Anti-alpha-enolase Antibody as a Serologic Marker and its Correlation with Disease Severity in Intestinal Behçet's Disease

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감사의 글

2005년 시작한 박사학위가 여러 우여 곡절 끝에 5년 만에 무사히 마칠 수 있기까지 도움을 주신 모든 분에게 감사 드립니다. 먼저 박사 과정 동안 많은 지도와 관심을 가져주신 김진홍 교수님께 깊이 감사 드리고, 바쁘신 와중에도 귀중한 시간을 내주시어 아낌없는 충고를 해 주신 조성원, 유병무, 이기명, 고광현 교수님께도 깊은 감사 드립니다.

초등학교 다니는 두 아이를 키우면서 더욱 더 느끼는 바이지만, 제가 태어나서 여기까지 올 수 있도록 항상 든든한 버팀목이 되어 주시고 사랑을 베풀어 주시며 제게 가장 큰 행복을 만들어 주신 아버님과 어머님께 감사 드리며, 아름답고 현명하게 아내를 키워주신 장모님께도 깊은 감사를 드립니다. 그리고, 바쁜 와중에도 제가 병원일과 학교 일을 무사히 할 수 있도록 도움을 주신 매형, 누나 그리고 조카 미경이 에게도 고마움을 전합니다. 그리고, 멀리 떨어져서 자주 보지는 못하지만 미국에 있는 하연이, 수연이 가족과도 이 기쁨을 나누고 싶습니다.

마지막으로 제 인생의 반려자로 저에게 항시 끝없는 조언과 내조로 제 삶의 가장 큰 행운을 가져다 준 아내에게 고마움을 전하고, 어느덧 불쑥 커버려 이제는 듬직해진 아들 중혁과 항상 웃는 얼굴로 아빠를 즐겁게 해주는 딸 지수에게 너희들이 아빠가 하늘에서 받은 가장 큰 선물임을 전하며 이 논문을 바칩니다.

저자 씀

-ABSTRACT-

Anti-alpha-enolase Antibody as a Serologic Marker and its Correlation with Disease Severity in Intestinal Behçet's Disease

Intestinal Behçet's disease (BD) is a chronic inflammatory bowel disease, as are Crohn's disease (CD) and ulcerative colitis (UC). But unlike CD and UC, serologic markers for intestinal BD are not well known. Recently, anti-α-enolase antibody (AAEA) has been detected in sera from BD patients. The aim of this study was to evaluate the prevalence of AAEA in intestinal BD and its clinical correlations. The study sample included 80 patients with intestinal BD and 23 healthy controls. IgM AAEA was detected by ELISA. The positivity of IgM AAEA was defined as an optical density greater than three standard deviations above the mean of the control sera. Other parameters, such as demographic information, subtype of BD, colonoscopic findings, disease severity and treatment modality, were analyzed retrospectively. The prevalence of IgM AAEA was 67.5% in intestinal BD and 0% in the control group. The positivity rate of IgM AAEA was higher in complete or incomplete BD than in suspected BD (77.5% vs 51.6%, $p = 0.016$). The mean HBI score was higher in antibody positive patients than in antibody negative patients (5.60 vs 4.61, $p = 0.003$). The cumulative probability of steroid use for aggravation of intestinal and extra-intestinal symptoms was higher in antibody positive patients than in antibody negative patients (p=0.012). The number of patients with systemic involvement was higher in the AAEA positive group than in the negative group. Monitoring IgM AAEA may be helpful for diagnosis of intestinal BD and could be used to predict clinical course and disease severity.

Key words: Anti-α-enolase antibody, Disease severity, Intestinal Behçet's disease, Serologic marker

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ABBREVIATIONS

BD, Behçet's disease; **CD,** Crohn's disease; **UC,** ulcerative colitis; anti–endothelial cell antibody (AECA); **pANCA,** perinuclear antineutrophil cytoplasmic autoantibody; **ASCA,** Anti-*Saccharomyces cerevisiae* antibody; **AAEA**,anti-α-enolase antibody; **HBI**; Harvey-Bradshaw index;

I. INTRODUCTION

Behçet's disease (BD) is a rare multisystem disorder characterized by vasculitis. Its clinical expression may be dominated by orogenital ulcerations, skin lesions, intraocular inflammation and less commonly by arthritic, vascular, gastrointestinal, and neurologic manifestations (Kaklamani et al, 1998; Sakane et al, 1999; Yurdakul et al, 2004). The complete etiology and pathogenesis of BD remain unknown, and the clinical course is characterized by exacerbations and remissions of unpredictable duration and frequency. Due to the lack of a definitive diagnostic test for BD, diagnosis is made solely on clinical manifestations.

