

타카야수 동맥염의 임상적 고찰

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Clinical Characteristics of Takayasu's Arteritis

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ABSTRACT

Background and Objectives : Takayasu's arteritis is a disease of unknown etiology which has recently been reported to be a systemic disease. This is a prospective study of the clinical features and angiographic findings of Takayasu's arteritis from a single center. **Subjects and Methods** : Forty five patients were diagnosed as Takayasu's arteritis according to the Numano's diagnostic criteria, where patients satisfying at least one criterion from elevated ESR or CRP, arterial wall enhancement at MRA or CT angiography, or carotid tenderness are categorized into the active group. A disease duration of one year was used to define the division of the disease into either acute or chronic. Ueno's and Numano's classifications obtained through various imaging studies, were used. **Results** : At the time of diagnosis, 60% of patients were in the active stage while 40% were in inactive stage. Levels of ESR, CRP and fibrinogen were found to differ significantly according to disease activity. The most common type of Takayasu's arteritis was type III according to the Ueno's classification, and type V according to the Numano's. The left subclavian artery was involved most frequently (78.5%). The most commonly involved segment of the aorta was the abdominal aorta (64.4%). Mean systolic blood pressure of the right arm in the renal artery stenosis group was 156 ± 39 mmHg, which was significantly higher than that in the group without renal artery stenosis (113 ± 46 mmHg) ($p = 0.005$). ESR and CRP were correlated with aortic signal intensity on contrast-enhanced MR imaging (ESR ; $r = 0.685$, $p = 0.007$ /CRP ; $r = 0.596$, $p = 0.041$). **Conclusion** : Takayasu's arteritis is a disease of unknown causes, especially among young female patients, and exhibits nonspecific and various symptoms. ESR and CRP remain as valuable indicators of disease activity. The MR enhancement intensity of the arterial wall shows a positive correlation with both ESR and CRP level and it therefore may be correlated to disease activity and represent a useful diagnostic indicator. (Korean Circulation J 2001;31(11):1106-1116)

KEY WORDS : Angiography ; Takayasu's arteritis.

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대상 및 방법

환자선택

1994 10 2000 4

Table 1. Diagnostic criteria for Takayasu's arteritis by Sharma and Numano³⁾

Three major criteria	
1. Left mid subclavian artery lesion	The most severe stenosis or occlusion present in the mid portion from the point 1 cm proximal to the vertebral artery orifice up to that 3 cm distal to the orifice determined by angiography
2. Right mid subclavian artery lesion	The most severe stenosis or occlusion present in the mid portion from the right vertebral artery orifice to the point 3 cm distal to orifice determined by angiography
3. Characteristic signs and symptoms of at least one month duration	These include limb claudication, pulselessness or pulse differences in limbs, an unobtainable or significant blood pressure difference (> 10 mmHg systolic blood pressure difference in limb), fever, neck pain, transient amaurosis, blurred vision, syncope, dyspnea or palpitations.
Ten minor criteria	
1. High ESR	Unexplained persistent high ESR > 20 mm/h(Westergren) at diagnosis or presence of the evidence in patients history
2. Carotid artery tenderness	Unilateral or bilateral tenderness of common arteries on palpation. Neck muscle tenderness is unacceptable.
3. Hypertension	Persistent blood pressure > 140/90 mmHg brachial or > 160/90 mmHg popliteal
4. Aortic regurgitation or annuloaortic ectasia	By auscultation or Doppler echocardiography or angiography. By angiography or two-dimensional echocardiography.
5. Pulmonary artery lesion	Lobar or segmental arterial occlusion or equivalent determined by angiography or perfusion scintigraphy, or presence of stenosis, aneurysm, luminal irregularity or any combination in pulmonary trunk or in unilateral or bilateral pulmonary arteries determined by angiography.
6. Left mid common carotid lesion	Presence of the most severe stenosis or occlusion in the mid portion of 5 cm in length from the point 2 cm distal to its orifice determined by angiography.
7. Distal brachiocephalic trunk lesion	Presence of the most severe stenosis or occlusion in the distal third determined by angiography.
8. Descending thoracic aorta lesion	Narrowing, dilation or aneurysm, luminal irregularity or any combination determined by angiography : tortuosity alone is unacceptable.
9. Abdominal aorta lesion	Narrowing, dilation or aneurysm, luminal irregularity or aneurysm combination.
10. Coronary artery lesion	Documented on angiography below the age of 30 years in the absence of risk factors like hyperlipidemia or diabetes mellitus.
Presence of two major criteria or one major criteria and two minor criteria or four minor criteria suggests a high probability of Takayasu arteritis. ESR : erythrocyte sedimentation rate	

