Takayasu arteritis: epidemiological, clinical, and immunogenetic features in Greece

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ABSTRACT

Objective. *Takayasu arteritis (TA) is an uncommon disease with clinical heterogeneity across different ethnic groups. We aimed to evaluate the epidemiological, clinical, and immunogenetic features of TA in Greece.*

Methods. *Demographic, clinical, laboratory, angiographic, and therapeutic data of 42 patients from 4 large referral centers were retrieved. Serology and Human Lymphocyte Antigen (HLA) typing was performed in 22 patients.*

Results. *We studied 37 women and 5 men with a median age of 31 years at disease onset. Median delay in diagnosis was 24 months and median follow-up was 47 months (range 0-178). Constitutional or musculoskeletal symptoms were present in 86%, especially early in the disease course. Vascular findings were universal with reduced or absent pulse being the most common manifestation (98%). Hypertension was frequent (78%). Extensive disease prevailed and stenotic lesions were more common than aneurysms (95% vs. 40%). Erythrocyte sedimentation rate and C-reactive protein showed modest correlation with disease activity. HLA-B52 was expressed by 37% of the patients vs. 2.4% of the controls ($p<0.001$). Glucocorticoids and cytotoxic agents were used in most patients with remission rates of 83%. A total of 42 surgical procedures were performed with success rates of 87%.*

Conclusion. *TA in Greece clinically and epidemiologically resembles the pattern of disease in Japan and the Western hemisphere. There is considerable delay in diagnosis, which may partially reflect failure to recognize a rare disease. New surrogate markers are needed to assess disease activity. Glucocorticoids are the cornerstone of treatment and cytotoxic drugs are frequently used as steroid sparing agents.*

Introduction

Takayasu arteritis (TA) is a rare, chronic, inflammatory disease of the large arteries such as the aorta, the main aortic branches and the pulmonary arteries. It usually affects females in the reproductive age. The clinical spectrum involves inflammatory symptoms as well as ischemic manifestations, due to artery stenosis or occlusion. The etiopathogenesis is unknown, although both immunological and genetic mechanisms seem to be involved (1, 2). Associations with Human Lymphocyte Antigen (HLA) alleles have been observed in some populations, the strongest of which is with B52 in Japan and Korea and B5 in India (3-5).

The disease is more frequent in Southeast Asia, Japan and Latin American countries, while in North America and Europe the data are restricted (6-18). The estimated prevalence in the United States is 2.6 per million (19). This is probably an underestimate though, since the disease remains often undiagnosed. There seems to be a clinical variability related to geographical distribution; in Japanese patients the most commonly affected site is the aortic arch, whereas Indian patients have primarily abdominal aorta involvement (20).

In Greece, TA is uncommon and there are no available data with regard to its features. We retrospectively reviewed the medical records from all patients diagnosed with TA in 4 referral centers in Greece and evaluated the epidemiological, clinical, and immunogenetic features of the disease in this Mediterranean population.

Patients and methods

Patients

The medical records of all patients diagnosed with TA and registered in the Rheumatology clinics of 3 University and 1 General hospital in 4 different

cities in Greece (Athens, Thessaloniki, Heraklion and Ioannina) were retrospectively evaluated. More than 60% of the Greek population resides in these cities (Census 2001) and the abovementioned hospitals are major referral centers for the rest of the country. A total of 42 patients were identified, who were diagnosed between July 1984 and October 2006. All but two patients met the American College of Rheumatology 1990 criteria for the diagnosis of TA. Two patients met only two criteria (age at onset <40 years and typical angiographic abnormalities) but had a histological confirmation of the disease. Other clinical diagnoses were eliminated where appropriate. In patients with late onset disease (>40 years), the diagnosis of giant cell arteritis was excluded clinically.