Intestinal BD is generally accepted as a type of inflammatory bowel disease, a group of diseases that includes ulcerative colitis (UC) or Crohn's disease (CD). Some antibodies are highly specific for UC or CD. For example, perinuclear antineutrophil cytoplasmic autoantibody (pANCA) is recognized as a marker of UC (Saxon et al, 1990; Ruemmele et al, 1998; Peeters et al, 2001; Quinton et al, 1998). Anti-*Saccharomyces cerevisiae* antibody (ASCA) is useful as a highly specific serologic test for CD (Ruemmele et al, 1998; Peeters et al, 2001; Quinton et al, 1998; Sendid et al, 1996). However, unlike UC or CD, no antibody has ever been found to be associated with intestinal BD.

As a heterogeneous group of antibodies against various proteins on the surface of endothelial cells, anti–endothelial cell antibody (AECA) has been detected in various immune-mediated diseases (Adler et al, 1994; Meroni et al, 1995). AECA has also been demonstrated in the sera of patients with BD (Aydintug et al, 1993; Lee et al, 1999). Recently, Lee et al. reported that α-enolase is the target antigen recognized by AECA in the

sera of patients with BD, using human dermal microvascular endothelial cells (HDMECs) as a substrate (Lee et al, 2003). IgM anti-α-enolase antibody (AAEA) was found in 18 of 40 patients with BD (45.0%) (Lee et al, 2003). Based on their results, they suggest that AAEA has potential to be a diagnostic marker of BD.

In this study, we assessed the prevalence of IgM AAEA in patients with intestinal BD and evaluated the relationships between IgM AAEA and various intestinal BD-related clinical factors, including disease activity and severity.

II. MATERIALS AND METHODS

A. Patients

80 patients diagnosed with intestinal BD and 23 age- and sex-matched healthy controls were enrolled in the present study. Serum samples were obtained from all patients with intestinal BD at the time of diagnosis as well as from healthy controls and frozen at −70°C until use. Patients with diagnosed or suspected intestinal tuberculosis, CD, UC, infectious colitis, or malignancy were excluded.

BD was diagnosed according to the criteria from the 1987 Behçet's Disease Research Committee of Japan, which divide the disease into the following three types: complete, incomplete, and suspected (Mizushima et al, 1998). In addition to the Japanese criteria, we used the criteria of the International Study Group for Behçet's disease (ISGBD) from 1990, which require the presence of oral ulceration plus any two of the following: genital ulcerations, typical eye lesions, typical skin lesions, and positive results to a pathergy test (1990). Intestinal BD was diagnosed using a combination of clinical, endoscopic (Lee et al, 2001), radiologic (Chung et al, 2001), and pathologic findings. All patients were followed for at least one year after diagnosis of intestinal BD.

B. Analyzing factors

Patients with intestinal BD were divided into IgM AAEA positive and negative groups. Various parameters, such as clinical and laboratory findings, colonoscopic findings, and

treatment modality, were retrospectively collected from medical records. Endoscopic findings involving the number, size, location, distribution, depth, shape, and margin of ulcers were analyzed (Lee et al, 2001). The distribution pattern of intestinal lesions was classified as localized single, localized multiple, or multi-segmental. When two or more ulcers were observed, the diameter of the largest ulcer was used as the size for analysis. The depth of the ulcer was characterized as shallow or deep/undermining. The ulcer margin was divided into discreteness of border and marginal elevation. Patients were defined as experiencing a disease flare-up when they complained of abdominal symptoms that required additional medications such as steroids and immunosuppressants, operations, or admission. Because there is no activity index for intestinal BD, the disease activity was evaluated by the Harvey-Bradshaw index (HBI), which is used to estimate the disease activity of CD. The HBI was checked every month in the event of a disease flare-up and was otherwise checked every three months. Written informed consent was obtained from all participants.