10 mmHg 가 (BP discrepancy)

임상검사와 영상검사

ESR, CRP, (BUN), (Cr), Lp(a), homocysteine, plasminogen activator inhibitor(PAI) - 1, tissue plasminogen activator(tPA), immunoglobulin G(IgG), immunoglobulin M(IgM), immunoglobulin A(IgA), C3, C4, CH50, (ANA), [ACE(P)], methylene tetrahydrofolate reductase polymorphism [MTHFR(P)]

ACE(P) ACE intron 16 287 base insertion(I)/deletion(D) polymorphism DD homozygote⁷⁾

MTHFR homocysteine MTHFR(P) (677 C - to - T mutation) alanine(A) valine() MTHFR 가 , hyperhomocysteinemia⁸⁾

(40), adenosine thallium (20), (7) Du - plex (31), CT angiogram(12), (MRI & MRA)(33), conventional angiogram(24) stenosis, dilatation, aneurysm, ulcer, dissection, thrombus, calcification, wall thickening, wall enhancement가

자기공명 영상에 의한 대동맥벽 조영 증강 Gadolinium - enhanced MR imaging signal intensity가 signal

intensity 가

가 가 ,

통계처리 ESR, CRP Pearson's Student t - test² test

결과

임상소견 45 가 39 6.5 : 1 39 (14~61) 30 가 40 가 62% (Table 2). Ishigawa 40 Numano 44%(20/45) 15 (33.3%) 8 (17.8%), 4 (8.9%), 4 (8.9%) 45 1 creatinine 가 4 (8.9%) 가 2 (1), (2), (1), (1) 2 , 1 (Ta-

Table 2. Age and sex distribution

Age (years)	Sex (Male/Female)	Total (%)	Age at first diagnosis (%)
10 - 19	0/ 3	3 (6.7)	4 (8.9)
20 - 29	0/ 8	8 (17.8)	8 (17.8)
30 - 39	4/13	17 (37.8)	19 (42.2)
40 - 49	1/ 6	7 (15.6)	6 (13.3)
50 - 59	1/ 5	6 (13.3)	4 (8.9)
60 -	0/ 4	4 (8.9)	4 (8.9)
Total	6/39	45 (100)	45 (100)

Table 3. Clinical characteristics

Characteristics	Number (%)
Female (%)	39/45 (86.7%)
Mean age (years)	39 ± 13
Risk factors	
DM	0/45 (0%)
Hypertension	20/45 (44%)
Smoking (over 1 pack per day)	2/45 (4.4%)
Hypercholesterolemia (cholesterol >240 mg/dL)	4/45 (8.9%)
Combined diseases	
Tuberculosis history	2
Gastric polyp	1
Thyroid disease	2
Multiple myeloma	1
Hepatitis	1
Typhoid fever history	1

DM : diabetes mellitus

ble 3).

11.1%(5/45) ,
46.7%(21/45) ,
20.0%(9/45), 22.2%(10/45),
17.8%(8/45), 11.1%(; 2/45,
; 3/45), 6.7%(3/45) ,
35.6%(16/45) . 28.
9%(13/45) . 20.0%(9/
45) , 8.9%(4/45), 13.3%(6/
45) . 8.9%(4/45)
(Table 4). 8.9%(4/45)
.

임상 검사 소견과 활동성에 따른 변화

ESR 가 64.4%(29/
45) , CRP 가 37.2%(16/43)
18.2%(8/45) , 가 9.1%
(4/45) .

8
7
.
(; 23.3±7.1 me -
an ESR ; 78.7±15.6 mm/h, mean CRP ; 5.8±2.0
mg/dL) 8 (17.8%) , (; 43.

