

Manometric Evaluation of the Esophagus in Patients with Behçet's Disease

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Key Words

Behçet's disease · Esophagus · Manometry

Abstract

Introduction: Gastrointestinal (GI) involvement in Behçet's disease (BD) mainly appears in mucosa and affects 5–40% of patients, however the effects of the disease on lower esophageal sphincter (LES) pressure and esophageal contractions are not well known. The aims of this study were to evaluate esophageal motor function and to identify whether there was any specific motility pattern for patients with BD who had upper GI symptoms without endoscopic abnormality. **Materials and Methods:** 25 patients with BD, with a mean age of 43.1 (range 20–66) years, were admitted to our clinic whose main complaints were dyspeptic such as reflux, epigastric pain, vomiting and bloating. 25 healthy and age-matched individuals were also included in the study as controls. After one night fasting, LES pressure and esophageal contractions were measured. **Results:** Esophageal motor abnormalities were detected in 16% (4/25) of these patients with manometric studies (non-specific esophageal motor disorder in 1, esophageal hypomotility in 2, and LES hypotension in 1 patient); 16% (4/25) of these patients had endoscopic findings and overall 32% (8/25) of the cases showed esophageal pathology. All cases with esophageal motor abnormalities were suffering from reflux and endoscopy showed grade B esophagitis in 2 of these cases. Median LES pressure and LES relaxation were significantly lower in patients with BD compared to the control group (16.8 ± 10.5 vs. 20.4 ± 6.1 , $p = 0.02$, and 92.1 ± 10.1 vs. 96.4 ± 4.5 , $p =$

0.03 respectively). **Conclusion:** Esophageal involvement in BD is significantly high. We propose manometric studies are necessary to evaluate esophageal manifestations in BD patients with esophageal symptoms even without endoscopic findings.

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Introduction

Behçet's disease (BD) is a chronic, relapsing, inflammatory disease characterized by recurrent oral aphthae and any of several systemic manifestations including genital aphthae, ocular disease, skin lesions, neurologic disease, vascular disease or arthritis. BD is considered to be a type of vasculitis. The prevalence of gastrointestinal (GI) involvement varies, from a low frequency in Turkey (3–5%) to a high frequency in Japan (50–60%) [1]. Ileocecal ulcerations are the most common GI lesions. Esophageal involvement is uncommon, reported to be 2–11% of the patients with BD [2], and this involvement mainly consists of esophageal ulcers. The ulcers can mainly be found in the middle or lower esophagus and may range from small lesions to severe deep ulcers [3]. Some patients with esophageal involvement are symptomatic. In these cases, dysphagia and odynophagia can be a presenting symptom which warrants upper GI endoscopic examination. However, not all patients have endoscopic findings although they have upper GI symptoms such as abdominal pain, bloating, nausea and heartburn suggesting functional dyspepsia [4]. Some of these upper GI symp-

toms may be the result of esophageal motor dysfunction.

Esophageal manometry has not been systematically performed in patients with this particular disorder and no specific motility pattern has been attributed to the disease. Therefore, the aims of this study were to evaluate esophageal motor function and to identify whether there was any specific motility pattern for patients with BD who had upper GI symptoms without endoscopic abnormality.

Materials and Methods

The study population of 25 patients with BD, who were referred to the gastroenterology outpatient clinic due to dyspeptic symptoms, were enrolled into the study. All BD patients fulfilled the diagnostic criteria of the International Study Group for BD [5]. Patients with BD who had two or more active clinical features related to BD at the time of the study were considered to have active BD, and those who had no symptoms apart from recurrent oral ulcers for at least 1 month prior to the study were considered to have inactive BD [6]. 25 age-matched patients with functional dyspepsia, who were diagnosed according to the Rome II criteria, were also included in the study and served as a control group. None of the patients were on drugs that might alter esophageal motor function during motility testing.

