the well was read at 450 nm using a microplate reader. The antibodies were measured even for 16 healthy controls (2 men, 14 women; mean age 32.43 ± 6.74 years; mean ± SD; range 26–51).

Furthermore, we measured β-thromboglobulin (β-TG), platelet factor 4 (PF4), thrombin anti-thrombin III complex (TAT), D-dimer, protein C, protein S and thrombomodulin (TM), which is an index of the activation of vascular endothelial cells.

We also examined antinuclear antibody (ANA), rheumatoid factor (RF), myeloperoxidase (MPO)-antineutrophil cytoplasmic antibodies (ANCA), proteinase-3 (PR3)-ANCA, hepatitis B virus antigen (HBAg), hepatitis C virus (HCV) antibody, serologic reaction for syphilis, $CH_{50}$, $C_3$ and $C_4$, in addition to general laboratory investigations.

**4. Statistical analysis**

Statistical analyses were performed using JMP ver.10 (SAS Institute, Cary, NC, USA). A p-value of less than 0.05 was considered to indicate a statistical significance.

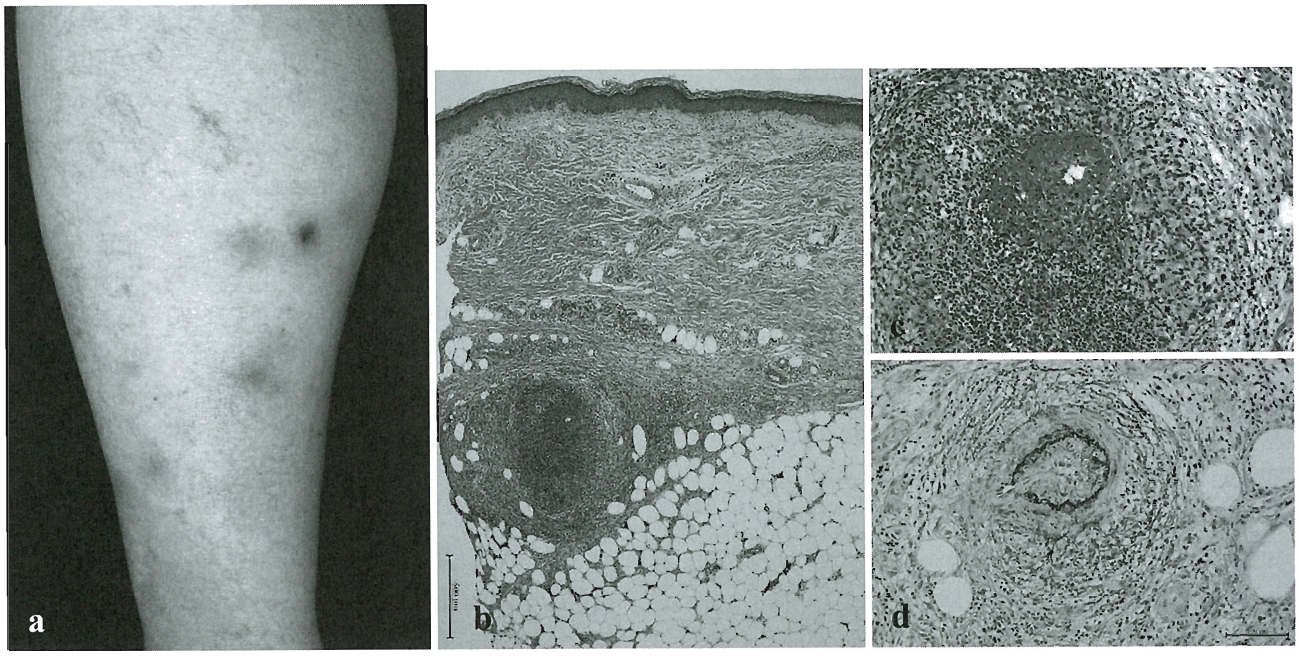


**Fig. 1** Clinical and histopathological features of cutaneous polyarteritis nodosa (case 7) Clinical features (a) Indurated erythemas on the lower extremities. Histopathological features. Necrotizing vasculitis of small muscular arteries in subcutaneous tissues (b, c). Elastica van Gieson staining reveals partial destruction of the internal elastic lamina (d).