Data collection

A specific form was used for data collection. The information extracted included: demographic features, date of disease onset, date of diagnosis, date of last follow up, family history, comorbidities, clinical features (at onset, at time of diagnosis and during the course of the disease), laboratory parameters (at time of diagnosis and at last follow up), angiographic and echocardiographic findings, histological findings and treatment modalities (medical and surgical). Angiographic classification was performed according to the criteria established in 1994 (21). Disease activity was evaluated at last follow up and the disease was classified as 'active', in 'complete remission' or in 'partial remission' according to the National Institute of Health criteria (15).

Serology and HLA typing

Blood samples from 24 patients were available. The sera of these patients were screened for anti-endothelial cell antibodies using flow cytometry (22). Twenty-two patients underwent HLA typing using a molecular technique, based on polymerase chain reaction [Micro SSP (TM) DNA Typing Trays (One Lambda, Inc)]. Lymphocytes were separated and typed for HLA-A, B and C in all these patients and B-lymphocytes were obtained for HLA DR, DQ and DRw typing in all but two. The compilation of the data collection forms was completed in October 2006.

Statistical analysis

Numerical data are presented as mean ± standard deviation (SD) and categorical data as percentages. Comparisons between numerical data were performed using the unpaired *t*-test and between categorical data using the chi-squared test or Fisher's exact test where appropriate. *P*-values (two-tailed) <0.05 were considered as statistically significant. Logistic regression analysis was performed to identify potential predictors for delayed (≥2 years) diagnosis of TA, using demographic, clinical, and laboratory parameters as independent variables. All analyses were performed using the Statistical Package for Social Sciences (version 13.0).

Results

Patients' characteristics

Forty-two patients, with a median follow up of 47±51 months (range, 0–178 months), were studied. All patients were Caucasian (Greeks). There were 37 females and 5 males (ratio 7.4:1). The median age at onset of first symptoms of the disease was 31 years (range, 13-59 years). At the disease onset, 10 patients (24%) were younger than 20 years and 6 patients (15%) were older than 40. The remaining of the patients (61%), had disease presentation in the third and forth decades of life. The median delay between the onset of first symptoms and the diagnosis was 24 months (range, 0–516 months). Patients with delay ≥2 years in diagnosis of the disease had increased rates of arthralgia (100% *vs*. 33%, p=0.002) and fatigue (85% *vs*. 30%, p=0.013) and lower rates of thrombocytosis (10% *vs*. 50%, p=0.011). In multivariate analysis, only fatigue at the time of diagnosis was associated with increased risk for delay in diagnosis (odds ratio=11.7; 95% confidence interval: 1.5–89.1, p=0.018). With regard to comorbidities, 2 patients had diabetes mellitus, 1 patient had Crohn's disease and another patient had Hashimoto thyroiditis. Two patients had rheumatic fever in childhood and 2 had a history of tuberculosis. Family history was negative for TA or other types of vasculitis in all patients.

Clinical features

The clinical features of all patients are shown in Figure 1.

Constitutional and musculoskeletal findings

Most patients (86%) had at least one constitutional or musculoskeletal symptom during the disease course. However, only 45% of them had such a symptom with disease presentation. Constitutional symptoms were reported by 67% of patients and they were more common early in the disease (Table I). Fatigue was noted in 59% and fever (≥37.5ºC) in 31% of patients. Only 3 patients (7%) presented with fever of >38.3ºC, fulfilling the criteria of fever of unknown origin. Musculoskeletal symptoms were also common (57%) and included arthralgias and myalgias (51% and 24% respectively), followed by thoracic and cervical pain. Frank synovitis was found in 24% of patients, with the wrists and the metacarpophalangeal joints being the most frequently affected joints.

Vascular findings

Vascular findings were present in virtually all patients. The most common finding was reduced or absent pulse (98%), followed by a bruit (92%). The most common site of a bruit was the carotid arteries (89%) and then the subclavian arteries (75%). Multiple bruits were found in 85% of patients. Differential blood pressure of the arms >10 mmHg was detected in 76% of patients. More than half had claudication of a limb. Almost 1 out of 3 patients had Raynaud's phenomenon, while carotodynia was rather uncommon (7%). Vascular findings were more common in upper than in lower limbs (83% *vs*. 56%, p=0.008). Thirty-two patients (78%) were hypertensive either at the onset or later in the course of the disease. Hypertension was not more common among patients with renal artery stenosis (85% *vs*. 82%, p>0.100).

