Is Takayasu's arteritis more severe in children?

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ABSTRACT

Objective. *Takayasu's arteritis (TAK) is a chronic vasculitis, affecting predominantly the aorta and/or its major branches. The aim of this study was to compare the differences between childhood and adult onset TAK.*

Methods. *We retrospectively evaluated 179 TAK patients followed between August 2005 and July 2019. Demographic characteristics, laboratory features, disease activity, echocardiographic data at diagnosis and treatment regimens in the disease course were compared between the paediatric and adult onset patients.*

Results. *Twenty-five paediatric-onset (<18 years of age at diagnosis) and 154 adult-onset patients (≥18 years of age at diagnosis) were enrolled. The mean age at diagnosis for children and adults were 13.6±4 and 35.6±13, respectively. Paediatric onset TAK patients had more intense inflammation at the time of diagnosis reflected in their clinical findings. Acute phase reactants were high in all paediatric patients and significantly higher in patients with paediatric-onset TAK (p=0.006 and p=0.005, respectively). Abdominal predominant disease was more common in the paediatric group, in contrast, focal disease and aortic arch predominant disease were more common in the adult group. Ascending aortic dilatation, left ventricular hypertrophy and moderate-severe aortic insufficiency were more frequent in echocardiography findings of paediatric onset TAK patients. In comorbidities, hypertension was more common in paediatric TAK patients during follow-up, whereas cerebrovascular disease was more common in adult patients.*

Conclusion. *Our paediatric onset TAK patients presented with a more severe inflammation and more widespread vascular involvement. Multicentre studies from different geographic areas are needed to verify our observation and understand the underlying causes.*

Introduction

International Chapel Hill Consensus Conference Nomenclature of Vasculitides 2012 (CHCC2012) defines Takayasu's arteritis (TAK) as arteritis, often granulomatous, affecting predominantly the aorta and/or its major branches (1). TAK is an interesting disease that affects individuals younger than 40 and is more common among certain ethnic groups (2, 3). In Turkey, an eastern Mediterranean country, is one of the geographic areas where the disease is more frequent than in Europe (3, 4). The diagnostic pathway relies on clinical consideration and imaging. The diagnosis of TAK is especially challenging for the paediatrician due to the insidious onset, rare occurrence and large differential of many inflammatory conditions.

There are certain differences between the adult and paediatric rheumatic diseases. Certain vasculitis target only certain ages such as Kawasaki disease and temporal arteritis. Some rheumatic diseases tend to be milder in children such as IgAV (immunoglobulin-A associated vasculitis-HSP) whereas some tend to be more severe such as SLE (5, 6). The aim of this study was to compare the differences between the childhood and adult onset TAK in the main referral centre for central Turkey.

Methods

Study protocol and patients

We retrospectively evaluated the medical records of TAK patients followed at Division of Rheumatology of the Department of Internal Medicine and Division of Paediatric Rheumatology of the Department of Paediatrics in Hacettepe University, Ankara, Turkey between August 2005 and July 2019. Twenty-five paediatric-onset (<18 years of age at

diagnosis) and 154 adult-onset patients (≥18 years of age at diagnosis) fulfilled the EULAR/PReS/PRINTO endorsed Ankara 2008 and the American College of Rheumatology (ACR) 1990 criteria for TAK, respectively (7-9). Demographics, baseline laboratory features, distribution of involved arterial territories, disease activity and treatment regimens in the disease course were compared between the paediatric and adult onset patients. These 179 patients were assigned to Numano classification (Type I affects primarily the branches from the aortic arch; Type IIa affects the ascending aorta, aortic arch and its branches; Type lIb affects the ascending aorta, aortic arch with its branches and thoracic descending aorta; Type III affects the thoracic descending aorta, abdominal aorta and/or renal arteries; Type IV affects only the abdominal aorta and/or renal arteries; Type V affects the combined features of both type lIb and IV) and also to the latest proposed clusters of disease subsets (Cluster 1: Abdominal Predominant, Cluster 2: Aortic Arch Predominant, Cluster 3: Focal Disease) as suggested previously (10, 11).

