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Comparison of Clinical and Histopathologic Findings of Pathergy Test with Disposable/Sharp and Nondisposable/Blunt Needles in Behçet's Disease

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Aim: The aim of this study was to determine whether using blunt instead of sharp needles presented any advantage and whether the histopathological interpretation prevailed over the clinical interpretation.

Materials and Methods: This study was performed on 60 Behçet's disease (BD) patients and 20 control subjects. The pathergy test was applied to all subjects intradermally with sharp and blunt needles and the histopathology of each test result was studied.

Results: In the active period of BD (40 patients), positive test results were obtained in 34 (85.0%) patients using blunt needles and in 13 (32.5%) using sharp needles (P = 0.0001). In the active group, there was a significant difference in results when compared with the histopathologic findings (P < 0.05). In the remission period group (20 patients), positive results were obtained in 9 (45.0%) patients with blunt needles and in 2 (10.0%) with sharp needles (P = 0.013). In the remission group, there were no significant differences in results when compared with the histopathologic findings. In the control group patients, all blunt and sharp needle pathergy tests were negative.

Conclusions: This study has demonstrated that a higher positivity rate is obtained in pathergy tests using blunt needles when compared with sharp needles. We suggest that clinical interpretation of the pathergy test with blunt needles is adequate to determine activity of BD; histopathologic interpretation does not provide any extra advantages.

Key Words: Behçet's disease, blunt needles, histopathological interpretation, pathergy test, sharp needles

Behçet Hastalarında Künt ve Sivri Uçlu İğnelerle Yapılan Paterji Testinin Klinik ve Histopatolojik Bulgularının Karşılaştırılması

Amaç: Bu çalışmanın amacı künt uçlu iğnelerle yapılan uygulamanın sivri uçlu iğnelerle yapılana ve histopatolojik değerlendirmenin klinik değerlendirmeye bir üstünlük sağlayıp sağlamadığını değerlendirmektir.

Yöntem ve Gereç: Çalışmaya 60 Behçet hastası ve 20 kontrol grubu hastası alındı. Paterji testi tüm hastalara künt ve sivri uçlu iğnelerle intradermal olarak uygulandı ve test sonuçları histopatolojik olarak değerlendirildi.

Bulgular: Aktif dönemdeki 40 Behçet hastasından künt uçlu iğne uygulanan hastaların 34'ünde (% 85) ve sivri uçlu iğne uygulanan hastaların 13'ünde (% 32.5) pozitiflik saptandı (p=0.0001). Aktif dönemde histopatolojik bulgular arasında da belirgin farklılıklar vardı (P < 0.05). Remisyon dönemindeki grupta (20 hasta) künt uçlu iğne uygulanan 9 (% 45) ve sivri uçlu iğne uygulanan 2 (% 10) hastada pozitif sonuç alındı (P = 0.013). Remisyon grubunda histopatolojik bulgulardaki farklılıklar istatistiksel olarak anlamlı değildi. Kontrol grubunda hem künt, hem de sivri uçlu iğnelerle yapılan paterji testi sonuçları negatifti.

Sonuç: Bu çalışmada künt uçlu iğnelerin kullanılmasıyla sivri uçlu iğnelere göre daha yüksek oranda pozitiflik elde edildiği görülmüştür. Künt uçlu iğnelerle uygulanan paterji testinin klinik olarak değerlendirilmesinin Behçet hastalığı aktivitesini değerlendirmede yeterli olduğunu ve histopatolojik değerlendirmenin ekstra bir avantaj sağlamadığını düşünmekteyiz.

Anahtar Sözcükler: Behçet hastalığı, künt uçlu iğne, histopatolojik değerlendirme, paterji testi, sivri uçlu iğne

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Introduction

Behçet's disease (BD) is a type of vasculitis with unknown etiology that can affect multiple systems of the human body (1,2). Unfortunately, there is no specific laboratory test to diagnose BD. All the criteria for BD recognized by the International BD Study Group are based on clinical signs and symptoms, except for the pathergy test (PT) (3). Recently, questions have arisen regarding the positivity of PT in the diagnosis of BD (4). It has been considered that the thickness of the needle affects PT positivity, and also that the histopathologic examination of the skin lesion that occurs after PT can be useful in confirming BD diagnosis (5,6).