C. Detection of anti-alpha-enolase antibody by ELISA

Enzyme-linked ammunosorbent Assay (ELISA) for recombinant α-enolase isolated by gene cloning was performed on serum samples from healthy controls and patients with intestinal BD, as outlined previously (Lee et al, 2003).

Purified α-enolase protein was plated in microtiter plates. Then 100 μl of serum, diluted 1:50 in Hanks' balanced salt solution (HBSS) with divalent cations (Irvine Scientific) and 1% bovine serum albumin (BSA; Sigma), was added to each well. Peroxidase-conjugated goat anti-human IgM, diluted 1:1,000 in HBSS with divalent cations and 1% BSA, were

added to each well, and the plates were incubated for 1 hour at 37°C. Antibody binding was quantified colorimetrically by adding tetramethylbenzidine (Sigma) as substrate. One microliter of 30% H_2SO_4 was added immediately prior to use. The chromogenic reaction was stopped with 8N H_2SO_4, and the plates were read spectrophotometrically at 450 nm on an ELISA reader (Dynatech, Alexandria, VA, USA). Positivity was defined as an optical density (OD) greater than three standard deviations (3SD) above the mean of the control sera (Lee et al, 2003).

D. Statistical analysis

Statistical analysis was carried out using the SPSS Base 11.0 statistical package. Values were given as mean ± SD. Continuous data were analyzed using the Student's *t*-test, and categorical data were compared using the chi-square test. The relationships between HBI scores and IgM AAEA were evaluated using Pearson's correlation test. Analysis of cumulative steroid use was performed using the Kaplan-Meier method, and the differences between the two groups were assessed using the log-rank test. Statistical significance was denoted by $p<0.05$. All p values were two-tailed.

III. RESULTS

A. Measurement of serum IgM AAEA and its prevalence in intestinal BD

The mean OD value of IgM AAEA measured by ELISA in intestinal BD patients was 0.4520 ± 0.2212. This value was significantly higher in intestinal BD patients than in healthy controls, who showed a mean value of 0.1215 ± 0.1792. The cut-off value was an OD of 0.34, which was defined previously as the mean plus 3SD for the 23 healthy control sera (Fig. 1) (Lee et al, 2003). The positivity rates of IgM AAEA for intestinal BD patients and control group were 67.5 % and 0.0%, respectively (Table 1).