Cardiological evaluation

Patients were evaluated by a standard two-dimensional and Doppler echocardiography. Echocardiography data were obtained according to a study-specific protocol only at baseline (from diagnosis to the first three months). Echocardiographic evaluations were performed using a GE Vivid E9 with XD clear or GE Vivid S5 (GE Healthcare, Horten,70 Norway) with 5 or 6 MHz matrix transducer probe. Standard examination was performed in the apical four-chamber, parasternal short and long axis, subcostal and suprasternal views. Cardiac chamber quantification, Doppler echocardiography and M-mode echocardiographic measurements (Left atrial diameter, interventricular septal thickness, posterior wall thickness, left ventricular internal dimension, fractional shortening, and left ventricular ejection fraction) were performed according to the established standards of the American Society of Echocardiography (12). Valvular regurgitation stages were classified according to the American College of Cardiology/ American Heart Association practice guidelines (13). Left ventricular mass was calculated using the formula given by Devereux *et al*. according to the American Society of Echocardiography guidelines: left ventricular mass (g) = 0.81(1.04 [inter- ventricular septum thickness + posterior wall thickness + left ventricular internal dimension]^3 – [left ventricular internal dimension]^3) + 0.06 (14). Left ventricular mass index was derived by dividing left ventricular mass in grams by the patient's body surface area. Relative wall thickness, defined as the ratio of end-diastolic left ventricular posterior wall thickness to left ventricular internal dimension ([2x posterior wall thickness]/left ventricular internal dimension), was determined to be < or ≥0.42. Left ventricular geometry was considered normal if left ventricular mass index was <95th percentile and relative wall thickness <0.42; concentric remodelling was reported if left ventricular mass index was <95th percentile and relative wall thickness ≥0.42; concentric hypertrophy was reported if left ventricular mass index was ≥95th percentile and relative wall thickness ≥0.42; and eccentric hypertrophy was reported if left ventricular mass index was ≥95th percentile and relative wall thickness <0.42 (12).

Statistical analysis

Statistical analysis was performed using SPSS v. 23.0 (IBM, Armonk, NY, USA). Continuous data were described as median (inter-quartile range, IQR) and categorical variables as percentages. Chi-square test was used to compare categorical variables and Mann-Whitney U-test/ Student's t-test was used to compare continuous variables. Kaplan-Meier test was used for survival analysis. *P*-values of <0.05 were considered as significant.

This study has been approved by Hacettepe University Ethics Commission (approval no: GO 17/157-23).

Results

Demographic and clinical features

Twenty-five (14%) patients had paediatric-onset TAK. 161 patients were female (80% and 91.6% of patients with paediatric-onset and adult-onset TAK, respectively). The mean age at diagnosis for children and adults were 13.6±4 and 35.6±13 respectively. The most common presentation of the patients with TAK was claudication (19%) followed by the constitutional symptoms (12.8%) (Table I).

Overall, the paediatric patients presented with a more inflammatory state including increased incidence of fatigue, constitutional symptoms and increased acute phase reactants. (Table I) This was reflected in the extent of vessel involvement according to the Numano classification as well (Table II). The paediatric patient with TAK had numerous hospital visits with a wide range of symptoms depending on the vessel involved. Almost all of them complained of fatigue or limitations in their daily life. They presented with symptoms ranging from severe abdominal pain, flank pain, syncope and chest pain. When they were diagnosed in our clinic weak pulses and difference in blood pressure were present in only 36% (n=9) of the paediatric patients. On the other hand, the adult patients presented with more subtle findings and most had discrepancies in pulses and blood pressures (Table I).

Adult TAK patients had a wider distribution for disease onset age. Even if not statistically significant, a higher female predominance was found. As a sign of the early systemic phase, however, non-specific inflammatory features were less a reflection of later stages. Clinical characteristics were not different from paediatric patients.

Disease activity and acute phase reactants

Paediatric onset TAK patients had higher inflammation at disease onset. Although ITAS-A and ITAS-2010 scores were comparable between adults and children, baseline median erythrocyte sedimentation rate and C-reactive protein levels were significantly higher in patients with paediatric-onset TAK (p=0.006 and p=0.005, respectively) (Table I).