We designed this prospective study to determine whether using nondisposable/blunt needles instead of disposable/sharp needles presented any advantage and whether the histopathologic interpretation prevailed over the clinical interpretation. Secondly, we aimed to ascertain if the PT could be a criterion in determining disease activity.

Materials and Methods

The PT was performed in 60 BD patients (27 M, 33 F) who were diagnosed with BD according to the International BD Study Group criteria (3). Twenty patients with dermatoses (11 F, 9 M) were selected to serve as the control group. The average age of the BD patients was 33.50 ± 9.64 years and of the control group was 30.50 ± 14.89 years. All subjects were informed about the procedure and provided written informed consents.

The patients in the study group with one or more clinical symptoms were assigned to the active period group (n: 40), and patients with prior diagnosis of BD but without any recent symptoms or signs were assigned to the remission period group (n: 20). The patient and control groups did not take immunosuppressant drugs, steroids, colchicine or non-steroidal anti-inflammatory drugs (NSAIDs) for at least one month before the test. In the control group, patients with any history of clinical symptoms similar to BD, any history of positive PT diseases such as pyoderma gangrenosum, erythema elevatum diutinum and inflammatory bowel diseases were excluded.

Pathergy test was performed with disposable/sharp and nondisposable/blunt needles in all patients. Nondisposable/blunt and disposable/sharp needles of type 20 G = No.1 were used in the tests. Hairless and avascular regions in the flexor part of both forearms were chosen to perform PT. Skin was cleaned with alcohol before the test. PT was done with nondisposable/blunt needles on the right forearm and with disposable/sharp needles on the left forearm. The test was applied intradermally for each type of needle without any rotational movements and was evaluated clinically after 24 and 48 hours (h). The occurrence of erythema without any indurations was considered as 'negative' and the occurrence of papules and pustules was considered as 'positive'. For histopathologic examination, biopsy at the intradermal puncture site was taken after 48 h.

The statistical analysis was carried out using SPSS (Statistical Package for Social Sciences) 10.0 for Windows. The Pearson chi-square test and continuity correction test were used for statistical analysis. *P* values less than 0.05 were defined as statistically significant.

Results

Clinical Results

Among the 40 patients in the active period of BD, positive PT results were obtained in 34 patients (85.0%) using nondisposable/blunt needles and in 13 patients (32.5%) using disposable/sharp needles, and the difference between the two groups was statistically significant (P = 0.0001).

Among the 20 patients in the remission period group, positive PT results were obtained in 9 patients (45.0%) using nondisposable/blunt needles and in 2 patients (10.0%) using disposable/sharp needles, and the difference between the two groups was statistically significant (P = 0.013).

When active and remission periods were compared, PT positivity with nondisposable/blunt needle was found to be statistically higher in active period patients (P = 0.001). PT positivity with disposable/sharp needle was higher in the active period, but the difference was not statistically significant (P = 0.058). PT positivity results with nondisposable/blunt and disposable/sharp needles in the BD patients are shown in Table 1.

In the control group patients, the results of PT with both nondisposable/blunt and disposable/sharp needle were negative. Difference in PT positivity with nondisposable/blunt and disposable/sharp needle in both the active and remission period groups was statistically significant when compared with the control group (P = 0.001, P = 0.002; P = 0.001, P = 0.04, respectively).

Table 1. Comparison of pathergy test results with nondisposable/blunt and disposable/sharp needles in the active and remission periods.

	Nondisposable/blunt needle		Disposable/sharp needle	
	Positive	Negative	Positive	Negative
Active period (%)	34 (85.0)	6 (15)	13 (32.5)	27 (67.5)
Remission period (%)	9 (45)	11 (55)	2 (10)	18 (90)

Histopathologic Results

Table 2 gives the histopathologic results of the PT in the patient and control groups. When positive and negative PT results with nondisposable/blunt needle and disposable/sharp needle were compared in the active period patients, the presence of perivascular lymphocytic infiltration, thickening of blood vessel walls, and extravasations of erythrocytes, and the coexistence of these three symptoms, which indicate blood vessel damage, were found statistically significantly more common in patients with positive PT using nondisposable/blunt needle than in patients with negative PT using nondisposable/blunt needle ($P < 0.05$, $P < 0.05$, $P < 0.05$ and $P < 0.05$, respectively). They were also found statistically significantly more common in patients with disposable/sharp needle positive PT than in patients with disposable/sharp needle negative PT ($P < 0.05$, $P < 0.05$, $P < 0.05$ and $P < 0.05$, respectively).