### 5. Ethical considerations

The protocol for this study was approved by the Ethics Committee of Tokyo Women's Medical University.

## Results

### 1. Clinical features

In the 24 CPN cases, indurated erythemas, about 10 mm in diameter, on the lower extremities were the most common skin manifestations which were observed in 21 patients (87.5%) (Fig. 1a). Fifteen of the CPN patients (62.5%) had livedo reticularis and 8 (33.3%) had subcutaneous nodules on the lower extremities, while 3 patients (12.5%) had purpuric lesions and 2 (8.3%) had skin ulcers. Eight patients (33.3%) had numbness on the lower extremities and 4 of those 8 patients showed neuropathy of the legs confirmed by low conductive speed. Two of the CPN patients (8.3%) had arthralgia of the foot joints or hip joints, and none of the patients had myalgia. We found no significant findings of internal organs and other collagen diseases in any of the CPN patients.

Ten of the 11 LV patients (90.9%) had both smaller indurated erythemas than the CPN patients and purpura, 9 (81.8%) had atrophie blanche, 8 (72.7%) had skin ulcers, and 7 (63.6%) had livedo reticularis on the lower extremities and/or feet (Fig. 2a-c). Two of the LV patients (18.1%) had subcutaneous nodules on the lower extremities and feet, and 4 patients (36.3%) had numbness on the lower extremities with mild low conductive speed in 3 patients, which were relieved by vasodilatation therapy. None of the LV patients had arthralgia, myalgia, internal involvement or other collagen diseases.

### 2. Histological findings

Histologically, all 24 CPN cases showed vasculitis of small muscular arteries in the deep dermis or subcutaneous tissues (Fig. 1b, c). Elastica van Gieson staining revealed destruction of the internal elastic lamina (Fig. 1d) in 15 cases, but not in the remaining 7 cases, although histological findings showed fibrinoid degeneration/fibrin deposit of the artery walls with dense infiltration of neutrophils and/or lymphocytes in all cases. Nineteen CPN cases had accumulations of plasma protein or fibrin thromboses in the vessels of the dermis and subcutaneous tissues. Immunofluorescence staining was