Table 4. Symptoms and signs of Takayasu's arteritis

Symptoms	Number (%)
Constitutional symptoms	5 (11.1)
Fever	5 (11.1)
General weakness	1 (2.2)
Cardiovascular symptoms	21 (46.7)
Dyspnea	10 (22.2)
Chest pain	9 (20.0)
Palpitation	2 (4.4)
BP discrepancy	16 (35.6)
Claudication	8 (17.8)
Extremity pain	5 (11.1)
Extrimity weakness	3 (6.7)
Neurologic symptoms	13 (28.9)
Headache	9 (20.0)
Dizziness	10 (22.2)
Syncope	4 (8.9)
Paralysis	3 (6.7)
Visual disturbance	6 (13.3)
Gastrointestinal symptoms	4 (8.9)
Abdominal pain	3 (6.7)
Nausea/vomiting	1 (2.2)
Ulcer	1 (2.2)
Others	10 (22.2)
Thrombophlebitis	1 (2.2)
Neck pain	4 (8.9)
Bone lesions	5 (11.1)

BP : blood pressure

6 ± 13.0 mean ESR ; 42.5 ± 6.3 mm/h, mean CRP ;
1.4 ± 6.5 mg/dL) 19 (42.2%), (;
41.2 ± 10.8 mean ESR ; 12.7 ± 3.0 mm/h, mean
CRP ; 0.1 ± 0.0 mg/dL) 18 (40.0%) .

ESR C₃ 가 가 ,
ESR, CRP , fibri -
nogen 가 가
(Table 5).

ESR, CRP, fibrinogen CH₅₀ 가
가 (Table 5).
ACE(P) 가 14 II/ID/DD
가 0.14/0.79/0.07 MTHFR(P)

가 11 AA/AV/VV 가 Ueno III 52.4%(22/
0.36/0.45/0.18 가 42) 가 I (9/42), IV
(II/ID/DD ge - (8/42), II (3/42) . Numano
notype ; 0.35/0.49/0.16, n = 826 ; AA/AV/VV ge - V 57.1%(24/42)
notype ; 0.39/0.47/0.14, n = 200) ² test II (9/42 ; IIa 4, IIb 5), I
(Ta - (6/42), IV (2/42), (1/42)
ble 6). (Fig. 1).

분 류 혈관영상소견
45 3 62%(28/
가가 가 가 42 45) 가 ,

Table 5. Laboratory data

Parameters (Abnormal value)	No. of abnormal value (%)	Mean value			p		
		Active		Inactive	A [†]	B [‡]	C [§]
		Acute	Chronic				
Age (years)		23.3± 7.1	43.6± 13.0	41.2± 10.8	0.000	NS	NS
ESR (>20 mm/h)	29/45* (64.4)	78.7± 15.6	42.5± 6.3	12.7± 3.0	0.017	0.000	0.000
CRP (>0.8 mg/dL)	16/43* (37.2)	5.8± 2.0	1.4± 6.5	0.1± 0.0	NS	0.041	0.014
WBC (>10000 /mm ³)	4/45* (9.1)	8991± 1442	6519± 493	6868± 8.54	NS	NS	NS
PAI-1 (>43 ng/mL)	5/18* (27.8)	59.2± 22.7	25.2± 6.5	25.0± 11.4	NS	NS	NS
tPA (>12 ng/mL)	0/17* (0.0)	5.8± 1.6	5.7± 0.5	4.6± 1.2	NS	NS	NS
Fibrinogen (<210 mg/dL)	2/12* (16.7)	468± 73	368± 26	276± 11	NS	0.019	0.005
Lp (a) (>25 mg/dL)	4/13* (30.8)	21.7± 7.3	28.4± 9.5	35± 8.9	NS	NS	NS
IgG (>1618 mg/dL)	7/22* (31.8)	1714± 132	1767± 307	310± 17	NS	NS	NS
IgA (>378 mg/dL)	12/22* (54.5)	468± 44	368± 58	271± 56	NS	NS	NS
IgM (>263 mg/dL)	4/22* (18.2)	205± 32	168± 30	50± 19	NS	NS	NS
C3 (<88 mg/dL)	8/22* (36.4)	131.3± 15.0	80.8± 7.3	94.8± 4.6	0.015	NS	NS
C4 (<12 mg/dL)	1/22* (4.5)	25.7± 3.1	24.1± 5.4	22.5± 0.9	NS	NS	NS
CH50 (<25 /mL)	7/18* (38.9)	44.7± 4.5	38.5± 4.7	30.8± 3.0	NS	NS	0.030
Homocysteine (>15.3 mol/L)	4/14* (28.6)	9.1± 4.7	15.2± 4.6	15.3± 2.6	NS	NS	NS
Hb (<10 mg/dL)	8/45* (18.2)	10.4± 2.2	12.1± 1.7	12.4± 2.3	NS	NS	NS
FANA (positive)	4/12* (33.3)	3/5	1/4	0/3	NS	NS	NS