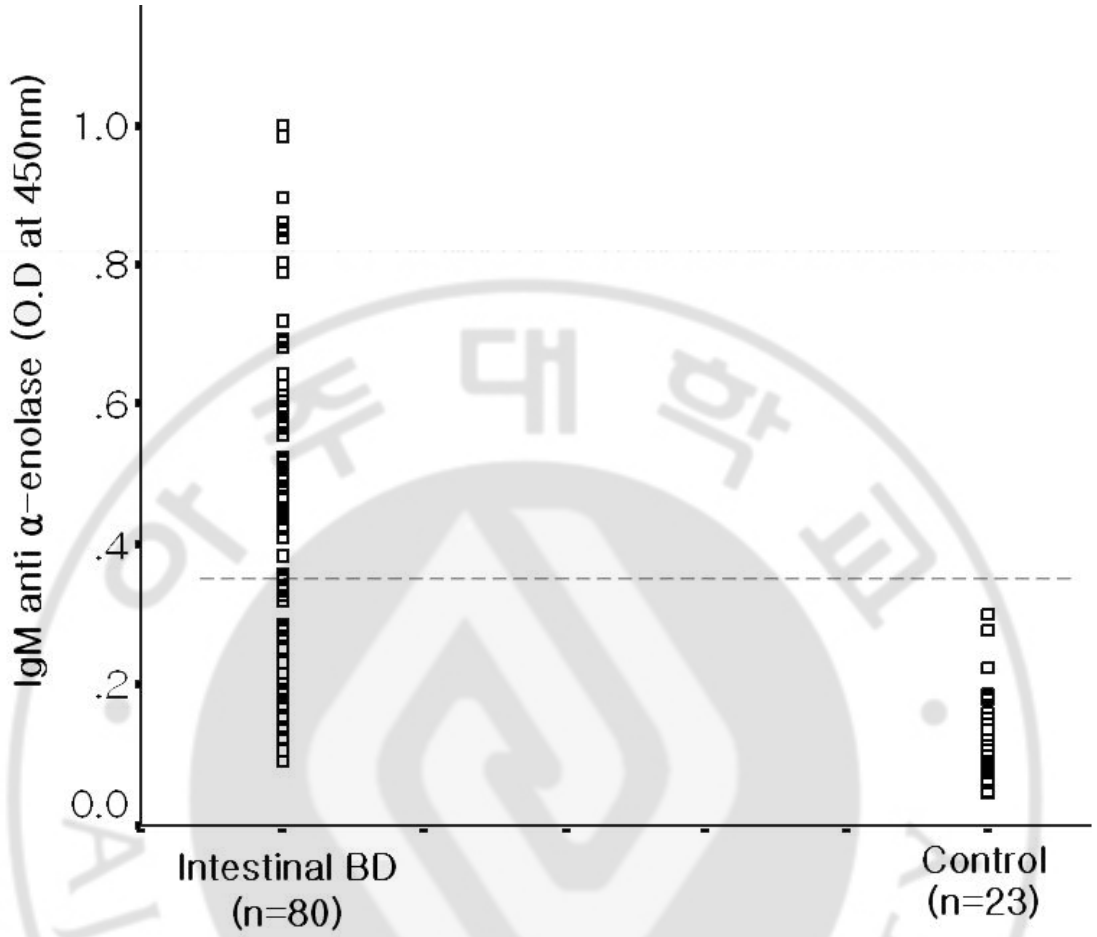

Fig. 1. Titers of IgM anti-α-enolase antibody in intestinal BD patients and controls. The horizontal dotted line represents 3SD above the mean value of IgM anti-α-enolase antibody in normal controls

Table 1. The frequency of IgM anti-α-enolase antibody for recombinant α-enolase, refined by gene cloning, in sera from healthy controls and intestinal Behçet's disease patients.

	Mean value of IgM anti-α-enolase antibody (OD) *	Positivity of IgM anti-α-enolase antibody
Healthy controls (n=23)	0.1215 ± 0.1792	0 (0.0%)
Intestinal BD† patients (n=80)	0.4520 ± 0.2212	54 (67.5%)

*OD: optical density

†BD: Behçet's disease

B. Clinical characteristics and laboratory findings of IgM AAEA positive and negative groups

There were 47 male (58.8%) and 33 female (41.2%) intestinal BD patients, and the mean follow-up period after the diagnosis of intestinal BD was 88.9 ± 51.9 months. Mean age at the time of diagnosis of BD was 36.5 ± 9.6 years, and the time interval between the diagnosis of BD and intestinal BD was 10.5 ± 20.7 months.

The mean age of healthy controls was 35.4 ± 8.2 years, of whom 13 (56.5%) were male and 10 (43.5%) were female. There were no differences in mean age or sex ratio between healthy controls and BD patients.

Table 2 shows the differences in demographics, laboratory parameters, and BD-related manifestations between the IgM AAEA positive and negative groups. In males, the numbers of AAEA positive and negative patients were similar (57.4% vs 42.6%). But, in females, there were more AAEA positive patients (81.8% vs 18.2%). There was no difference between the two groups in terms of age at diagnosis with BD, diagnostic interval between BD and intestinal BD, BD-related clinical manifestations, or laboratory findings. However, the total number of BD-related systemic manifestations, such as oral ulcers, genital ulcers, skin lesions, eye lesions, arthritis, epididymitis, GI lesions, vascular lesions and CNS lesions, was higher in the positive group than in the negative group (3.90±1.23 vs 3.30±1.25, p=0.046).

Table 2. Demographics, laboratory parameters, and Behçet's disease-related manifestations in IgM anti-α-enolase antibody positive and negative groups.