Involvement of vasculature

Splanchnic arteries were more commonly affected in paediatric-onset

Table I. Clinical and demograhic features of TAK patients.

	All TAK (n=179)	Paediatric-onset TAK (n=25)	Adult-onset TAK (n=155)	*p*
Female, n (%)	161 (89.9)	19 (79.2)	142 (91.6)	0.072
Age at TAK diagnosis, years, mean ± SD	30.9 ± 14.8	12.8 ± 4.6	35.7 ± 12.7	<0.001
Median disease duration, years (IQR)	4.6 (6.7)	3.2 (4.8)	5.5 (7.9)	0.51
Median time for diagnostic delay, months (IQR)	5 (23)	7.6 (16.8)	4.0 (24.3)	0.48
Median ESR at TAK diagnosis, mm/h (IQR)	60 (53)	87 (67)	54 (50)	0.006
Median CRP at TAK diagnosis, mg/dL (IQR)	4 (9)	11 (12)	3.4 (8)	0.005
Median Hb at TAK diagnosis, mg/dL (IQR)	11 (3)	10.2 (2)	11.3 (3)	0.054
Median ITAS-2010 score (IQR)	7 (4)	8 (5)	6 (3)	0,57
Median ITAS-A score (IQR)	9 (5)	11 (4)	8.5 (4)	0,24
Comorbidities, n (%)				
Hypertension	59 (33.1)	13 (54.2)	46 (29.9)	**0.019**
Diabetes mellitus	14 (7.8)	0 (0)	14 (9.0)	0.22
Myocardial infarction and/or heart failure	2 (1.1)	0 (0)	2 (1.3)	0.75
Cerebrovascular accident	22 (12.3)	0 (0)	22 (14.2)	**0.048**
Pulmonary hypertension	5 (2.8)	1 (4.2)	4 (2.6)	0.52
Malignancy	6 (3.4)	0 (0)	6 (3.9)	1
Inflammatory conditions, n (%)				
Psoriasis	1 (0.6)	0	1 (0.6)	1
Familial Mediterranean fever	1 (0.6)	0	1 (0.6)	1
Spondyloarthritis	13 (7.3)	1 (4.2)	12 (7.7)	1
Inflammatory Peripheral Arthritis	3 (1.7)	0 (0)	3 (1.9)	1
Enteropathy (Coeliac disease or inflammatory bowel disease)	5 (2.8)	2 (8.3)	3 (1.9)	0.13
Glomerulonephritis (FSGS)	1 (0.6)	0	1 (0.6)	1
Death, n (%)	8 (4.5)	2 (8.3)	6 (3.9)	0.29

Table II. Vascular involvement in paediatric-onset and adult-onset TAK.

		All TAK (n=179)	Paediatric-onset TAK (n=25)	Adult-onset TAK (n=154)	*p*
Ascending aorta		58 (32.4)	10 (41.7)	48 (31)	0.30
Aortic arch		98 (54.7)	16 (66.7)	82 (52.9)	0.55
Brachiocephalic trunk		74 (41.3)	11 (45.8)	63 (40.6)	0.63
Common carotid arteries		119 (66.5)	17 (70.8)	102 (65.8)	0.63
Subclavian arteries		142 (79.3)	14 (58.3)	128 (82.6)	0.01
Descending thoracic aorta		107 (59.8)	17 (70.8)	90 (58.1)	0.23
Abdominal aorta		92 (51.4)	15 (62.5)	77 (49.7)	0.24
Coeliac and/or mesenteric arteries		68 (38)	14 (58.3)	54 (34.8)	0.04
Coeliac Artery		41 (22.9)	11 (45.8)	30 (19.4)	0.004
Superior mesenteric artery		55 (30.7)	10 (41.7)	45 (29.0)	0.21
Inferior mesenteric artery		13 (7.3)	1 (4.2)	12 (7.7)	1
Renal arteries		54 (30.2)	11 (45.8)	43 (27.7)	0.07
Common iliac arteries		16 (8.9)	2 (8.3)	14 (9.0)	1
Pulmonary arteries		29 (16.2)	5 (20.8)	24 (15.5)	0.55
Numano classification	**Unclassified***	1 (0.6)	0 (0)	1 (0.6)	0.19
	Type 1	34 (19)	1 (4.2)	33 (21.3)	
	Type 2a	9 (5)	2 (8.3)	7 (4.5)	
	Type 2b	18 (15.6)	4 (16.7)	24 (15.5)	
	Type 3	7 (3.9)	1 (4.2)	6 (3.9)	
	Type 4	4 (2.2)	2 (8.3)	2 (1.3)	
	Type 5	96 (53.6)	14 (58.3)	82 (52.9)	
A novel disease classification	**Cluster 1 (Abdominal predominant)**	47 (26.3)	11 (45.8)	36 (23.3)	0.064
	Cluster 2 (Aortic Arch predominant)	71 (39.7)	7 (29.3)	64 (41.3)	
	Cluster 3 (Focal disease)	61 (34.1)	6 (25.0)	55 (35.5)	