Neurologic findings

Seventy per cent of patients had some evidence of central nervous system

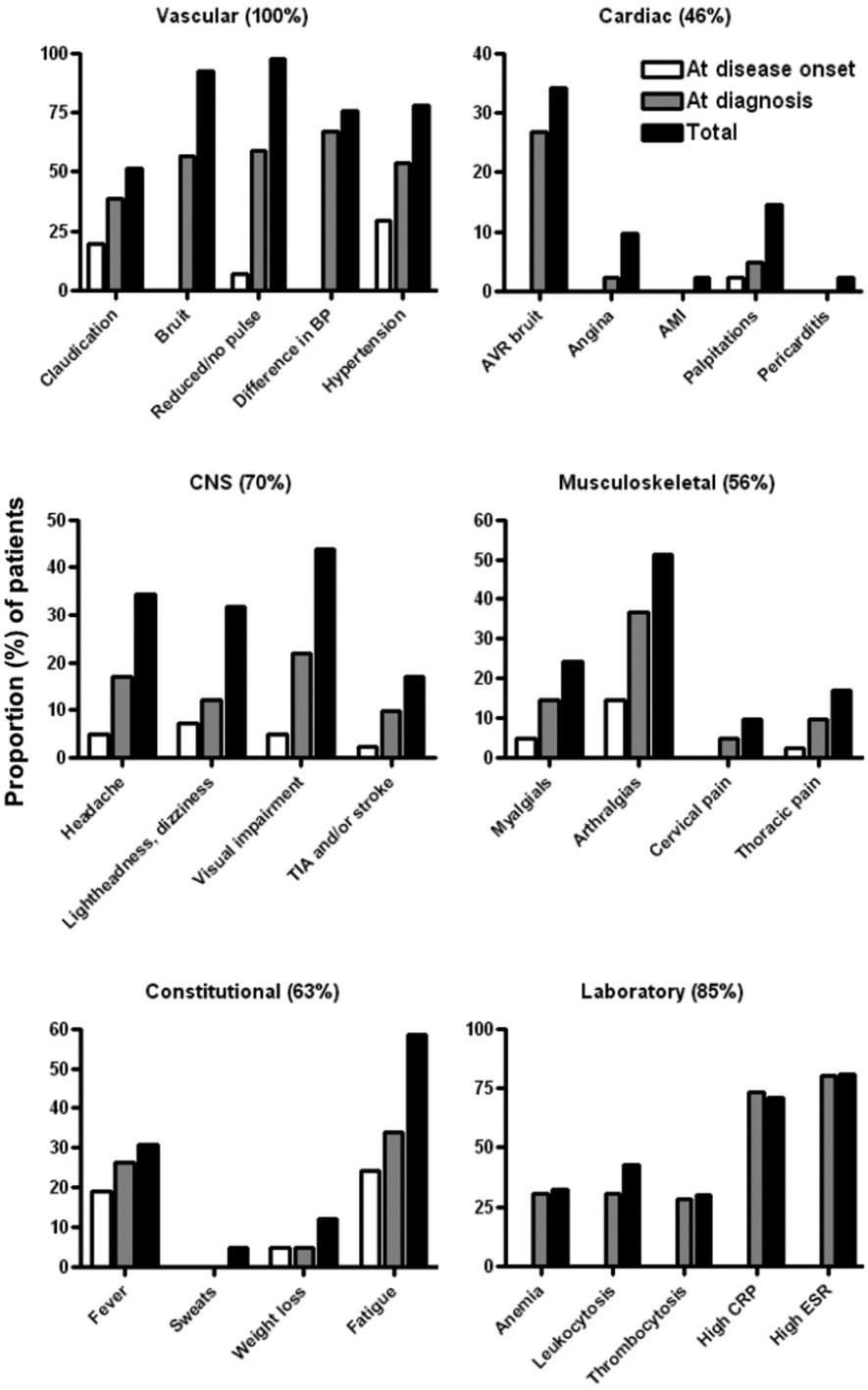

Fig 1. Clinical and laboratory findings in 42 Greek patients with Takayasu arteritis .
Frequency of clinical and laboratory findings in patients with Takayasu arteritis at disease onset (white bar), at the time of diagnosis (grey bar) and at any time point (black bar), from disease onset until the last follow-up. The cumulative prevalence of clinical and laboratory findings is also reported in parentheses.

involvement; dizziness and headache were reported by 32% and 34% of patients respectively. Seven patients (17%) had a stroke or a transient ischemic attack (TIA). Headache and stroke or TIA were associated with the presence of lesions in the carotid arteries (43% *vs*. 20%, p=0.356 and 17% *vs*. 0%, p=0.565, respectively) but not the vertebral arteries. Eighteen patients (44%) had visual impairment, which was almost always bilateral. Sixteen of these patients had stenosis in at least one carotid artery. Symptoms were transient in most patients. One patient had occlusion of the central retinal artery of one eye, which resulted in monocular blindness. Of the 15 patients, who underwent fundoscopy, 12 (80%) were found to have hypertensive retinopathy and 7 (47%) were found to have ischemic retinopathy related to disease.

Cardiac findings

Cardiac disease was found in 46% of patients. Fifteen per cent had palpitations and 10% had angina. One patient suffered from an acute myocardial infarction. Six patients underwent coronary angiography. Half of them had lesions either in the left coronary artery alone (2 patients) or in both coronary arteries (1 patient). In more than one third of patients an aortic valve regurgitation murmur was heard. Twenty-eight patients had heart ultrasound. Asymptomatic aortic valve regurgitation (mild to moderate) was found in 34% and hypertrophy