When PT results with nondisposable/blunt needle and disposable/sharp needle were compared in active period patients, the coexistence of perivascular lymphocytic infiltration, thickening of blood vessel walls, and extravasations of erythrocytes was found statistically significantly more common using nondisposable/blunt needle than disposable/sharp needle ($P = 0.044$).

Lymphocytic vasculitis was observed in 2 of the positive PT patients with nondisposable/blunt needles (7.4%), whereas no lymphocytic vasculitis was determined in the negative PT patients with nondisposable/blunt needles. In addition, neutrophilic infiltration was seen in 10 of the positive PT patients with nondisposable/blunt needles (29.4%), but in only 2 of the negative PT patients with nondisposable/blunt needles (33.3%).

Comparisons of the positive and negative test results with nondisposable/blunt needles and disposable/sharp needles in the remission period patients revealed no statistically significant differences. Comparisons of the histopathologic findings between nondisposable/blunt and disposable/sharp needles in the remission period patients also revealed no statistically significant differences.

Comparison of histopathologic findings of PT using nondisposable/blunt needles in the active and remission period patients, ignoring the results of the clinical interpretation of PT, revealed that the occurrence of edema in the upper layer of the dermis, perivascular neutrophilic infiltration, periadnexal neutrophilic infiltration, erythrocyte extravasations, neutrophilic leukocyte infiltration located in the dermis, neutrophilic vascular reaction, lymphocyte infiltration in fat tissue, and lymphocyte exocytosis in the epidermis was also statistically significantly higher in the active period than in the remission period ($P = 0.001$, $P < 0.005$, $P < 0.005$, $P < 0.005$, $P = 0.004$, $P = 0.001$, $P = 0.0019$, $P = 0.037$, respectively).

Discussion

Pathergy test is the nonspecific hyperactivity of the skin. Positive PT is the one of the important diagnostic criteria for BD; however, the incidence of PT positivity has declined in recent years. In the literature, the rate of positive PT in Turkey was shown as approximately 80% before 1984; however, the positivity rate decreased after 1986 (1,7). Studies have shown that the sharpness of the needle has a significant role in the positivity rate of PT (4,5,8). The wide use of the blunt and nondisposable needle before 1986 might be a reason for the high positivity rate of PT. After 1986, sterile and disposable needles began to be used routinely to avoid spread of infectious diseases, such as human immunodeficiency virus (HIV) and hepatitis B virus (HBV). The same situation is true for other developing countries. The

Table 2. Histopathologic findings in the Behçet's disease and control groups.

Patient/Control	Active period				Remission period				Control group			
Needle	ND/B +	ND/B −	D/S +	D/S −	ND/B +	ND/B −	D/S +	D/S −	ND/B +	ND/B −	D/S +	D/S −
n	34	6	13	27	9	11	2	18	0	20	0	20
EdE	11	0	5	2	3	0	1	0	0	0	0	0
Lpyi	34	6	13	22	10	8	2	15	0	19	0	13
Npvi	31	4	4	12	5	3	2	3	0	1	0	0
Lpai	24	2	6	4	8	1	2	1	0	1	0	1
Npai	14	2	1	0	6	1	1	1	0	0	0	1
BVT	17	1	4	2	5	1	1	2	0	7	0	2
EE	16	1	5	3	2	0	0	4	0	1	0	0
AE	3	0	1	0	1	0	0	0	0	0	0	0
DBL	16	4	3	1	3	2	1	3	0	6	0	3
Nİ	21	3	3	3	5	1	2	1	0	5	0	2
V	2	0	0	0	1	0	0	0	0	0	0	0
NVR	10	2	1	1	1	0	0	0	0	0	0	0
LIFT	10	0	1	0	3	1	1	0	0	0	0	0
ExE	10	0	6	3	3	0	0	1	0	1	0	0