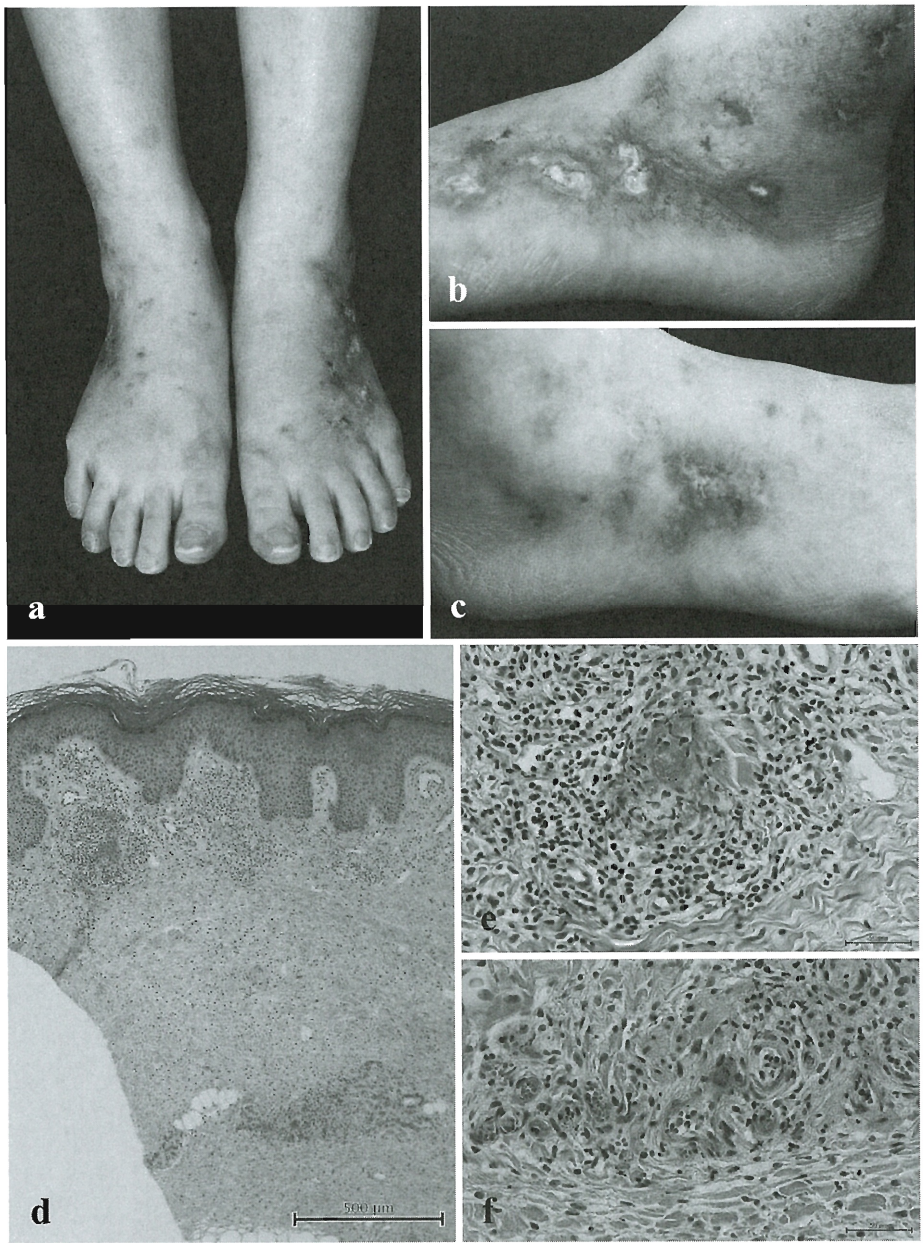


**Fig. 2** Clinical and Histopathological features of livedo vasculopathy (case 5)
Clinical features (a ～ c). Indurated erythemas, purpura, ulcers and atrophie blanche on the lower extremities and feet. Histopathological features (d ～ f). Thrombosis in the small vessels of the dermis and subcutaneous tissues with perivascular lymphocytic infiltrations.

performed in 20 cases, and showed positive reactions for fibrinogen in 6 cases, $C_3$ in 4 cases, $C_1$, IgG, IgM and IgA in 1 case on the artery walls.

Histologically, all 11 LV cases had thrombosis in the small vessels of the dermis and/or subcutaneous tissues with perivascular lymphocytic infiltrations (Fig. 2d-f). Immunofluorescence staining was performed in all 11 cases, and showed positive reactions for $C_3$ and fibrinogen in 9 cases, IgM in 8 cases, $C_1$ in 7 cases, IgG in 6 cases, IgA in 2 cases and a negative reaction in 1 case on the artery walls.

**3. Laboratory data** (Table 2)

IgG aCL antibodies were detected in 1 of the 22 CPN patients and in 1 of the 11 LV patients. LAC was detected in 2 of the 23 CPN patients and in 1 of the 11 LV patients. IgG anti-PS/PT antibodies were detected in 3 of the 21 CPN patients and in 2 of the 11 LV patients. IgM aCL antibodies and IgG anti-$\beta_2$ GPI/CL antibodies were not detected in any of the patients. On the other hand, the mean titer of IgM