*Only pulmonary arterial involvement.

Table III. Comparison of treatment agents used in paediatric and adult-onset TAK patients.

	All TAK (n= 179)	Pediatric-onset TAK (n=25)	Adult-onset TAK (n=154)	*p*
Ever usage of immunosuppressive agents, n (%)				
Methotrexate	103 (57.5)	16 (66.7)	87 (56.1)	0.33
Azathiopurine	56 (31.3)	7 (29.2)	49 (31.6)	0.81
Leflunomide	11 (6.1)	3 (12.5)	8 (5.2)	0.17
Cyclophosphamide and/or biologics	93 (52)	21 (87.5)	72 (46.5)	**<0.001**
Cyclophosphamide	66 (36.9)	15 (62.5)	51 (32.9)	**0.005**
Biologics	54 (30.2)	17 (70.8)	37 (23.9)	**<0.001**
TNF-α inhibitors	27 (15.1)	12 (50)	15 (9.7)	**<0.001**
Interleukin-6 blockage	38 (21.2)	10 (41.7)	28 (18.1)	**0.009**
Endovascular intervention and/or vascular surgery, n (%)	32 (17.9)	5 (20.8)	27 (17.4)	0.77
Endovascular intervention	19 (10.6)	0 (0)	19 (12.3)	0.08
Vascular surgery	19 (10.6)	5 (20.8)	14 (9.0)	0.14

Table IV. The echocardiographic data of paediatric-onset and adult-onset TAK patients.

Parameters, median (IQR)		Adult-onset (n=27)	Peadiatric-onset (n=15)	*p*
Gender, women, n (%)		22 (%84.6)	11 (%73.3)	0.38
Age, mean ± SD		32.4 ± 12.48	12.77 ± 4.73	<0.001
Length (cm)		164 (8.25)	154 (28)	0.017
Weight (kg)		65 (15.75)	42 (26)	0.001
Body mass index (BMI) (kg/m^2)		23.4 (5.28)	17.7 (3.61)	0.002
Body surface area (m2)		1.74 (0.24)	1.4 (0.51)	0.014
Frequency of hypertension, n (%)		**6 (23.1%)**	**8 (53.3%)**	**0.049**
Pulmonary artery systolic pressure* >40 mmHg, n (%)		4 (14.8%)	2 (15.4%)	1
Presence of pericardial effusion, n (%)		2 (7.4%)	1 (6.7%)	1
Decreased ejection fraction, n (%)		2 (7.4%)	3 (20%)	0.329
Ascending aortic dilatation, n (%)		**1 (3.7%)**	**7 (50%)**	**0.001**
Increased left ventricular mass index (LVMI), n (%)		**5 (25%)**	**9 (60%)**	**0.036**
Increased relative wall thickness (RWT) , n (%)		11 (40.7%)	7 (46.7%)	0.710
VENTRICULAR GEOMETRY	NORMAL	8 (%29.6)	4 (26.7%)	0.68
	EXCENTRIC HYPERTROPHY	8 (%29.6)	5 (33%)	
	CONCENTRIC REMODELLING	7 (25.9%)	2 (13.3%)	
	CONCENTRIC HYPERTROPHY	4 (14.8%)	4 (26.7%)	
Mitral valve insufficiency	Normal-mild	23 (85.2%)	13 (86.7%)	1
	Moderate-severe	4 (14.8%)	2 (13.3%)	
Tricuspid valve insufficiency	Normal-mild	22 (81.5%)	15 (100%)	0.142
	Moderate-severe	5 (18.5%)	0 (0%)	
Aortic valve insufficiency	**Normal-mild**	**24 (88.9%)**	**8 (53.3%)**	**0.020**
	Moderate-severe	**3 (11.1%)**	**7 (46.7%)**	
Pulmonary valve insufficiency	Normal-mild	27 (100%)	15 (100%)	NA
	Moderate-severe	0 (0%)	0 (0%)	

