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SHORT COMMUNICATION

Significance of Two Skin Biopsy Performances with Consecutive Deeper Sections in the Differential Diagnosis Between Cutaneous Polyarteritis Nodosa and Livedo Vasculopathy

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Cutaneous polyarteritis nodosa (CPN) is a necrotizing vasculitis of medium-sized arteries within the skin, without the involvement of internal organs (1, 2). Histopathology is the gold standard diagnostic tool for CPN (3). Deeper sections of tissue specimens are used in many laboratories to enhance the sensitivity of diagnosis (4–9). This study retrospectively investigated the utility of taking 2 skin biopsies with consecutive deeper sections in improving diagnostic accuracy in patients with CPN.

PATIENTS AND METHODS

A total of 101 patients (30 men, 71 women; mean age 45.4 ± 17.9 years) with CPN seen at the Department of Dermatology, St Marianna University School of Medicine between 2003 and 2012 were investigated retrospectively. In all patients, necrotizing vasculitis shown histopathologically was observed in the lower dermis and/or the subcutaneous fat. Patients were diagnosed according to criteria outlined in our previously reported articles (3, 10–12). None of the patients had been treated with corticosteroids, immunosuppressants or vasodilators at the time of serum sampling. Anti-neutrophil cytoplasmic autoantibodies were negative. Furthermore, none of the patients demonstrated any evidence of a co-existing malignancy, other autoimmune diseases or viral hepatitis, nor were any of the patients positive for mixed cryoglobulinaemia.

Until 2008, the standard patient handling protocol in our department was to take a single skin biopsy from the cutaneous lesions. However, as it was considered necessary to improve the accuracy of our histopathological findings for the diagnosis of CPN, in 2009 we began taking 2 skin biopsies from 2 cutaneous lesions at the same time from each patient, with their informed consent. Deeper sections in the present study indicate a series of the 50th, 100th, and 150th of 3-μm cut intervals from a paraffin block of a skin biopsy sample. When there was no evidence of necrotizing vasculitis in the initial section, we proceeded to the consecutive deeper sections.

All data are expressed as means ± standard deviations (SD). A p-value < 0.05 was considered to be statistically significant. Differences among qualitative results were compared using the χ^2 test. All analyses were performed using SPSS (SPSS Inc., Chicago, IL, USA).

This study was approved by the St Marianna University Ethics Committee, and informed consent was obtained from all patients (No. 1117).

RESULTS

Case report

A 23-year-old woman was admitted to our hospital with a 3-week history of skin lesions distributed over her lower extremities to her feet. She presented with cutaneous nodules, purpuric lesions, and erythematous macules with livedo racemosa on her legs (Fig. 1A, C). Skin biopsy specimens were obtained from 2 cutaneous nodules on her left lower extremity and the internal portion of her right sole. Following our standard procedures, microscopic examination of cutaneous nodules on her right sole showed necrotizing vasculitis in the subcutaneous fat in the initial section by standard histopathological methods (Fig. 1B). However, cutaneous nodules on her left lower extremity did not reveal necrotizing vasculitis in the initial section (Fig. 1C). Upon further examination of consecutive deeper sections, we detected necrotizing vasculitis in the 100th cut intervals from the paraffin block, but not in the 50th or 150th (Fig. 1D, E).

Retrospective analysis

The 101 patients were divided into 2 groups: Seventy-nine patients (Group 1) underwent one skin biopsy and the other 22 patients (Group 2) underwent 2 skin biopsies at the same time in the retrospective study.

In Group 1 (26 men, 53 women; mean age 46.4 ± 18.5 years), 69 patients showed histopathological evidence of necrotizing vasculitis in the initial section according to the standard method. A further 10 patients showed histopathological evidence of necrotizing vasculitis only in the consecutive deeper sections; 2 were diagnosed by the 50th section, 5 by the 100th section, and 3 by the 150th section.

In Group 2 (4 men, 18 women; mean age 42.2 ± 15.4 years), 10 patients showed histopathological evidence of necrotizing vasculitis in initial sections of both skin biopsies. The other patients showed histopathological evidence of necrotizing vasculitis only in consecutive deeper sections or in an initial section of only one of the skin biopsies. Overall, it was possible to diagnose 12 additional CPN patients in Group 2 using consecutive deeper sections of 2 skin biopsy samples.