Patients entering the study were asked to complete a symptom questionnaire concerning the presence of heartburn, regurgitation, epigastric pain, nausea and vomiting. All patients had undergone upper GI endoscopic examination and esophageal motility testing on 2 separate days. Endoscopic examinations were performed by one of the investigators using a standard videogastroscope. Esophageal manometry was performed by using a single catheter containing 8 solid-state pressure transducers spaced at 5-cm intervals and attached to an online computer (MMS, Medical Measurement Systems, The Netherlands). Patients came to the laboratory after at least 8 h of fasting. The 8-channel catheter was lubricated and passed nasally and advanced into the stomach. A slow station pull-through was performed at 1-cm increments. Once the lower esophageal sphincter (LES) was profiled, the distal pressure transducer which included four lumens was placed in the high-pressure zone of the LES, so that the proximal pressure transducers were located 5, 10, 15 and 20 cm above the LES. A series of 10 wet swallows (with 5-ml water bolus) were given at 20–30 s intervals. Each contraction was recorded and then analyzed by a computerized software system (MMS) for amplitude, contraction and velocity. LES relaxation and residual pressures were also recorded.

The present study was approved by the Institutional Review Board of Ankara University Medical School and all patients signed informed consent before entering the study.

Statistical analyses were performed with SPSS 11.5 for Windows (SPSS Inc., Chicago, Ill., USA). All values were expressed as mean \pm SE unless otherwise stated. The differences between the groups were evaluated by Student's *t* test or the Mann-Whitney *U* test, depending on the normality of the data. A *p* value <0.05 was considered as significant.

Results

The mean age of the patients enrolled in the study ($n = 25$, 15 women) was 43.2 (range 21–64) years. Mean BD duration was 12.8 years and 13 of the patients had active disease during the study period. The clinical manifestations of BD, endoscopic and manometric findings, and GI symptoms in our cases are summarized in table 1. All patients in this study complained of upper GI symptoms, predominantly of heartburn ($n = 19$). Of the 25 patients who had undergone upper GI endoscopy, 4 showed endoscopic abnormalities which consisted of esophagitis according to the Los Angeles classification (1 grade A, 3 grade B) [7]. Manometry was abnormal in 4 patients (non-specific esophageal motor disorder in 1, esophageal hypomotility in 2, and LES hypotension in 1 patient). All cases were suffering from reflux symptoms and endoscopy showed grade B esophagitis in 2 of these cases. Upper endoscopies were normal in 2 other patients.

As a manometric finding, median LES pressure (mm Hg) and LES relaxation (%) were significantly lower in patients with BD compared to the control group (16.8 ± 10.5 vs. 20.4 ± 6.1 , $p = 0.02$, and 92.1 ± 10.1 vs. 96.4 ± 4.5 , $p = 0.03$ respectively) (table 2). There was no significant difference between LES relaxation duration (s) (8.4 ± 2.5 vs. 9.1 ± 1.7 , $p = 0.07$), contraction amplitude (mm Hg) (56.1 ± 22.3 vs. 59.9 ± 17.7 , $p = 0.73$) and peak velocity (s) (3.2 ± 1.1 vs. 3.5 ± 3.1 , $p = 0.89$) in patients with BD compared to the control group (table 2).

Median LES pressure (mm Hg), LES relaxation (%) and contraction amplitude (mm Hg) were 13.4 ± 5.6 , 89.2 ± 12.9 , and 55.6 ± 26.2 in active BD patients and 20.4 ± 13.3 , 95.1 ± 4.5 , and 56.7 ± 18.1 in inactive BD patients, respectively ($p = \text{NS}$, table 3).

Discussion

In our study, 25 BD patients with upper GI symptoms were evaluated. Esophageal motor abnormalities were detected in 16% of the patients with manometric studies; 16% of these patients had endoscopic findings and overall 32% of the cases showed an esophageal pathology. When the manometric evaluation of BD patients was compared with the functional dyspepsia control group, in BD cases a lower LES pressure and lower LES relaxation percentage were statistically significant.

Houman et al. [8] studied esophageal findings of 23 BD patients with or without GI symptoms by using endoscopy, manometric studies and histological evaluation.

