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Notalgia paresthetica: The histopathological findings of 17 cases

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Introduction: **Notalgia paresthetica (NP) is a chronic disease characterized by sensory neuropathy which holds the skin, characterized by pruritus in which pain, paresthesia and/or hypersthesia were concomitant, and accompanied by remission and aggravation. Although NP is a common condition, it is rarely diagnosed by clinicians. For this reason, there are not too many series with many cases in the literature investigating this entity. In this study, we tried to reveal the histopathological findings of NP in the series with the highest number of cases in the literature and contribute to the clarification of the pathogenesis of the disease.** ***Materials and methods:*** **Punch biopsy materials of 17 patients diagnosed with notalgia parestetica in Çorum Erol Olçok Education and Research Hospital were included in the study. 4 mm diameter punch biopsy material was obtained from each patient. Tissues were embedded in paraffin blocks and after fixation, 5 pieces of sections with 4 micron thickness were obtained from each tissue with a microtome device. Three of the sections were stained with Hematoxylin Eosin, 1 of them were stained with Crystal violet for amyloid determination and 1 of them were stained with Perioidic Acid Schiff (PAS) for the detection of fungi and vasculitis. The satined slights were examined in light microscope (Nikon Ci). Each slights were evaluated by a single pathologist in detail in terms of epidermal changes and dermal changes.** ***Results:*** **Of the 17 patients included in the study, 13 (76.5%) were female and 4 (23.5%) were male. The age of the patients ranged from 19 to 63 years, with an average of 44.2 years. Epidermal changes were detected in 8 (47%) cases. The average age of the patients with epidermal changes was 31.6 years and the average age of the patients without epidermal changes was 48.7 (p <0.001) Hyperpigmentation in the basal of the epidermis was seen in 3 (17.6%) cases. The two most common findings in dermis were perivascular lymphocytes and melanophages. Perivascular lymphocyte infiltration was observed in 15 (88.2%) cases while melanophages were observed in 13 (76.4%) cases. Amyloid accumulation was not detected in any of the 17 cases with crystal violet. In 2 cases lymphocytic vasculitis was observed in the dermis.** ***Conclusion:*** **NP is a chronic disease accompanied by epidermal and dermal changes. The most common epidermal change is single cell necrosis and dermal change is perivascular lymphocyte infiltration and melanin incontinence. In addition to the literature, lymphocytic vasculitis was found in two cases in our study. However, more cases and studies are needed to assess whether vasculitis is a cause or consequence of the disease.**

INTRODUCTION

Notalgia paresthetica (NP) is a chronic disease characterized by sensory neuropathy which holds the skin, characterized by pruritus in which pain, paresthesia and/or hypersthesia were concomitant, and accompanied by remission and aggravation. (1 - 4) It is a well-limited hyperpigmented patch lesion, which its dermatologic finding is thought to be due to chronic irritation and pruritus (5-8). Before being clinically identified, NP cases received different diagnoses such as psychosomatic disorder, cutaneous dorsal amyloidosis or lichen amyloidosis. (9–12, 22)

Although NP is a common condition, it is rarely diagnosed by clinicians. For this reason, there are not too many series with many cases in the literature investigating this entity. There are very few studies examining the histopathology in particular (13-15). In this study, we tried to examine the histopathological findings of NP and to demonstrate the pathological findings observed in punch biopsies, thus contributing to the elucidation of the pathogenesis of the disease.

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MATERIALS AND METHODS

Punch biopsy materials of 17 patients diagnosed with notalgia parestetica in Çorum Erol Olçok Education and Research Hospital were included in the study. 4 mm diameter punch biopsy material was obtained from each patient. The materials were fixed in 10% formaldehyde solution for 18-24 hours and each tissue was divided into 2 mm slices and placed in tissue cassettes. After fixation, 5 sections with 4 microns thickness were obtained with microtome device from each of the tissues embedded in paraffin blocks. Three of the sections were stained with Hematoxylin Eosin, 1 of them were stained with Crystal violet for amyloid determination and 1 of them were stained with Perioidic Acid Schiff (PAS) for the detection of fungi and vasculitis. The satined slights were examined in light microscope (Nikon Ci). Each slights were evaluated by a single pathologist in detail in terms of epidermal changes and dermal changes. The data were controlled for normal distribution. No normality was found and Mann whitney U test was used to compare averages. P <0.05 was accepted as the statistical significance limit. Statistical analyzes were evaluated using SPSS program 21.0 version (SPSS Inc., Chicago, Ill, USA).