of the left ventricle in 25% of them. One patient developed severe congestive heart failure, which could not be attributed to her well-controlled arterial hypertension. Coronary and pulmonary angiograms were normal. Disease related cardiomyopathy was suspected, but she died before a biopsy was done.

Angiographic findings

All patients had at least one angiographic study; in 2 of them the data were not available. Almost half had ultrasound studies as well. Most patients (70%) had disease above and below the diaphragm. According to current classification criteria, this is type V disease. Seven patients (17.5%) had involvement of the aortic branches only (type I). In 3 patients (7.5%) the lesions involved the aortic arch and its branches (type II) and in 2 (5%) the abdominal aorta only (type IV). No patient had type III disease (descending thoracic and abdominal aorta only). Pulmonary arteriography was performed in 4 patients, because pulmonary hypertension was suspected. Three of them had stenotic lesions: 2 in the main pulmonary arteries and 1 in small branches bilaterally. Stenosis was the most common lesion (95%), followed by aneurysm (40%) and occlusion (35%).

Table I. Early versus late appearance of constitutional and musculoskeletal symptoms in Takayasu arteritis patients.

	Early (≤2 years after disease onset) n. (%)	Late (>2 years after disease onset) n. (%)
Constitutive symptoms		
Fatigue (n=23)*	13 (56)	10 (44)
Weight loss (n=5)	2 (40)	3 (60)
Fever (n=11)	9 (82)	2 (18)
Sweats (n=2)	0 (0)	2 (100)
Any of the above (n=26)	17 (65)	9 (35)
Musculoskeletal symptoms		
Arthralgias (n=21)	11 (52)	10 (48)
Myalgias (n=10)	3 (30)	7 (70)
Thoracic pain (n=7)	3 (43)	4 (57)
Cervical pain (n=4)	2 (50)	2 (50)
Any of the above (n=24)	12 (50)	12 (50)

*Number of patients who developed the specific symptoms during the disease course.

Table II. Angiographic findings in 42 Greek patients with Takayasu arteritis.