* : the number of the patients from whom the test was requested, † : between acute active group and chronic active group, ‡ : between chronic active group and inactive group, § : between active (both acute and chronic) and inactive group, : number of patients with positive test per number of patients from whom the test was requested, ESR : erythrocyte sedimentation rate, CRP : C-reactive protein, WBC : white blood cell, PAI-1 : plasminogen activator inhibitor, tPA : tissue plasminogen activator, Lp : lipoprotein, IgG : immunoglobulin G, IgA : immunoglobulin A, IgM : immunoglobulin M, Hb : hemoglobin, FANA : fluorescent antinucleus antibody

Table 6. Frequency of ACE polymorphism & MTHFR polymorphism in patients with Takayasu's arteritis and normal population

	Control	Takayasu's arteritis	² test
ACE (P) (II/ID/DD genotype)	0.35/0.49/0.16	0.14/0.79/0.07	NS
MTHFR (P) (AA/AV/VV genotype)	0.39/0.47/0.14	0.36/0.45/0.18	NS

oACE (P) : angiotensin converting enzyme (polymorphism), MTHFR (P) : methylene tetrahydro folate reductase (polymorphism)

고혈압과 신동맥 협착과의 상관 관계
(38% ; 17/45)
156 ± 39 mmHg
113
± 46 mmHg 가 (p
= 0.005).

ESR, CRP와 동맥벽 조영 증강과의 상관 관계
ESR

19.0%(8/45)
(64.4%),
(37.8%),
(37.8%)
(46.7%),
(Table 7).
9 7
2 (2/45, 4.4%) 3
(Table 7).

Table 7. Site of involvement on CT or MR imaging in patients with Takayasu's arteritis

	Site of involvement	Number	Percent (%) [*]
Aorta	Ascending thoracic aorta	17	37.8
	Aortic arch	17	37.8
	Descending thoracic aorta	21	46.7
	Abdominal aorta	29	64.4
Branches	Right brachiocephalic trunk	22	52.4
	Subclavian artery (right/left)	33 (15/28)	78.5
	Common carotid artery (right/left)	31 (24/26)	73.8
	Internal carotid artery (right/left)	9 (6/ 6)	21.4
	Vertebral artery (right/left)	8 (6/ 4)	19.0
	Celiac artery	4	9.5
	Superior mesenteric artery	7	16.7
	Inferior mesenteric artery	0	0.0
	Renal artery (right/left)	17 (11/14)	40.5
	Iliac artery (right/left)	9 (5/ 6)	21.4
	Pulmonary artery (right/left)	8 (3/ 5)	19.0
	Coronary artery (RCA/LAD/left main) [†]	2 (1/1/1)	4.8
	Femoral artery (right/left)	7 (4/ 5)	16.7

* : total number = 45 patients, † : positive finding at coronary angiogram, RCA : right coronary artery, LAD : left anterior descending coronary artery