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Table 1 Histopathological evaluation results of the cases

	sex	age	Epidermal changes	Basal hyperpigmentation	Perivascular lymphocyte infiltration	Dermal amyloidosis	Melanophages in dermis	Other dermal changes
Case 1	F	40	necrotic keratinocytes	None	Moderate	None	Moderate	
Case 2	F	58	None	Mild	None	None	None	
Case 3	M	33	Irregular acanthosis	None	Intense	None	Mild	
Case 4	F	63	None	None	Mild	None	Intense	
Case 5	M	42	Mild spongiosis and spongiotic vesicle formation	None	Mild	None	None	
Case 6	M	19	Necrotic keratinocytes and irregular acanthosis	None	Mild	None	None	
Case 7	F	32	Necrotic keratinocytes and irregular acanthosis	Mild	Mild	None	Moderate	
Case 8	F	37	None	None	Moderate	None	Mild	
Case 9	F	23	Necrotic keratinocytes	None	Mild	None	Mild	
Case 10	F	55	None	None	Intense	None	Mild	Lymphocytic vasculitis
Case 11	F	45	None	None	Intense		Mild	
Case 12	F	68	None	None	Mild	None	Mild	
Case 13	F	37	Necrotic keratinocytes	None	Mild	None	Mild	
Case 14	M	35	None	None	Moderate	None	Mild	
Case 15	F	58	None	Moderate	None	None	None	
Case 16	F	57	None	None	Mild	None	Mild	
Case 17	F	50	Spongiosis	None	Intense	None	Moderate	Lymphocytic vasculitis