The accuracy of diagnosis for necrotizing vasculitis in the skin biopsies of our patients was significantly higher in Group 2 compared with Group 1 ($\chi^2 = 17.72$, $p = 0.0000255$).

DISCUSSION

We could detect histopathologically diagnosed necrotizing vasculitis more accurately in Groups 1 and 2 using the consecutive deeper sections skin biopsy method.

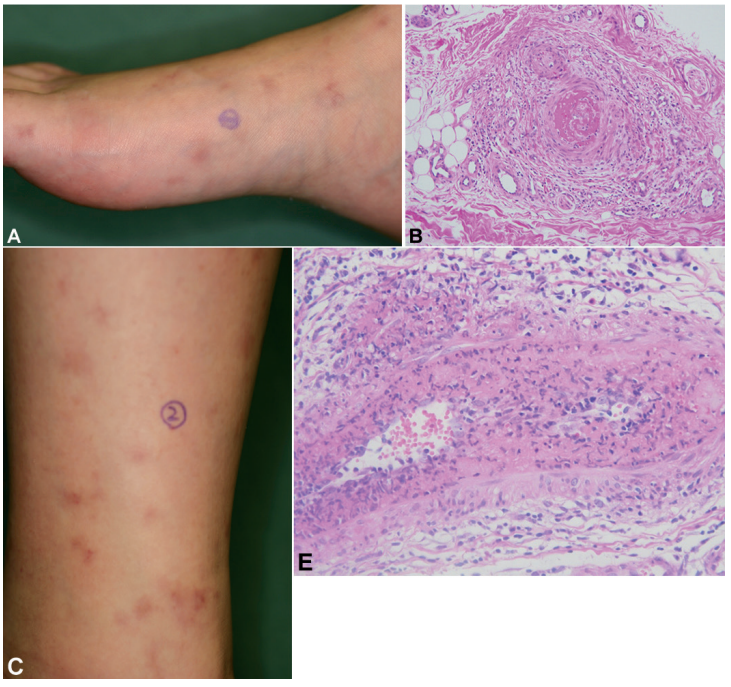

Fig. 1. (A) Purpuric cutaneous nodules on the right sole. (B) Fibrinoid necrosis, admixture of neutrophils and lymphocytes in and around blood vessels, and nuclear dust characteristics of necrotizing vasculitis in the subcutaneous fat were found by an initial section. (C) Cutaneous nodules and purpuric lesions with livedo in the left lower extremity. (D) Consecutive deeper sections in the skin biopsy specimen in the cutaneous nodule on the left lower extremity indicated #2 in (C) (See Fig. 1 (A–E)[1]). (E) Necrotizing vasculitis in the 100th deeper section.

Furthermore, we found a higher rate of detection of necrotizing vasculitis shown histopathologically from 2 biopsies with deeper sections (Group 2) compared with a single skin biopsy with deeper sections (Group 1). Based on these findings, we suggest that consecutive deeper sections and taking 2 skin biopsy samples at the time of evaluation could lead to increased rates of detection of necrotizing vasculitis in patients with CPN. Bruecks et al. (13) examined the utility of consecutive deeper sections in improving diagnostic accuracy for small skin biopsies. This more careful histopathological analysis could facilitate the detection of hidden necrotizing vasculitis in skin biopsy samples.

Livedo vasculopathy is diagnosed based on clinical features such as livedo appearance, skin ulcerations, and purpuric lesions on the lower extremities (14). A skin biopsy is used to confirm that there is no histopathological evidence of necrotizing vasculitis. In contrast, a diagnosis of CPN requires the presence of necrotizing vasculitis shown histopathologically as a key finding. The distinction between CPN and livedo vasculopathy is sometimes subtle from a dermatological point of view and the disease entities are controversial among expert dermatologists. Confusion can occur due to inconclusive skin biopsy findings, leading to failure to confirm necrotizing vasculitis in some cases. If we had diagnosed CPN patients in the present study using only an initial section without the consecutive deeper section method, some of them would have been diagnosed with livedo vasculopathy instead of CPN. We propose that 2 skin biopsy performances with consecutive deeper sections are required to establish an accurate diagnosis in patients with CPN.

[1]http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1603

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