		Anti-α-enolase antibody		*p*-value
		Negative Group (n=26)	Positive Group (n=54)	
Sex	Male	20 (42.6%)	27 (57.4%)	0.022
	Female	26 (18.2%)	27 (81.8%)	
Age diagnosed as BD* (y)		37.19±9.90	36.09±9.58	NS†
Diagnostic interval between BD and intestinal BD (months)		14.19±27.84	8.72±16.51	NS
BD-related manifestations				
	Oral ulcers	25 (96.2 %)	53 (98.1%)	NS
	Genital ulcers	10 (38.5%)	29 (53.7%)	NS
	Skin lesions	12 (46.2%)	32 (59.3%)	NS
	Eye lesions	2 (7.7%)	13 (24.1%)	NS
	Arthritis	7 (26.9%)	24 (44.4%)	NS
	Epididymitis	0 (0.0%)	1 (1.9%)	NS
	GI lesions	26 (100%)	54 (100%)	NS
	Vascular lesions	3 (11.5%)	3 (5.6%)	NS
	CNS Lesions	1(3.8%)	1 (1.9%)	NS
Total number of manifestations		3.30±1.25	3.90±1.23	0.046
Laboratory Data				
	WBC (/mm3)	9,544±2,855	8,530±4,140	NS
	Hb (g/dl)	12.20±1.48	11.52±1.93	NS
	ESR (mm/hr)	32.5±18.3	35.5±19.4	NS
	CRP (mg/dl)	2.43±2.57	2.86±3.51	NS

	ANCA‡ negative	16 (100.0%)	40 (93.0%)	NS
	positive	0 (0.0%)	3 (7.0%)	

* BD: Behçet's disease

† NS: non-significant

‡ ANCA: antineutrophil cytoplasmic autoantibody (n=59)

C. Comparison of diagnostic criteria between IgM AAEA positive and negative groups

Comparing the AAEA positive and negative groups using the Japanese criteria, the portion of complete and incomplete patients was significantly higher in the AAEA positive group than in the negative group (p=0.033). More patients met the ISGBD criteria in the AAEA positive group than in the negative group; however, the difference was not statistically significant (Table 3).

Table 3. Application of Japanese criteria revised in 1987 and ISGBD criteria in IgM anti-α-enolase antibody positive and negative groups.

	Anti α-enolase antibody		*p*-value
	Negative Group (n=26)	Positive Group (n=54)	
Japanese criteria			0.033
Complete	0 (0.0%)	4 (7.4%)	
Incomplete	11 (42.3%)	34 (63.0%)	
Suspected	15 (57.7%)	16 (29.6%)	
ISGBD criteria			NS*
Satisfaction	8 (30.8%)	27 (50%)	
Non-satisfaction	18 (69.2%)	27 (50%)	

*NS: non-significant

D. Colonoscopic findings in IgM AAEA positive and negative groups

Most (97.5%) of the patients had ulcerations in the ileocecal area. The number of ulcerations was higher in the AAEA positive group than in the negative group (2.42±2.29 vs 1.57±0.98, p=0.024). However, no differences were found between the two groups with regard to the size, distribution, depth, shape, or margin of the ulcer (data not shown).

E. Disease course and treatment modality in IgM AAEA positive and negative groups

The mean HBI score was higher in the AAEA positive group than in the negative group (5.60±1.44 vs 4.61±1.12, p=0.003) (Table 4), and there was a weak correlation between the OD level of IgM AAEA and the HBI score (r=0.224, p=0.046) (Fig. 2).

Considering only intestinal lesions, treatment modalities did not differ between the two groups. But when extra-intestinal lesions were included, steroids were used more frequently in the AAEA positive group than in the negative group. Also, the cumulative rate of steroid use for both intestinal and extra-intestinal lesions was higher in the AAEA positive group (p=0.022) (Fig. 3).

Table 4. Disease course and treatment modality in IgM anti-α-enolase antibody positive and negative groups.

	Anti-α-enolase antibody		*p*-value
	Negative Group (n=26)	Positive Group (n=54)	
Disease course			
Mean HBI* score	4.61±1.12	5.60±1.44	0.003
No. of intestinal operations	1.70±0.95	1.70±1.06	NS†
No. of relapses for intestinal lesions	2.35±1.82	3.24±2.17	NS
Treatment modality			
Medical treatment for intestinal BD‡			
Intestinal lesions only			NS
5-ASA only	13 (50.0%)	22 (40.8%)	
5-ASA+Steroid	6 (23.1%)	14 (25.9%)	
5-ASA+Steroid+immunosuppressant	7 (26.9%)	18 (33.3%)	
Including extra-intestinal lesions			0.047
5-ASA only	12 (46.1%)	11 (20.4%)	
5-ASA+Steroid	6 (23.1%)	23 (45.6%)	
5-ASA+Steroid+immunosuppressant	89 (30.8%)	20 (37.0%)	