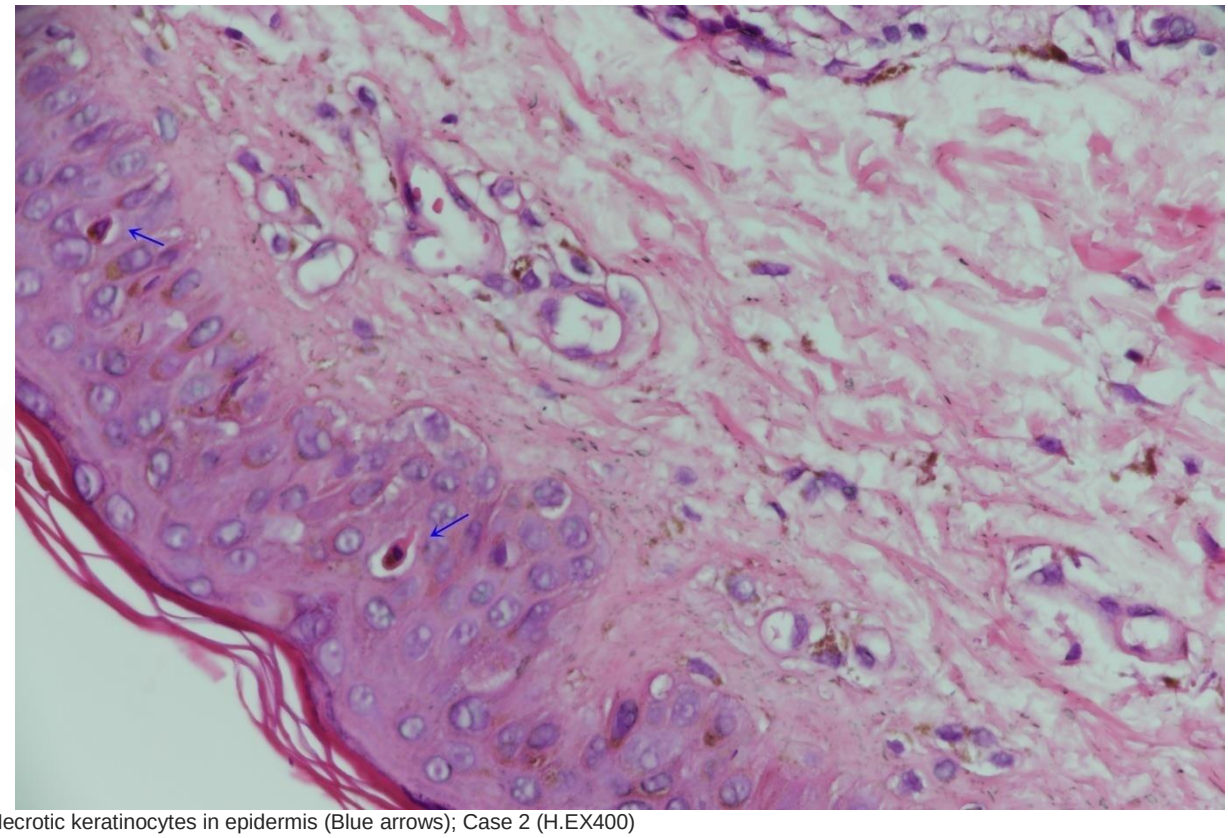

Figure 1 Necrotic keratinocytes in epidermis (Blue arrows); Case 2 (H.EX400)

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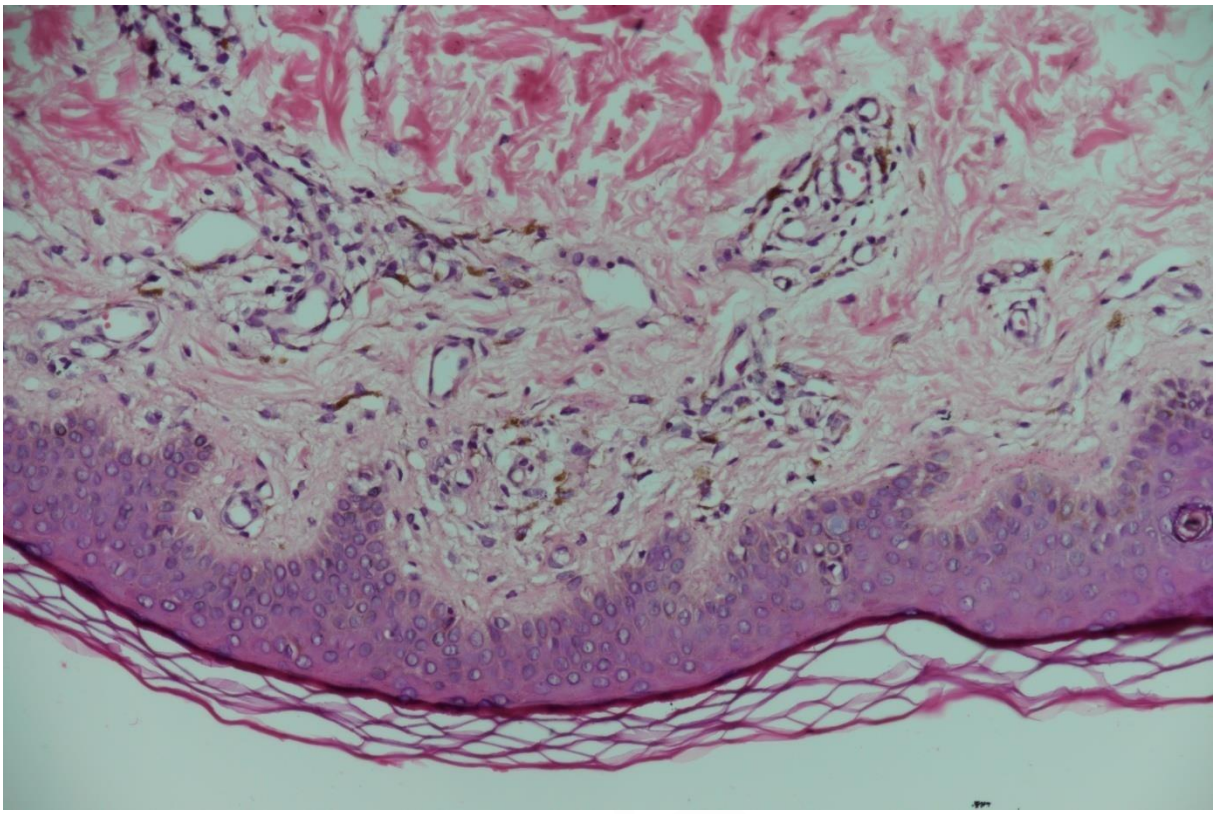