		Type of abnormality		
Vessel	Any type	Stenosis	Occlusion	Aneurysm
Aorta	23/36 (64%)	17/36 (47%)	1/36 (3%)	9/36 (25%)
Ascending	9/35 (26%)	3/35 (9%)	–	7/35 (20%)
Thoracic	9/22 (41%)	4/22 (18%)	–	5/22 (23%)
Abdominal	21/29 (72%)	16/29 (55%)	1/29 (4%)	6/29 (21%)
All three	7/36 (19%)	1/36 (3%)	–	3/36 (8%)
Innominate artery	8/33 (24%)	3/33 (9%)	2/33 (6%)	5/33 (15%)
Carotid artery	31/34 (91%)	30/34 (88%)	5/34 (15%)	4/34 (12%)
Right	23/34 (68%)	22/34 (65%)	5/34 (15%)	3/34 (9%)
Left	28/34 (82%)	28/34 (82%)	2/34 (6%)	3/34 (9%)
Bilateral	21/34 (62%)	20/34 (59%)	2/34 (6%)	2/34 (6%)
Basilar artery	11/23 (48%)	11/23 (48%)	5/23 (22%)	1/23 (4%)
Right	5/23 (22%)	5/23 (22%)	1/23 (4%)	1/23 (4%)
Left	8/23 (35%)	8/23 (35%)	5/23 (22%)	1/23 (4%)
Bilateral	2/23 (9%)	2/23 (9%)	1/23 (4%)	1/23 (4%)
Subclavian artery	29/30 (97%)	27/30 (90%)	11/30 (37%)	6/30 (20%)
Right	18/29 (62%)	17/29 (59%)	1/29 (4%)	5/29 (17%)
Left	28/30 (93%)	27/30 (90%)	11/30 (37%)	2/30 (7%)
Bilateral	16/30 (53%)	16/30 (53%)	1/30 (3%)	1/30 (3%)
Renal artery	19/30 (63%)	19/30 (63%)	3/30 (10%)	2/30 (7%)
Right	13/31 (42%)	13/31 (42%)	0/31 (0%)	1/31 (3%)
Left	17/30 (57%)	17/30 (57%)	3/30 (10%)	2/30 (7%)
Bilateral	10/30 (33%)	10/30 (33%)	0/30 (0%)	1/30 (3%)
Mesenteric artery				
Superior	6/31 (19%)	5/31 (16%)	4/31 (13%)	1/31 (3%)
Inferior	0/31 (0%)	0/31 (0%)	–	–
Celiac artery	2/6 (33%)	2/6 (33%)	1/6 (17%)	–
Iliac artery	10/16 (63%)	10/16 (63%)	3/16 (19%)	1/16 (6%)
Right	10/16 (63%)	10/16 (63%)	2/16 (13%)	0/16 (0%)
Left	9/16 (56%)	9/16 (56%)	2/16 (13%)	1/16 (6%)
Bilateral	9/16 (56%)	9/16 (56%)	1/16 (6%)	0/16 (0%)
Coronary artery	3/6 (50%)	3/6 (50%)	1/6 (17%)	–
Right	1/6 (17%)	1/6 (17%)	–	–
Left (anterior)	3/6 (50%)	3/6 (50%)	1/6 (17%)	–
Bilateral	1/6 (17%)	1/6 (17%)	–	–
Any vessel	40/40 (100%)	38/40 (95%)	14/40 (35%)	16/40 (40%)

The subclavian artery was the most frequently affected vessel (97%) followed by the carotid artery (91%), the aorta (64%) and the renal artery (63%) (Table II). Calcification was uncommon and when present, it involved the thoracic and abdominal aorta.

Laboratory findings

Laboratory tests were routinely performed in all patients during follow up (Fig. 1). The erythrocyte sedimentation rate (ESR) and the C-reactive protein (CRP) were elevated in 75% and 67% of patients with active disease respectively. Forty-one per cent and 30% of patients in remission (partial or complete) however, also had elevated values of ESR and CRP respectively. The sera of 24 patients were screened for anti-endothelial cell antibodies but none was positive.