* HBI: Harvey-Bradshaw index

† NS: non-significant

‡ BD: Behçet's disease

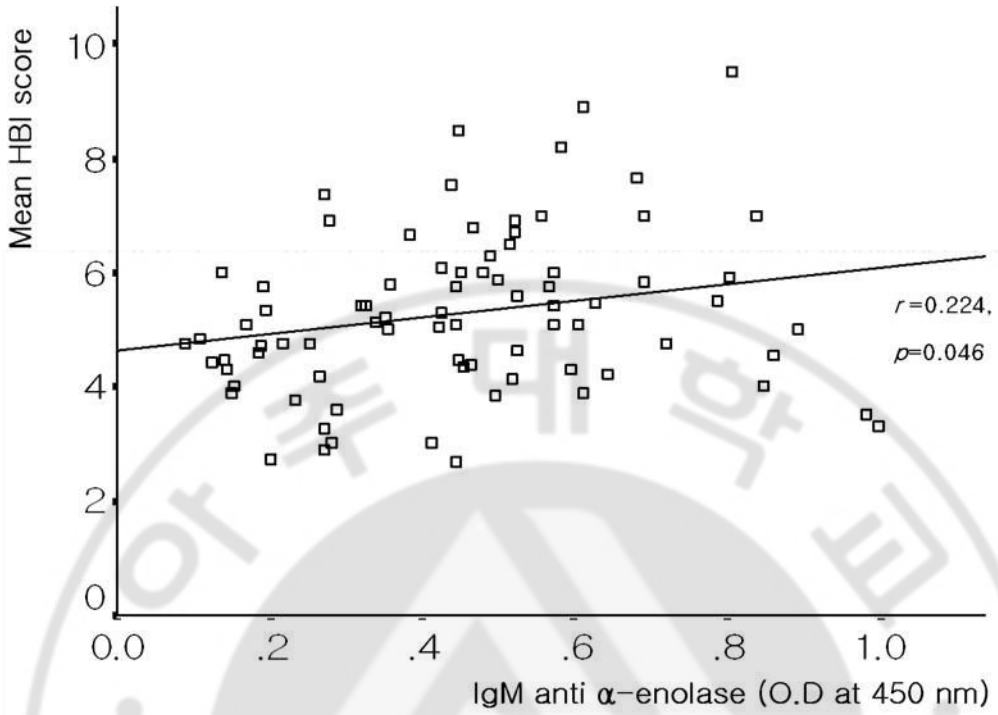

Fig. 2. Correlation between the OD of IgM anti-α-enolase antibody and HBI score in intestinal BD patients. There was a positive correlation between IgM anti-α-enolase antibody and the HBI score (r=0.224, p=0.046; Pearson correlation test).