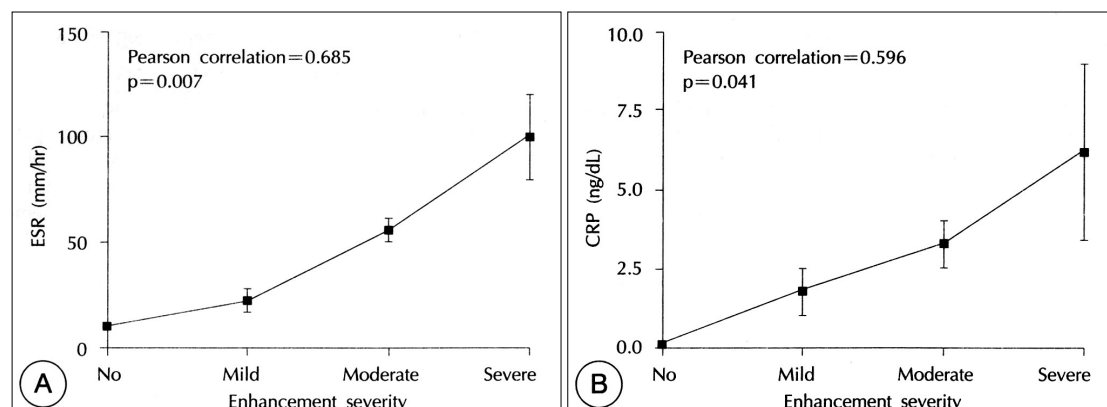


Fig. 2. Graphs show relationship between ESR (A) or CRP (B) levels and arterial signal intensity relative to myocardial signal intensity on contrast-enhanced MR imaging. ESR : erythrocyte sedimentation rate, CRP : C-reactive protein

Table 8. Management of Takayasu's arteritis

Modality	Number*
Medical	26 (57.8%)
Immunosuppressant	16 (35.5%)
Antiplatelet agent	19 (42.2%)
Anticoagulation	2 (4.4%)
Antihypertensives	25 (55.6%)
Intervention (PTA)	16 (35.5%)
Abdominal aorta	2
Subclavian artery (right/left)	3 (2/1)
Renal artery (right/left)	6 (4/2)
Common iliac artery (right/left)	3 (2/1)
Vertebral artery	1
Coronary artery (RCA/LAD)	2 (1/1)
Thoracic aorta	1
Surgery (CABG)	1 (2.2)
Left main coronary artery	1
Observation	2 (4.4)

* : total number = 45 patients, RCA : right coronary artery, LAD : left anterior descending coronary artery, PTA : percutaneous transluminal angioplasty, CABG : coronary artery bypass graft

0.685 0.007 ESR
(Fig.

2A). CRP

0.596 0.041
CRP
(Fig. 2B).

치 료

26 (57.8%),
가 16 (35.5%, 18),
1 (CABG), 2
35.5%
4.4%, 42.2%,
55.6% (Table 8).
18 5
6 (; 4 ,
; 2)
(3), (3), (2),
(2), (1), (1)
1 가
(Table 8). 가 .

고 찰

임상양상

1.6 : 1~8 : 1⁹⁾¹⁰⁾
25~41
,¹¹⁾¹²⁾ 3/4 ,¹³⁾
가 6.5 : 1 ,
39 Nu -
mano 40
(17/45, 37.8%)
3 40
2/3 가 40
가
8
가

74%

44%

Mayo Clinic

6%

¹⁴⁾

70%

8.9%(4/45)

치료방법

가 me -
MTHFR(P) thotrexate
16
가 가 5 me -
thotrexate가 가 가

영상검사와 이에 의한 침범부위의 분류

16)
Ueno , Nu -
mano V 가 ,
1)
가 ,
가 ,
15)
62% 가
가 18)
1 35.5%
18 5
40%
가 가
가

요 약

ESR, CRP 가 ,
16)
, CT,⁶⁾ MR imaging

배경 및 목적 :

, contrast enhanced MR imaging

방 법 :

4)5) ESR, CRP 1994 10 2000 4
MR imaging 가 Numano
45 ESR
MR imaging 21 CRP가 0.9 ,
가 ,
가

1
Duplex, CT angiogram,
(MRI, MRA)
Ueno, Numano
결 과 :
60%,
40% 가 ESR
CRP fibrinogen Ueno
III Numano V
가 (78.5%),
가 (64.
4%).
156 ± 39 mmHg, 113 ± 46 mmHg
가 (p=0.005). ESR, CRP MR
imaging 가
(r=0.685, p=0.007 ; r=0.596, p=0.041).
결 론 :
가 ESR, CRP
MRI 가
중심 단어 :

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