Table 1. Clinical and laboratory features of patients with Behçet's disease

No.	Age	Sex	OU	GU	A	PT	U	PPE	EN	VT	NB	GI symptom	E	Manometry
1	42	F	+	+	-	+	-	-	-	-	-	Heartburn, bloating	N	N
2	64	F	+	+	-	+	+	-	-	+	-	Dysphagia	N	N
3	52	M	+	+	-	-	+	-	-	-	-	Heartburn	N	N
4	42	F	+	+	-	+	-	-	-	-	-	Heartburn	N	NEMD
5	37	M	+	+	-	-	-	-	-	-	-	Heartburn	N	N
6	57	M	+	+	-	+	-	-	-	-	-	Dysphagia	N	N
7	36	F	+	+	-	-	-	+	+	-	-	Heartburn	N	N
8	42	F	+	+	-	-	-	+	+	-	-	Heartburn	EA	N
9	49	F	+	-	-	-	-	-	-	-	-	Heartburn	N	EH
10	42	M	+	+	-	-	+	-	-	-	-	Dysphagia	N	N
11	57	F	+	+	-	-	-	-	-	-	-	Heartburn	N	N
12	21	F	+	+	-	-	+	-	-	-	-	Heartburn, bloating	N	N
13	47	F	+	+	-	+	-	+	+	-	-	Heartburn	EB	N
14	51	M	+	+	-	+	-	+	-	+	-	Heartburn, bloating	N	N
15	42	M	+	-	-	+	-	-	-	-	-	Heartburn	EB	EH
16	44	F	+	+	+	+	-	-	-	-	-	Dysphagia	N	N
17	22	F	+	+	-	+	-	-	-	-	-	Nausea, vomiting	N	N
18	51	F	+	+	-	+	-	+	-	-	-	Heartburn	N	N
19	28	M	+	-	-	-	-	-	-	-	-	Heartburn	N	N
20	43	M	+	+	+	+	-	+	-	-	-	Heartburn	N	N
21	57	M	+	+	+	+	-	+	+	-	-	Heartburn	EB	LH
22	43	F	+	+	-	-	+	-	+	+	-	Heartburn	N	N
23	30	M	+	-	-	+	-	+	+	-	+	Heartburn	N	N
24	49	F	+	+	+	-	-	-	-	-	-	Epigastric pain	N	N
25	34	F	+	+	-	-	-	+	-	-	-	Heartburn	N	N

OU = Oral ulceration; GU = genital ulceration; A = arthritis; PT = pathergy test; U = uveitis; PPE = papulopustular eruptions; EN = erythema nodosum; VT = vascular thrombosis; NB = neuro-Behçet; E = endoscopy; N = normal, EA = esophagitis grade A; EB = esophagitis grade B; NEMD = nonspecific esophageal motor disorder; EH = esophageal hypomotility; LH = lower esophageal sphincter hypotension.

Table 2. Esophageal manometric findings in patients with Behçet's disease and control group

	Behçet's disease (n = 25)	Control group (n = 25)	p
LES pressure, mm Hg	16.8 ± 10.5	20.4 ± 6.1	0.02
LES relaxation, %	92.1 ± 10.1	96.4 ± 4.5	0.03
Duration of LES relaxation, s	8.4 ± 2.5	9.1 ± 1.7	0.07
Esophageal contraction amplitude, mm Hg	56.1 ± 22.3	59.9 ± 17.7	0.73
Peak velocity, s	3.2 ± 1.1	3.5 ± 3.1	0.89

LES = Lower esophageal sphincter, s = seconds.

In this study group it is observed that 66% (14/21) of the cases had pathological findings. From the group of 20 patients that were evaluated with manometric studies, 4 of the patients had lower LES pressure, 2 had repetitive contractions, and 2 (1 also had a lower LES pressure) had lower amplitude of the contractions in the middle por-

tion of the esophagus. Abnormal findings were observed in the sum of 7 (35%) patients. In this study all the patients with esophageal motility problems demonstrated normal endoscopic findings. Esophageal involvement was not significantly correlated with disease duration, disease activity or any other aspect of BD. Apart from

Table 3. Esophageal manometry results in patients with active and inactive Behçet's disease (BD)

	Disease activity		p
	active BD (n = 13)	inactive BD (n = 12)	
LES pressure, mm Hg	13.4 ± 5.6	20.4 ± 13.3	0.2
LES relaxation, %	89.2 ± 12.9	95.1 ± 4.5	0.2
Duration of LES relaxation, s	8.6 ± 3.1	8.2 ± 1.8	0.8
Esophageal contraction amplitude, mm Hg	55.6 ± 26.2	56.7 ± 18.1	0.8
Peak velocity, s	3.3 ± 1.1	3.1 ± 0.9	0.8

LES = Lower esophageal sphincter; s = seconds.

microscopic findings in 1 case who showed vasculitis, all other endoscopic, manometric and histological abnormalities were non-specific. In our study it is also noted that esophageal involvement was not significantly correlated with disease duration or disease activity of BD.