HLA studies

HLA typing was performed in 22 patients. The results were compared with published reports from the general Greek population (23) (Table III). Thirty-eight per cent of TA patients expressed the B52 antigen compared to only 2.4% of controls (healthy donors). This association was statistically significant ($p<0.001$).

Medical treatment

At the last follow up visit, 90% of patients were receiving either glucocorticoids or immunosuppressive treatment. Glucocorticoids were prescribed in 87% of patients at some point during their disease course and immunosuppressive agents in 82%. Only 2 patients were treated with immunosuppressive agents without glucocorticoids. Two patients received no treatment at all: one because of long-lasting remission and the other because of no compliance. The most commonly prescribed immunosuppressant was azathioprine (69%), followed by methotrexate and mycophenolate mofetil (both 22%) and cyclophosphamide (13%). In 4 patients, infliximab, a chimeric monoclonal antibody against tumor necrosis factor-alpha (TNF-α,) was used (24). The initial dose was 3mg/kg every 8 weeks, following the regimen of rheumatoid

Table III. Prevalence of HLA haplotypes in 22 Greek patients with Takayasu arteritis.

Haplotype	Takayasu patients	Healthy controls*	*p*-value**	*p*-value‡
HLA-DRB1*07	6/20 (30.0%)	33/246 (13.4%)	0.101	–
HLA-DRB1*1502	6/20 (30.0%)	12/246 (4.9%)	0.047	–
HLA-DQA1*0303	2/14 (14.3%)	8/246 (3.3%)	0.189	–
HLA-DQA1*0501	3/14 (21.4%)	151/246 (61.4%)	0.008	–
HLA-DQB1*0301	6/13 (31.6%)	134/246 (54.5%)	0.090	–
HLA-DQB1*0601	4/19 (21.1%)	12/246 (4.9%)	0.040	–
HLA-A32	0/22 (0.0%)	33/246 (13.4%)	0.098	–
HLA-B44	0/19 (0.0%)	32/246 (13.0%)	0.158	–
HLA-B49	3/19 (15.8%)	10/246 (4.1%)	0.113	–
HLA-B52	7/19 (36.8%)	6/246 (2.4%)	<0.001	<0.001

*Data obtained from reference 23.
**Fisher's exact test. Only associations with crude *p*-values <0.200 are shown.
‡*p*-values adjusted for multiple comparisons.

Table IV. Surgical procedures in 42 Greek patients with Takayasu arteritis.

Procedure	Site	Procedures	n. of patients
Angioplasty		17	9
	Renal	11	
	Subclavian	2	
	Carotid	1	
	Iliac	2	
	Popliteal	1	
By pass		16	10
	Carotid	6	
	Subclavian	3	
	Renal	2	
	Iliofemoral	3	
	Mesenteric	1	
	Coronary	1	
Aneurysm repair		5	5
	Aorta	4	
	Subclavian	1	
Aortic valve replacement		1	1
Endarterectomy		3	2
	Carotid	2	
	Aorta	1	
Total		42	18

arthritis but an increase to 5mg/kg was necessary. All patients were followed for a median period of 15 months. Three of them responded and were able to reduce steroids. The most serious side effect seen was hemorrhagic cystitis, in a patient treated with cyclophosphamide. Two more patients discontinued azathioprine, one due to liver toxicity and the other due to leucopenia. No major infections were encountered. Steroid-related toxicity involved cushingoid face, osteoporosis, myopathy (2 patients), catarrhact and glaucoma (1 patient each). Infliximab was generally safe. Remission was achieved in 83% of patients (55% partial and 28% complete remission). There was no difference in the medical regimens used between the two groups. Antihypertensive treatment was received by 62% and antiplatelet agents by 57% of patients.