**Table 2** Serologic features
Serologic findings in 24 CPN patients and 11 LV patients.

| Patient no. | Age | Sex | IgG aCL | IgM aCL | β2GPI/CL | LAC (dRVVT) | LAC (PL) | LAC (APTT) | IgG aPS/PT | IgM aPS/PT |
|---|---|---|---|---|---|---|---|---|---|---|
| Normal range | | | <10 Units/ml | <8 Units/ml | <3.5 Units/ml | <1.3 sec | <6.3 sec | <55.5 sec | <12 Units/ml | <17.7 (cut off value) Units/ml |
| CPN | | | | | | | | | | |
| 1 | 58 | F | <8 | <5 | <1.2 | 1.18 | ND | ND | <5 | 20.5 |
| 2 | 27 | F | <8 | <5 | <1.2 | 1.03 | ND | ND | <5 | 18 |
| 3 | 56 | F | <8 | <5 | <1.2 | 1.09 | ND | ND | <5 | 10.7 |
| 4 | 38 | F | ND | ND | <0.7 | 1.2 | ND | ND | ND | ND |
| 5 | 52 | F | 14 | <5 | <1.2 | 1.05 | ND | ND | 9 | 14.6 |
| 6 | 77 | F | <8 | <5 | <1.2 | 1.09 | ND | ND | <5 | 9.8 |
| 7 | 64 | F | <8 | 7 | <1.2 | 1.09 | ND | ND | 9 | 23.6 |
| 8 | 69 | M | <8 | ND | <1.2 | 1.16 | ND | ND | ND | 0.5 |
| 9 | 32 | F | <8 | <5 | <1.2 | 1.2 | <0 | 47.2 | <5 | 13.6 |
| 10 | 45 | F | <8 | <5 | <1.2 | 1.1 | 1.7 | 42.9 | ND | 5.1 |
| 11 | 35 | F | <8 | <5 | <1.2 | 1.2 | 4.5 | 43.9 | <5 | 11.1 |
| 12 | 65 | F | <8 | <5 | 1.2 | 1.26 | 4.6 | 41.8 | 6 | 4.2 |
| 13 | 61 | F | <8 | <5 | <1.2 | 1.36 | 10.2 | 52.5 | 15 | 18.5 |
| 14 | 18 | F | <8 | <5 | <1.2 | 1.23 | 1.4 | 48.8 | <5 | 15.6 |
| 15 | 41 | F | <8 | <5 | <1.2 | 1.22 | 0.9 | 35.5 | <5 | 5.5 |
| 16 | 27 | F | <8 | <5 | <1.2 | 1.27 | 4.6 | 48.5 | 20 | 54.3 |
| 17 | 23 | F | <8 | 6 | <1.2 | ND | ND | ND | 5 | 36.2 |
| 18 | 23 | F | ND | <5 | <1.2 | 1.21 | <0 | 47 | 10 | 33.2 |
| 19 | 45 | F | 27 | <5 | <1.2 | 1.8 | 29.1 | 94.6 | 53 | 67.3 |
| 20 | 35 | F | <8 | <5 | <1.2 | 1.01 | <0 | 43.3 | 5 | 15.4 |
| 21 | 44 | F | <8 | <5 | <1.2 | 1.11 | 0.6 | 44.5 | <5 | 17.7 |
| 22 | 44 | F | <8 | <5 | <1.2 | 1.06 | 0.5 | 45.7 | <5 | 15.6 |
| 23 | 25 | F | <8 | <5 | <0.7 | 1.11 | <0 | 43.1 | <5 | 3.7 |
| 24 | 20 | F | <8 | <5 | <1.2 | 1.17 | 2.7 | 44.8 | <5 | 10.3 |
| LV | | | | | | | | | | |
| 1 | 30 | F | <8 | <5 | <1.2 | 1.1 | ND | ND | <5 | 6.4 |
| 2 | 24 | M | <8 | <5 | <1.2 | 1.16 | ND | ND | <5 | 7.1 |
| 3 | 42 | F | <8 | <5 | <1.2 | 1.09 | ND | ND | 13 | 8.7 |
| 4 | 34 | F | 11 | 6 | <1.2 | 1.14 | ND | ND | 10 | 61.1 |
| 5 | 23 | F | <8 | <5 | <1.2 | 1.16 | 1 | 45.9 | 28 | 21.6 |
| 6 | 74 | F | <8 | <5 | <1.2 | 1.16 | 1.8 | 36.7 | <5 | 0.4 |
| 7 | 77 | M | <8 | <5 | <1.2 | 1.19 | 10.7 | 54.2 | 7 | 0 |
| 8 | 18 | F | <8 | <5 | <1.2 | 1.11 | 1.2 | 44.4 | <5 | 12.9 |
| 9 | 43 | F | <8 | 6 | <1.2 | 1.11 | 2 | 45.7 | <5 | 19.8 |
| 10 | 49 | F | <8 | <5 | <1.2 | 1.12 | 0.7 | 53.8 | <5 | 11.8 |
| 11 | 74 | F | <8 | <5 | <1.2 | 1.11 | <0 | 38.6 | <5 | 0 |