Rohner et al. [9] studied intraluminal esophagus pressure in 3 BD patients and it is documented that all of these patients showed non-specific motility disorders. Rohner et al. comment that this motility disorder may be caused by neurological involvement.

Bottomley et al. [4] reported the first prospective study of esophagus in patients with BD. This study concerned 9 patients who underwent fiberoptic esophagogastroduodenoscopy; 3 patients were asymptomatic and 6 had upper GI symptoms at the time of endoscopy; 1 patient had evidence of grade I reflux esophagitis, 1 patient had an incidental pyloric canal ulcer, and 1 patient who had severe dysphagia on presentation was found to have a high esophageal stricture with accompanying ulceration. Although the number of patients was small in the study of Bottomley et al., the result obtained that the prevalence of esophageal involvement in BD was low (11%) and non-

specific. In this study it is noted that routine endoscopic evaluation is not necessary unless apparent esophageal symptoms are present.

In a retrospective analysis performed by Gürler et al. [10] in Turkey, GI involvement was observed in 62 (2.8%) of 2,147 BD patients. In this study, 7 cases with esophageal involvement were recorded while 55 others had ulcer in the terminal ileum, colon or in the rectum. Mori et al. [11] recorded lesions like esophageal erosion, ulcer, perforation, structure, etc., in the endoscopic evaluation of 5 BD patients in their study. In our study, 4 patients had different grades of esophagitis. It was also noted that reflux was the dominant symptom.

In conclusion, esophageal involvement in BD is significantly high. Esophageal involvement can be observed in 16% of BD patients if only endoscopic studies are performed. This ratio rises to one-third of all the patients by adding the manometric studies to this evaluation. We propose manometric studies are necessary to evaluate esophageal manifestations in BD patients with esophageal symptoms even without endoscopic findings.

References

- Sakane T, Takeno M, Suzuki N, Inaba G: Behçet's disease. *N Engl J Med* 1999;341:1284-1291.
- Bayraktar Y, Özaslan E, Van Thiel D: Gastrointestinal manifestations of Behçet's disease. *J Clin Gastroenterol* 2003;30:144-154.
- Lorenzetti ME, Forbes IJ, Roberts-Thompson IC: Oesophageal and ileal ulceration in Behçet's disease. *J Gastroenterol Hepatol* 1990;5:714-717.
- Bottomley WW, Dakkak M, Walton S, Bennett JR: Esophageal involvement in Behçet's disease. Is endoscopy necessary? *Dig Dis Sci* 1992;37:594-597.
- International Study Group for Behçet's Disease: Criteria for diagnosis of Behçet's disease. *Lancet* 1990;335:1078-1080.
- Ates A, Kinikli G, Düzgün N, Duman M: Lack of association of tumor necrosis factor alpha gene polymorphisms with disease susceptibility and severity in Behçet's disease. *Rheumatol Int* 2006;26:348-353.
- Lundell LR, Dent J, Bennett JR, et al: Endoscopic assessment of esophagitis: clinical and functional correlates and further validation of the Los Angeles classification. *Gut* 1999;45:172-180.
- Houman MH, Ben Ghorbel I, Lamloum M, et al: Esophageal involvement in Behçet's disease. *Yonsei Med J* 2002;43:457-460.
- Rohner HG, Wienbeck M, Sennekamp J, Rodermund OE: Esophageal manometry in Behçet's disease (abstract). *Z Gastroenterol* 1978;16:1-6.
- Gürler A, Boyabat A, Türsen U: Clinical manifestations of Behçet's disease: an analysis of 2,147 patients. *Yonsei Med J* 1997;38:423-427.
- Mori S, Yoshihira A, Kawamura H, Takeuchi A, Hashimoto T, Inaba G: Esophageal involvement in Behçet's disease. *Am J Gastroenterol* 1983;78:548-553.