Surgical treatment

Eighteen patients underwent 42 surgical procedures, with an average of 2.3 procedures per patient (Table IV). Transluminal angioplasty was performed in 9 patients and arterial by pass interventions in 10 patients. Five patients underwent aneurysm repair, 2 had endarterectomy and 1 had aortic valve replacement. The majority of the procedures were performed during the first 2 years after diagnosis. Main indications were cerebral hypoperfusion, renovascular hypertension and limb claudication. Involved vessels were the carotid, the subclavian, the renal and the iliofemoral arteries as well as the aorta. The mean postoperative follow up was 7.0±7.1 years. No major complications, apart from an episode of postoperative pancreatitis, were noted. Interventions altogether were successful in 87% of patients.

Discussion

We aimed to study 42 patients with TA in Greece, in order to identify the features of this rare disease in the Greek population.

The study suffers from some limitations. First, data were collected in a retrospective manner and thus, no causative inferences with regard the relationships between clinical and laboratory parameters or the treatment effects can be drawn. Patients were recruited from large tertiary care hospitals, which might have resulted in selection bias. Although discussions with other medical and surgical specialties commonly involved in the care of these patients were made during the data collection, one cannot exclude the possibility that a few patients not seen in the Rheumatology clinics were missed. Finally, the results may not be generalized to the Greek adult population since data came from four large cities where only 60% of the population resides. Despite these caveats, this study represents the first comprehensive analysis of the clinical, laboratory, and immunogenetic features of TA in Greece.

In our cohort, median age at disease onset was 31 years, similar to that in Asia and in Western countries (7, 10, 12, 15, 18, 25). This is opposed to the later age of onset (41 years) reported in previous European studies (16, 26). In a substantial minority of 15% of patients however, the first disease manifestation was reported after the age of 40, in accordance with other cohorts (15, 18, 27). Female predominance (7.4:1) is reminiscent of the Japanese

and Western population; this is in contrast to the almost equal occurrence in both sexes reported in India and Israel (28, 29). The median delay between the onset of symptoms and the diagnosis of 24 months was greater than this reported by others (10 and 15.5 months in United States and Italian cohorts respectively) (15, 18). Presence of constitutional symptoms at disease onset was associated with increased delay in diagnosis. The diverse spectrum of disease presentation, as well as the ignorance for the existence of the disease on the part of the physicians and therefore hesitance to do angiographic studies are possible explanations for the delay.

Most patients (70%) had extensive vascular disease, affecting the aorta and its branches above and below the diaphragm. Only 5% of patients had lesions confined to the aorta below the diaphragm, in accordance with the disease pattern described in Japan, United States, Brazil and Italy (7, 13, 15, 18). On the other hand, in India, Thailand, Korea and China, the widespread pattern is still the commonest but is followed by subdiaphragmatic involvement (9, 10, 12, 25). It seems that the disease process begins either at the aortic arch and/or its branches extending to the abdominal aorta or at the abdominal aorta extending to aortic arch depending on the geographical area (21).

Following the differences in angiographic pattern and in the female-to-male ratio, TA has been associated with different HLA alleles in different populations. In Japanese and Korean populations, there is an association with the B52 antigen, whereas in India an association with the B5 antigen has been described (3-5). These associations are suggestive of immune-mediated pathogenesis of TA. In our cohort and despite the small sample size, 38% of patients expressed the B52 antigen compared to only 2.4% of the healthy adult population (23).

Hypertension was common (78%) but there was no correlation with renal artery stenosis (8, 9, 15, 18). Dysfunction of baroreceptors and abnormal vascular compliance may also contribute to the pathogenesis of hypertension in TA (30). This is supported by the extensive involvement of carotid arteries and the aorta observed in our series. Middle aortic syndrome, that is atypical coarctation of the distal thoracic and abdominal aorta causing renal ischemia, has also been recognized as a cause of hypertension in TA (31). Although 55% of our patients had stenotic lesions either at the descending thoracic or the abdominal aorta, only in a minority of cases the stenosis was severe.