ND: not done, CPN: cutaneous polyarteritis nodosa, LV: livedo vasculopathy, M: male, F: female, aCL: anticardiolipin antibodies, β2GPI/CL: anti-β2-glycoprotein I dependent cardiolipin antibodies, LAC: lupus anticoagulant, aPS/PT: anti-phosphatidylserine-prothrombin complex antibodies

anti-PS/PT antibodies was 18.47 ± 16.01 (mean ± SD) U/ml in CPN, 13.61 ± 17.39 (mean ± SD) U/ml in LV and 11.28 ± 6.48 (mean ± SD) U/ml in healthy controls, however no significant differences were found between them (P = 0.06, Fig. 3). The cutoff value was 17.7 U/ml for IgM anti-PS/PT antibody by ROC curve between CPN and healthy controls. Finally, we detected some aPL in 10 CPN (41.6%) patients and 5 LV patients (45.4%).

β-TG and PF-4 were examined in 20 CPN and 11 LV cases, and TAT and D-dimer were examined in 22 CPN and 11 LV cases. Elevations of β-TG were shown in 4 CPN and 5 LV cases, PF-4 in 3 CPN and 4 LV cases, TAT in 1 CPN and LV case, respectively, and D-dimer in 6 CPN and 2 LV cases. Elevation of TM was shown in only 1 of the 20 CPN cases.

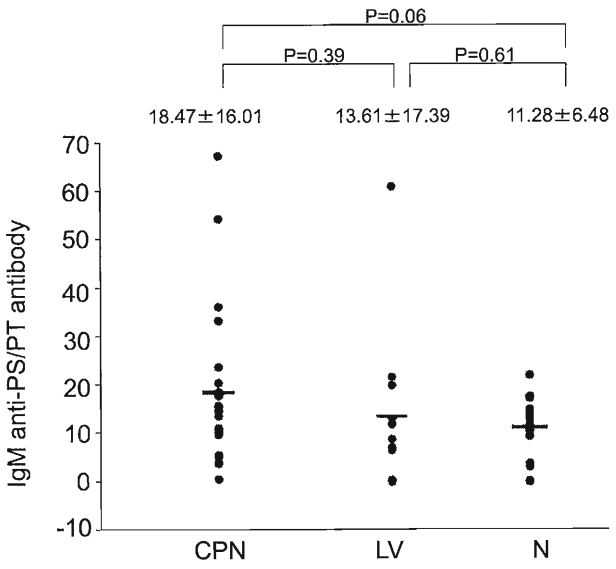


**Fig. 3** The titer of IgM anti-PS/PT antibodies in CPN (cutaneous polyarteritis nodosa), LV (livedo vasculopathy) cases and healthy controls
The mean level of IgM anti-PS/PT antibodies in CPN was 18.47±16.01 (mean±SD) U/ml, 13.61±17.39 (mean±SD) U/ml in LV cases, and 11.28±6.48 (mean±SD) U/ml in healthy controls (N), showing no statistical significance (CPN vs N; P=0.06, LV vs N; 0.61, CPN vs LV; 0.39).
The horizontal lines indicate the mean value in each group.

Protein C activity was low in 2 of the 19 CPN cases, and protein S activity was low in 2 of the 17 CPN cases tested. Statistically, no significant difference was observed between CPN and LV.