ND/B: nondisposable/blunt; D/S: disposable/sharp; EdE: edema on epidermis; Lpvi: lymphohistiocytic perivascular infiltration; Npvi: neutrophilic perivascular infiltration; Lpai: lymphohistiocytic periadnexal infiltration; Npai: neutrophilic periadnexal infiltration; BVT: blood vessel thickening; EE: erythrocyte extravasation; AE: acanthosis in the epidermis; DBL: degeneration in basal layer; NI: neutrophilic infiltration; V: vasculitis; NVR: neutrophilic vascular reaction; LIFT: lymphohistiocytic infiltration in fat tissue; ExE: exocytosis in epidermis; n: number of patients.

reason for the low positivity rate of PT in developed countries might be due to the use of sterile and disposable needles for years (4,8,9).

When the needle reaches the dermis, a pathergy reaction occurs. Dilsen et al. (4) and Akmaz et al. (5) compared the nondisposable/blunt and disposable/sharp needles in BH patients and showed more positive PT results with nondisposable/blunt needles. Dilsen et al. (4) suggested that calcium deposit accumulation at the tip of nondisposable/blunt needles occurred when they were sterilized in boiling water, and that they therefore became more traumatic than disposable/sharp needles.

The results of the test depend on the sharpness, type, sterility, and size of the needle, number of pricks, and disease activity (7). The most important factor that affects PT results is the thickness of the needle. There is no standard for measurement of needle thickness. The most important aim in the PT is to cause trauma to provoke neutrophilic vascular reaction or leukocytoclastic vasculitis. A thin needle may not be sufficient to induce reaction (4,5). Ozarmagan et al. (8) compared 20G and 26G disposable needles, and they found 65% positive results with 20G needles and 35% positive results with 26G needles. Dilsen et al. (4) compared needles of different thicknesses, and they demonstrated more positive results with 20G needles than wih 26G needles. For this reason, we used 20 G needles for the tests in our study group of patients.

Pathergy test gives more positive results in the active period than remission period (5,9). In Akmaz et al.'s (5) study, PT with nondisposable/blunt needles was positive in 81.3% in the active period and in 45.5% in the remission period. PT with disposable/sharp needles gave 18.8% positive results in the active period, but no positive results were obtained in the remission period. Friedman-Birnbaum and colleagues (9) found 45 positive results in 46 patients in the active period. In our analysis, the positivity rate with nondisposable/blunt needles was

found statistically higher than with disposable/sharp needles and overall positivity rate with both needles was statistically significant higher in the active period. Therefore, in light of our encouraging results, we advocate using PT as an activity criterion in BD.

The clinical use of PT is very important in the diagnosis of BD. On the other hand, misinterpretation of the test might cause false-positive or false-negative results. For that reason, immunopathologic and histopathologic tests are recommended with PT (10). The histopathologic results of PT depend on the time of the biopsy (10,11). In the first 6 h, polymorphonuclear leukocytes (PMNLs) are dominant in inflammatory exudate. After 24 h, mononuclear cell infiltration in dermal vessels, edema in vessel endothelium, and edema and leukocytoclasia in reticular dermis are seen (10,11). Leukocytoclastic vasculitis and neutrophilic vascular reactions also occur after 24 h. Lymphocytic vasculitis and lymphocytic perivascular infiltrations are found later (12-15). In this study, all biopsies were taken after 48 h for confident comparisons. In histopathology of the PT, the presence of the vasculitis and neutrophilic vascular reaction are definitive but not a requirement. The perivascular and periadnexal lymphohistiocytic infiltration of varying intensity and their penetration in the deep dermis and moderate neutrophilic infiltration in the dermis are also important findings (12). In this study, lymphohistiocytic infiltration, blood vessel wall thickening, and erythrocyte extravasation were found statistically higher in positive PT in both nondisposable/blunt and disposable/sharp needle groups in the active period. This result was consistent with Akmaz et al.'s (5) studies. When the same histopathologic comparisons were done for the remission period, no statistically significant difference was observed.

Overall, we have shown a significant correlation between BD activity and PT with nondisposable/blunt needle. We could not identify any additional impact of histopathological interventions in this regard. Consequently, we believe that histopathological analysis would be more helpful in the diagnosis of clinically negative PT cases.

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