We found good correlation between neurological manifestations (headache, stroke, TIA) and carotid lesions in TA patients. Nonetheless, 12% of patients had symptomatic coronary disease, which is in agreement with other studies (7, 15). In 3 out of 4 patients who underwent pulmonary angiography, stenotic lesions were found. The prevalence of pulmonary disease in TA is thought to be high but this is frequently asymptomatic and a workup is not usually done unless there is clinical suspicion (30).

ESR and CRP are widely used for the diagnosis and evaluation of disease activity in TA. Data about their sensitivity are conflicting (15, 32). In our series 1 out of 4 patients with clinically active disease had normal ESR and 1 out of 3 had normal CRP. On the contrary, only two thirds of patients in remission had normal ESR and/or CRP. Similar results were reported by the United States cohort (15). Altogether, the sensitivity of these markers may be considered poor. Other markers of disease activity, such as interleukin 6 and RANTES, have been tested but none have been proved superior to the standard ones so far (33). We suggest that inflammation markers are used in conjunction with the clinical assessment and angiographic studies to monitor disease activity and response to therapy in TA patients. Some investigators have reported high prevalence of anti-endothelial cell antibodies in TA correlating with disease activity (34, 35). We were unable to detect such antibodies in our patients' sera.

Glucocorticoids remain the cornerstone of treatment in TA. In our series 87% of patients were treated with glucocorticoids. Most of them also received immunosuppressive treatment, usually from the beginning, for steroid sparing purposes. This might have led to less steroid exposure and thus fewer side effects. Once remission was achieved, immunosuppressants were usually continued for maintenance of remission. Azathioprine was most frequently used, followed by methotrexate and mycophenolate mofetil. No direct comparison can be done among these agents, but they all seem to contribute equally to disease control. Although a remission rate of 83% may be considered satisfactory, only 28% of patients experienced complete remission.

Four patients received anti-TNF-α therapy with infliximab. Three of them had long standing disease, resistant to combination therapy. Infliximab was either added to the current treatment scheme or was combined with low dose methotrexate. Three of the 4 patients responded well and were able to reduce steroids (24). Other reports agree with our experience (36). Thus, infliximab might be an alternative for patients with disease resistant to immunosuppressive treatment. More than half of the patients were receiving antiplatelet agents, although clear benefit with regard to prevention of ischemic complications in TA has not been proved.

Surgical procedures in TA are usually performed when the disease is inactive, to achieve higher success rates (37, 38). Interestingly, as many as 40% of arterial biopsy specimens taken during such procedures show active inflammation (15). Our experience agrees with this finding (data not shown) and highlights the discrepancy between clinical assessment and actual disease activity. Arterial by pass procedures are popular in TA patients and the long-term viability of the grafts is 70–80% (39-41). Percutaneous transluminal angioplasty is commonly used in subclavian and renal disease, with lower success rates (42, 43). In our series, we had high success rates but the criteria used were purely clinical.

According to large series, 5- and 10-year survival rates in TA range 80-96% (7, 9, 11, 19). We had only one death (3%) in our cohort, due to sepsis after a long hospitalization for congestive heart failure. Another patient developed end stage renal disease due to renal artery stenosis and long-standing hypertension and is currently receiving peri-

toneal dialysis. Unfavorable prognostic factors in TA are severe hypertension, ischemic retinopathy, aortic or arterial aneurysms, severe aortic regurgitation, and progressive disease (44). Major causes of death are congestive heart failure, acute myocardial infarction, cerebrovascular disease, aneurysmal rupture, and end stage renal disease.

In summary, our work described the clinical and laboratory characteristics in a cohort of Greek patients with TA. Our findings highlight the high morbidity and the low rates of disease remission in TA patients, as well as the limitations in assessing disease activity and making therapeutic decisions based on current laboratory markers. It is becoming apparent that new inflammation markers and new vascular imaging techniques are needed to sensitively and effectively follow up TA patients. Apart from the traditional treatment modalities, anti-TNF-α agents may offer some benefit in cases of refractory disease.

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