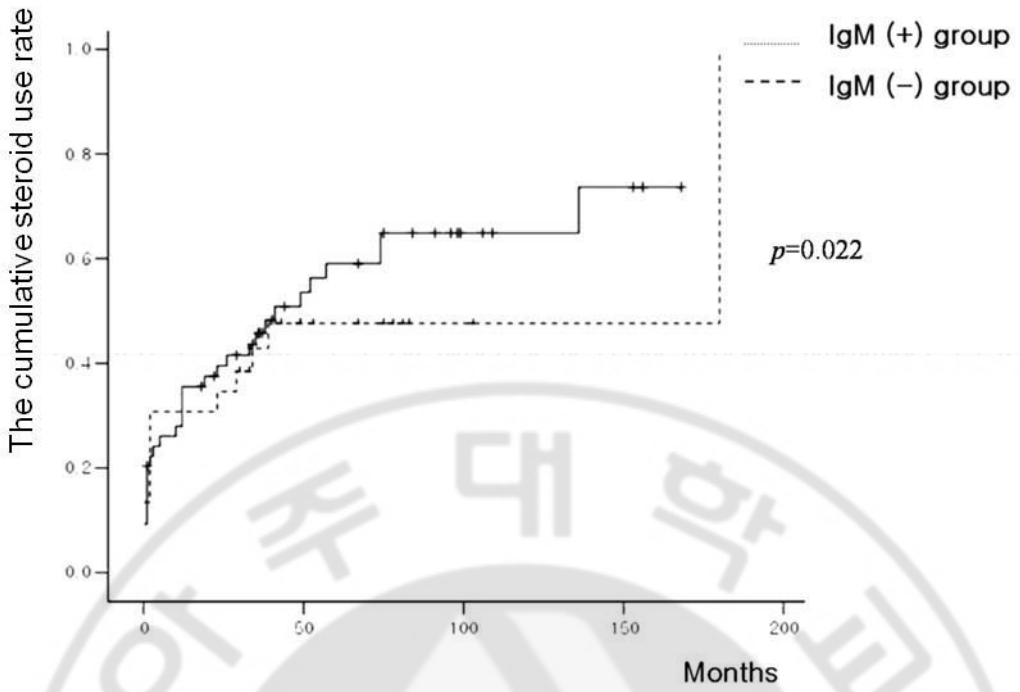

Fig. 3. Cumulative rate of steroid use for the IgM anti-α-enolase antibody positive and negative groups. Cumulative rate of steroid use for the IgM anti-α-enolase antibody positive and negative groups were 38 % and 31% at 1 year, 40% and 35% at 2 years, 46% and 43% at 3 years, 51% and 48% at 4 years, and 60% and 48% at 5 years, respectively (p=0.022).

IV. DISCUSSION

Because there are no pathognomonic symptoms or specific laboratory findings for BD, proper diagnosis of BD remains very difficult. BD may remain undiagnosed for several years until the clinical manifestations have fulfilled the criteria for Behçet's disease. Thus, efforts to find a serologic marker of BD have been made in order to diagnose BD before the fulfillment of diagnostic criteria.

AECA has been detected in various inflammatory diseases, including BD [9-12]. But there have been few studies focused on the characteristics of the antigen recognized by AECA. Recently, Lee et al found that α-enolase is the target protein of serum AECA in BD patients, and IgM or IgG AAEAs were found in 22 of 40 (55%) patients with BD (Lee et al, 2003). Among those 22 patients, 18 (45%) BD patients had IgM AAEA with reactivity for recombinant human α-enolase refined by gene cloning. They suggested that IgM AAEA might be used as a serologic marker of BD.

The α–enolase protein is a glycolytic enzyme with a molecular weight of 47 kD (Pratesi et al, 2000). This protein apparently serves as a plasminogen receptor on the surface of a variety of hematopoietic, epithelial, and endothelial cells and plays a crucial role in intravascular and pericellular fibrinolytic systems (Pancholi et al, 1998; Pancholi, 2001). This protein is also found on the surface of streptococci, which can cause acute rheumatic fever (Fontan et al, 2000), and has been identified as a type of heat-shock protein (Iida et al, 1985). The evidence suggests that α–enolase plays an important role in autoimmune and inflammatory diseases, such as rheumatoid arthritis, systemic lupus erythematosus, discoid lupus erythematosus, cancer-associated retinopathy, ANCA-positive vasculitis, systemic

sclerosis, endometriosis, primary membranous nephropathy, autoimmune liver disease, and mixed connective tissue disease (Pancholi, 2001; Gitlits et al, 2001; Saulot et al, 2002).

In our present study, IgM AAEA was positive in 54 of 80 (67.5%) intestinal BD patients. which was higher than the prevalence among BD patients (45.0%) reported by Lee et al (Lee et al, 2003). The rate of AAEA positivity was higher in intestinal BD than in other inflammatory bowel diseases, such as UC (10%) and CD (21%) (Roozendaal et al, 1998). Therefore, IgM AAEA may be a useful serologic marker of intestinal BD, similar to the use of ASCA in CD and pANCA in UC, especially in patients with intestinal involvement who lack systemic manifestations of BD. Although it could not be a used as a disease-specific serologic marker of intestinal BD given the broad spectrum of diseases associated with AAEA, it might play a role in discriminating intestinal BD from CD, two diseases that share several clinical similarities including mucocutaneous manifestations, gastrointestinal disease favoring the terminal ileum, and arthritis.

Regarding the disease activity index of IgM AAEA in intestinal BD, the mean HBI was higher in the AAEA positive group than in the negative group, although it has not been established whether the HBI score is appropriate for measuring disease activity of intestinal BD. There was also a weak positive correlation between the HBI score and OD level of IgM AAEA. Hence, we thought that the IgM AAEA level might reflect the disease activity of intestinal BD. Moreover, considering the higher rate of steroid use, more involvement of systemic organs, and more complete and incomplete groups according to the Japanese criteria in the IgM AAEA positive group, AAEA might be helpful for predicting the disease activity and severity, clinical course, and treatment modality in intestinal BD.

