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Letter to the Editor

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

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Dear Editor,

In a previous report entitled "Antiphospholipid Antibodies in Patients with Cutaneous Polyarteritis Nodosa and Livedo Vasculopathy: An Initial Report" published in this Journal[1)], we examined titers of IgM anti-phosphatidylserine-prothrombin complex (anti-PS/PT) antibodies in 23 patients with cutaneous polyarteritis nodosa (CPN), 11 with livedo vasculopathy (LV) and in 16 healthy controls. The mean titer of IgM 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 none of those differences was significant (P = 0.06). The cut-off value was 17.7 U/ml for IgM anti-PS/PT antibody by ROC curve between CPN and healthy controls. The facts that in CPN, IgM anti-PS/PT antibodies in particular were detected more frequently (39.1%) than other antiphospholipid antibodies (aPL), and the titer of those antibodies tended to be higher than in healthy controls, indicated that IgM anti-PS/PT antibodies might act as a pathogenic factor in CPN. In addition, 27.2% of LV cases also had high titers of those 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 this report, we add 2 more CPN cases and 38 healthy controls, and we reexamine the titers of IgM anti-PS/PT antibodies. As a result, a significant difference was detected between CPN and healthy controls.

IgM anti-PS/PT antibodies were measured using an ELISA method according to the manufacturer's protocol (Medical & Biological Laboratories Co., Ltd., Nagoya, Japan), the same method used in our previous report. The subjects included 25 patients

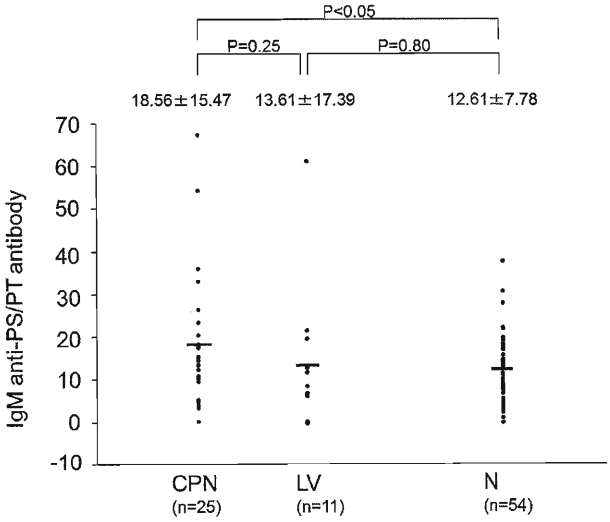

Figure The titer of IgM anti-PS/PT antibodies in CPN (cutaneous polyarteritis nodosa), LV (livedo vasculopathy) cases and healthy controls
The mean level of IgM anti-PS/PT antibodies in CPN was 18.56 ± 15.47 (mean ± SD) U/ml, 13.61 ± 17.39 (mean ± SD) U/ml in LV cases, and 12.61 ± 7.78 (mean ± SD) U/ml in healthy controls (N), Significant differences were found between CPN and healthy controls (P < 0.05), although no significant differences were found between CPN and LV (P = 0.25), between LV and healthy controls (P = 0.80).
The horizontal lines indicate the mean value in each group.

with CPN (1 man, 24 women; mean age 43.3 ± 16.7 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 February, 2013, and 54 healthy controls (10 men, 44 women; mean age 39.7 ± 12.4 years; mean ± SD; range 19–62), who were matched by age and sex. The protocol for this study was approved by the Ethics Committee of the Tokyo Women's Medical University.

The results showed that the mean titer of IgM anti-PS/PT antibodies was 18.56 ± 15.47 (mean ± SD) U/ml in CPN, 13.61 ± 17.39 (mean ± SD) U/ml in LV and 12.61 ± 7.78 (mean ± SD) U/ml in healthy controls. The difference in titer between CPN and healthy controls was significant ($P<0.05$, Figure), although no significant differences were found between CPN and LV ($P=0.25$) and between LV and healthy controls ($P=0.80$). The cutoff value was 9.8 U/ml for IgM anti-PS/PT antibody by ROC curve between CPN and healthy controls. In CPN, IgM anti-PS/PT antibodies had a tendency to be positive (80.0%), compared with other aPL. In addition, some LV cases (45.5%) also had the same antibodies.

These results strongly indicate that IgM anti-PS/PT antibodies in particular may 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 a pathogenic mechanism which is distinct from systemic polyarteritis nodosa. Our speculation is that a thrombotic change of small muscular arteries in the subcutaneous tissues might cause a progression to CPN due to vascular endothelial dysfunction, which may be related to IgM anti-PS/PT antibodies.

The authors indicate no conflict of interest.

References

1) **Wakabayashi N, Ishiguro N, Hayama M et al**: Antiphospholipid Antibodies in Patients with Cutaneous Polyarteritis Nodosa and Livedo Vasculopathy: An Initial Report. J Tokyo Wom Med Univ **83**: 86–94, 2013

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（追加報告）

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我々は2013年4月25日発行の本雑誌に発表した論文（若林奈津子ほか：東京女子医科大学雑誌　第83巻　第2号　86～94頁）で，皮膚型結節性多発動脈炎23例（計24例中，1例は欠測），リベド血管症11例，健常人コントロール16例で抗フォスファチジルセリン・プロトロンビン複合体（anti-PS/PT）IgM抗体を測定し，皮膚型結節性多発動脈炎におけるanti-PS/PT IgM抗体の関与の可能性について述べた．その後，皮膚型結節性多発動脈炎2例，健常人コントロール38例を追加し，皮膚型結節性多発動脈炎計25例，健常人コントロール計54例について再検討した結果，皮膚型結節性多発動脈炎と健常人コントロールの間でanti-PS/PT IgM抗体の値に有意差が得られたので，追加報告にて可及的速やかに報告する．

再検討の結果，皮膚型結節性多発動脈炎の25例中20例（80%）でanti-PS/PT IgM抗体が陽性であり，健康人コントロールと比較して有意差（$p<0.05$）をもって高値を示したことから，anti-PS/PT IgM抗体が皮膚型結節性多発動脈炎の発症機転において何らかの役割を担っていると考えた．一方，anti-PS/PT IgM抗体はリベド血管症でも11例中5例（45%）で陽性であり，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anti-PS/PT IgM抗体陽性という共通の基盤をもつことが示唆された．

以上より，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．