White blood cells were high in 5 CPN and 4 LV cases. CRP was high in 9 CPN cases (0.38 to 12.91 mg/dl) and 1 LV case (1.95 mg/dl). Liver and renal functions were normal in all CPN and LV cases. HBAg was negative in 21 CPN and 11 LV cases, HCV antibody was positive in only 1 of 21 CPN cases, and serologic reaction for syphilis was negative in 23 CPN and 11 LV cases. ANA was positive in 13 of the 24 CPN cases (×40 to ×640) and in 4 of the 10 LV cases (×80 to ×640). RF was positive in 2 of the 23 CPN cases and in none of the 10 LV cases. MPO-ANCA and PR3-ANCA were negative in all 24 CPN and 11 LV cases. $CH_{50}$ was elevated in 14 of the 21 CPN cases and in 5 of 9 LV cases, and was low in 1 of the 21 CPN cases. $C_3$ was elevated in 5 out of 22 CPN cases and was low in 1 of the 22 CPN cases. $C_4$ was high in 3 of the 22 CPN cases and in 1 of the 10 LV cases, and low in 2 of the 22 CPN cases. No significant differences were found in the data between CPN and LV.

## Discussion

CPN is a type of vasculitis limited primarily to the skin of the lower extremities without systemic involvements, although it shows the same cutaneous manifestations, indurated erythema, subcutaneous nodules, livedo reticularis, purpura, ulceration and gangrene, and the same histopathological findings as PAN. CPN usually occurs in 20 to 40 year-old women, which is a younger age group than PAN. On PAN, immune complexes and antiendothelial cell antibodies have been proposed as a pathogenic mechanism[4]. The association of PAN and APS is uncommon, and it is thought that aPL is not a direct cause of PAN but one factor to increase a thrombotic event, although there are a few reports of PAN complicated by APS[5][6]. The exact etiology of CPN is unknown, however there have been reports of aPL detected in CPN cases[1][7]~[9]. Katayama et al. reported that aCL antibodies may play a role in CPN in the development of occlusive vascular lesions in a manner different from immune complex-mediated vascular injury, and they suggested the possible effect of aCL antibodies on thromboxane production from platelets and prostaglandin production from vascular endothelial cells[7]. In 2007, it was reported that anti-PS/PT antibodies and/or LAC are detected in all CPN patients[2]. It was suggested from the study that those antibodies could serve as markers of CPN due to the reason that the mean IgM anti-PS/PT antibody level in patients with CPN was significantly higher than in patients with SLE, while levels were within normal limits in all patients with microscopic polyangiitis and in healthy controls (cutoff value; 10 U/ml)[2]. However, there have been only a few reports[9] regarding anti-PS/PT antibodies in CPN to date.

On the other hand, LV is a most common disease in young to middle-aged women. The disease shows necrotic purpuric lesions and small painful ulcerations often with surrounding livedo reticularis and atrophie blanche on the lower extremities, and reveals thrombosis rather than vasculitis histopa-

thologically. Although the pathogenesis of LV is also unknown, LV has recently been divided into two types, idiopathic and secondary. In the latter, various causes, factor V Leiden mutation, decreased protein C or protein S activity, aPL and hyperhomocystinaemia have been implicated[10]. In aPL, aCL antibodies (subclass unknown)[11][12], IgM aCL antibodies[13], IgG aCL antibodies[13][14], anti-β2GPI/CL antibodies[12][14] and IgM anti-PS/PT antibodies[3] were detected.

Thus, we characterized aPL in CPN and LV patients and examined the possible association between these 2 diseases. The results show that some aPL were detected in 10 CPN patients (41.6%) and 5 LV patients (45.4%). Laboratory data, including platelet activity, coagulation and immunological data, did not reveal significant differences between CPN and LV. In CPN, IgM anti-PS/PT antibodies in particular, had a tendency to be positive, compared with other aPL, and levels of antibodies in CPN tended to be high, compared with healthy controls. Some LV cases (27.2%) also had the same antibodies compared with healthy controls (6.2%). We may be able to find a significant difference between CPN and healthy controls if we increase the number of cases, since the p-value was very close to less than 0.05 in this study.