Figure 2 İntense melanophages in dermis and mild perivascular lymphocytes; Case 4 (H.EX200)

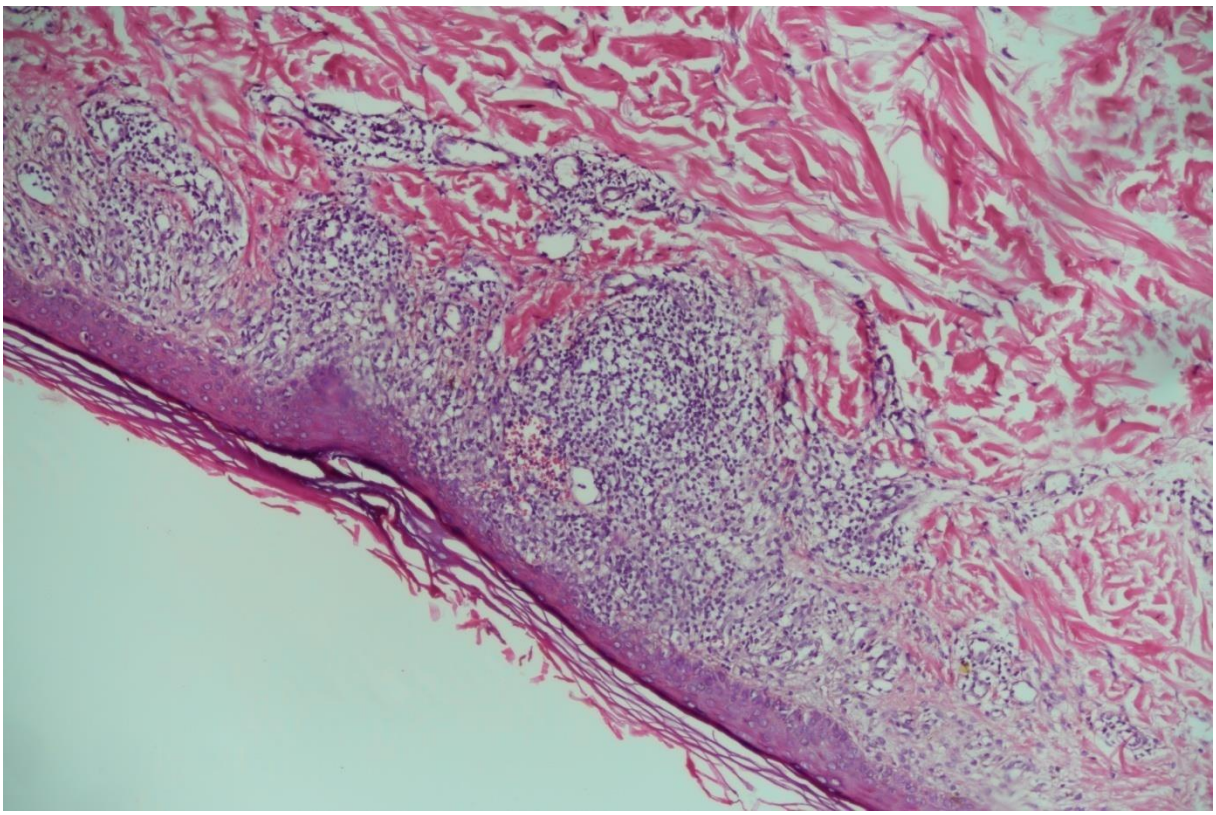

Figure 3 İntense perivascular lymphocytes in dermis, axtravaze erythrocytes and endothelial swelling; Lymphocytic vasculitis, case 10 (H.EX100)