Our study had several limitations. First was the issue of whether patients with intestinal involvement but lacking the systemic manifestations of BD could be diagnosed with

intestinal BD. Several diagnostic criteria have been introduced, such as the ISGBD criteria and the Behçet's Disease Research Committee of Japan in 1987. However, the ISGBD criteria do not allow for variations in BD symptoms (Lee, 1997). We used the Japanese criteria to account for this defect in the ISGBD criteria. Because all of the proposed criteria have not yet been met in clinical practice, improved criteria for BD are needed. The second limitation was that disease activity for intestinal BD was calculated using an HBI score, because an activity index has not yet been established for BD. However, considering the similarities in the clinical manifestations of BD and CD and the items of the HBI, which consisted of general well-being, abdominal pain, number of liquid stools daily, abdominal mass, and systemic complications, we thought that the HBI score could reflect the activity of intestinal BD. The third limitation was that we compared the prevalence of AAEA in intestinal BD to other inflammatory bowel diseases using previously published data for the prevalence of AAEA in UC and CD. More studies are needed to estimate the prevalence of AAEA among the three diseases simultaneously. The final limitation was the variation in collection time for the serum samples. Some were obtained while BD was in the active stage and others in the remission stage of the disease. Therefore, it is necessary to study whether there is a change of IgM AAEA level between the active stage and remission stage of intestinal BD.

V. CONCLUSION

In conclusion, we analyzed IgM AAEA in intestinal BD patients and found that IgM AAEA can be helpful for the diagnosis of intestinal BD, especially in patients without systemic manifestations of BD. AAEA may be associated with disease activity and severity. Thus, further studies on both the pathogenetic role and the clinical relevance of IgM AAEA in intestinal BD are needed.

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- 국문요약 -

장베체트병에서 혈청학적 표지자 및 질병 중증도 평가 도구로서 Anti-alpha-enolase Antibody 의 유용성

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장베체트 병은 크론씨병 및 궤양성 대장염 등과 같은 만성 염증성 장질환의 일종이나, 크론씨병의 ASCA (Anti-*Saccharomyces cerevisiae* antibody), 궤양성 대장염의 pANCA (perinuclear antineutrophil cytoplasmic autoantibody) 등과 같은 혈청학적 표지자는 알려져 있지 않다. 최근 들어, anti-α-enolase antibody (AAEA)가 베체트병 환자의 혈청에서 발견되었으며 이에 저자는 장베체트병에서 AAEA 의 유병률을 구하고 또한 AAEA 와 질병의 중증도와의 상관관계에 대하여 알아보고자 하였다. 본 연구를 위하여 장베체트병 환자 80 명과 대조군으로 건강한 사람 23 명에서 혈청을 채취하였으며 IgM AAEA 는 EIISA 법을 이용하여 측정하였다. IgM AAEA 양성은 대조군의 광학 밀도 (optical density) 측정값의 3SD (standard deviation) 이상일 경우로 정의하였으며, AAEA 존재여부와 환자의 일반적인 특징, 베체트병의 아형(subgroup)의 종류, 대장 내시경 소견, 질병이 중증도 및 치료 형태와의 연관성

을 후향적으로 비교 분석하였다. IgM AAEA 유병률은 장베체트병 환자에서 67.5%, 대조군은 0.0%였으며, IgM AAEA 양성군에서 suspected 베체트병 보다는 complete, incomplete 베체트병이 많았고 (77.5% vs 51.6%, p = 0.016), 또한 평균 HBI (Harvey-Bradshaw index)점수가 IgM AAEA 양성군에서 음성군에 비하여 높았다 (5.60 vs 4.61, p = 0.003). 또한 IgM AAEA 양성군에서 장베체트병 및 베체트병으로 인한 스테로이드의 사용률이 시간이 경과함에 따라 음성군에 비하여 증가하는 소견을 보였으며(p=0.012), 전신 질환 침범이 나타날 경우가 많았다. 결론적으로 IgM AAEA 는 장베체트병의 진단 및 질병의 경과 그리고 중증도를 예측하는데 도움이 되리라 생각된다.

핵심어: Anti-α-enolase antibody,질병의 중증도, 장베체트병, 혈청 표지자