In 1996, anti-PS/PT antibodies were detected in LAC positive patients[15]. Atsumi et al. examined anti-PS/PT antibodies in a large population of patients with autoimmune diseases and found that IgG anti-PS/PT antibodies were highly prevalent in patients with APS compared to patients with other diseases, and that the antibodies strongly correlated with the clinical manifestations of APS[16]. Sakai et al. also reported that the presence of anti-PS/PT antibodies highly correlated with increased thrombin generation in APS patients[17]. On the other hand, the correlation between clinical features and IgM anti-PS/PT antibodies are not clearly understood, however, positive IgM anti-PS/PT antibodies may be related with dysfunction of the peripheral circulation and thrombosis because these antibodies were detected in some cases of LV in past reports in addition to this study. In other words, LV cases with such antibodies are secondary LV cases and might be regarded as APS clinically, although this antibody is not yet included in the Sydney criteria[18].

The fact that in CPN, IgM anti-PS/PT antibodies in particular were detected more frequently than other aPL, and the titer of the antibodies tended to be higher than healthy controls, indicates that IgM anti-PS/PT antibodies might act as a pathogenic factor for CPN, although the mechanisms of CPN caused by IgM anti-PS/PT antibodies is still undisclosed. In addition, 27.2% (3/11) of LV cases also had the same antibodies and the titer of one case was much higher (61.1 U/ml) indicating that CPN might have a similar pathogenesis to some cases of LV. In fact, it has been reported that a case was finally diagnosed as CPN during treatment as LV[19]. CPN generally affects the lower extremities without any systemic involvement as does LV, and most CPN (79.1%; 19/24) cases had accumulations of plasma protein or fibrin thromboses in vessels of the dermis and subcutaneous tissues. In some CPN cases, antithrombotic agents are effective without systemic steroids or immunosuppressants[20][21]. This might be indirect evidence that CPN is initially induced by a local dysfunction of the circulation.

## Conclusion

Our speculation is that a thrombotic change of small muscular arteries in their subcutaneous tissues might progress to CPN due to vascular endothelial dysfunction, may be related to IgM anti-PS/PT antibodies, and that CPN might have another pathogenesis which is a distinct entity from PAN.

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The authors have no conflicts of interest to disclose.

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## 皮膚型結節性多発動脈炎とリベド血管症患者における抗リン脂質抗体（第一報）

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臨床的にリベドを呈し血管障害を認める疾患には，皮膚型結節性多発動脈炎，リベド血管症，抗リン脂質抗体症候群などがある．病理組織学的な所見は，皮膚型結節性多発動脈炎では真皮脂肪織境界部の小動脈炎を，リベド血管症，抗リン脂質抗体症候群では毛細血管～細血管の血栓像を呈するという違いがあるものの，3疾患の臨床症状には共通点が多くみられる．近年，皮膚型結節性多発動脈炎において抗リン脂質抗体の1つである抗ホスファチジルセリン・プロトロンビン複合体（anti-PS/PT）IgM 抗体が高率に検出され，発症への関与が示唆されている．

今回我々は皮膚型結節性多発動脈炎と臨床的に類似点を認めるリベド血管症患者における anti-PS/PT 抗体を含む抗リン脂質抗体の有無と血小板・凝固系検査としてβ-トロンボグロブリン，血小板第4因子，TAT，D-ダイマー，トロンボモジュリンなどについて検討した．

皮膚型結節性多発動脈炎24例中10例，リベド血管症11例中5例でなんらかの抗リン脂質抗体を検出し，皮膚型結節性多発動脈炎では，抗リン脂質抗体の中でも特に anti-PS/PT IgM 抗体の陽性例が多くみられた．統計学的な有意差はみられなかったが($p=0.06$)，健康人コントロールと比較して高い傾向がみられ，発症機転においてなんらかの関与をしている可能性を考えた．一方，anti-PS/PT IgM 抗体はリベド血管症でも27％に陽性であり，1例では高値を示したことから，皮膚型結節性多発動脈炎とリベド血管症の一部の症例では基盤に共通の因子の存在を疑った．皮膚型結節性多発動脈炎においては，リベド血管症でみられるような血栓形成が血管内皮障害をきたした結果，最終的に血管炎に発展することが推察され，全身型結節性多発動脈炎からは独立した clinical entity である可能性を考える．