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RESULTS

The study included 17 patients with NP dİagnosis. Of these patients, 13 (76.5%) were female and 4 (23.5%) were male. The patients' ages ranged from 19 to 63 years, with an average of 44.2 years. Epidermal changes were detected in 8 (47%) cases. The most common epidermal changes were necrotic keratinocytes and they were observed in 5 cases. (Figure 1)Irregular acanthosis was observed in 3 cases and spongiosis was observed in 2 cases. The average age of the patients with epidermal changes was 31.6 years, and the average age of the patients without epidermal changes was 48.7 ($p < 0.001$). The average age of the patients with epidermal changes was lower in a statistically significant way lower than those without epidermal changes. Hyperpigmentation in the basal of the epidermis was seen in 3 (17.6%) cases.Mild pigmentation was observed in 2 cases while moderate pigmentation was observed in 1 case (Table 1).

The two most common findings in dermis were perivascular lymphocytes and melanophages (Figure 2). Perivascular lymphocyte infiltration was observed in 15 (88.2%) cases and melanophages were observed in 13 (76.4%) cases. Perivascular lymphocyte infiltration was mild in 9 cases, severe in 3 cases, and moderate in 1 case. Melanophages in the dermis were mild in 9 cases, moderate in 3 cases and intense in 1 case (Table 1). Amyloid accumulation was not detected in any of the 17 cases with crystal violet. In 2 cases, lymphocytic vasculitis was observed in the dermis (Case 10 and 17). Two of the patients with lymphocytic vasculitis were women and their ages were 50 and 55 years (Table 1), (Figure 3).

DISCUSSION

Although NP is considered to be sensory neuropathy, its pathogenesis is still not fully elucidated. (12) The accused factors include genetics, increased dermal innervation, thinning of the spinal nerves, trauma or compression (5, 15, 17,18).

In a study including 12 cases conducted by N.raison Peyron et al., F/M ratio was found to be 3:1. (14) In a study including 10 cases conducted by Ekin Şavk et al., this rate was found to be 4:1.In our study, this ratio is 3:1 and complies with the literature.

The diagnosis of NP is usually made in the middle and advanced age, and the average age of the patients varies between 59 and 62 years in the literature (2.6,14,19-20). In our study, the average age of the patients was found to be 44.2 years and it was found to be lower than the literature. This may be because the number of patients in our study is higher than the case series in the literature.

In the study including 10 cases conducted by Ekin Ş. et al, epidermis in 9 cases was observed as normal and in only 1 case mild hyperkeratosis was observed (13). N.raison Peyron et al., in their 12-case study, except epidermis basal hyperpigmentation, no epidermis features were seen. In their study of Weber PJ, necrotic keratinocytes were detected in the epidermis (14). In our study, epidermal pathology was observed in 8 cases. The most common pathology was necrotic keratinocyte detected in 5 cases. The average age of the patients with epidermal change was found to be 31. 6 years, and the average age of the patients without epidermal change was found to be 48. 6 years. The probable cause of this may be the detection of epidermal changes in early periods and the regression in epidermal changes as the duration of exposure to disease increases and dermal changes come to the fore. In the literature, dermal changes in NP have been reported as perivascular lymphocytes and melanin incontinence (13-14). In our study, the two most common findings in the dermis were melanin incontinence and perivascular lymphocyte infiltration. The main reason for this may be postinflammatory hyperpigmentation due to chronic pruritus revealed in the case.

In the studies, amyloid deposition was detected in NP cases in varying proportions in dermis (14-15). However, Ekin Şavk et al. reported no amyloid deposition in any of 10 cases. (13) Also in our study, no amyloid deposition was observed in any of the 17 cases. Westermark et al. indicated that macular amyloidosis and NP were two different entities and suggested that cases with amyloid should not be evaluated as NP (21). Our study also supports this suggestion and no cases of amyloid accumulation have been detected in our cases.

In our study, unlike the literature, lymphocytic vasculitis was observed in 2 cases. Two of these patients were female. No NP cases accompanied by lymphocytic vasculitis have been reported previously in the literature.

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