*Estimated by measuring the tricuspid regurgitation jet maximum velocity by continuous wave Doppler plus estimated right atrial pressure.

TAKs (%58.3 *vs*. % 34.8, *p*=0.04) (Table II). Similarly, in paediatric-onset TAKs, there was a trend toward higher frequency for involvement of renal arteries (45.8% *vs*. 27.7%, *p*=0.07). On the other hand, subclavian artery involvement was more frequently seen in adult-onset disease (82.6% *vs*. 58.3%, *p*=0.01). Abdominal predominant disease was more common in the paediatric group, in contrast, focal disease and aortic arch predominant disease were more common in the adult group (*p*=0.06). Type 1 disease and focal disease was very rare in children according to Numano classification; in fact, the extent of vessel involvement tended to be more severe in children (Table II).

Cardiological evaluation

The echocardiographic data of 15 paediatric and 27 adult patients with TAK from the diagnosis to the first three months are summarised in Table IV. Echo-

Table V. Comparison of clinical and laboratory features of patients with paediatric and adult-onset Takayasu's arteritis.

	Number of patients (Paediatric/ Adult)	Study location	Age at disease onset (years) (Paediatric/ adult)	Female (n/%) (Paediatric/ adult)	Vascular involvement	Clinical manifestations	Laboratory features	Treatment regimens	Death (Paediatric/ Adult) (n/%)
Bolek *et al.*	25 children 154 adult	Turkey	13.6 ± 4 35.6 ± 13	19 (79.2) 142 (91.6)	Abdominal predominant disease* Splanchnic arteries* Subclavian artery**	Fatigue, constitutional symptoms* Discrepancies in pulses and blood pressures**	Elevated baseline ESR and C-reactive protein levels*	The total dose of corticosteroids used were lower in the pediatric group Cyclophosphamide and all biological therapies*	2 (8.3) 6 (3.9)
Jales-Neto *et al.* (15)	17 children 45 adult	Brazil	16 (1–18) 29 (21–53)	11 (64.7) 40 (88.8)	Left renal stenosis* Subclavian artery**	Clinical manifestations of TAK were similar apart from weight loss*	NA	The use of corticosteroid and immunosuppressive therapy was similar	2 (11.7) 4 (8.8)
Aeschlimann *et al.* (16)	29 children 48 adult	Canada	12.1 (9.8 –13.8) 31.2 (26.9-40.1)	22 (76) 48 (100)	Aorta and renal arteries* Subclavian arteries**	Arterial hypertension and decreased pulses of the lower extremities* Arthritis/arthralgia and claudication of the extremities**	Acute phase reactants in children were slightly high, but not statistically significant	Corticosteroids only** CS+ Cyclo* CS + MTX* CS + anti-TNF*	No deaths
Cong *et al.* (17)	31 children 94 adult	China	13.7 (6–18) 26.9 (6–65) (all patients)	24 (77.4) 84 (89.4)	Aortic arch branches**	Constitutional symptom and pulse deficit **	Elevated ESR**	NA	4 (12.9) 4 (4.2) s

ESR: erythrocyte sedimentation rate; NA: not available; CS: corticosteroid; Cyclo: cyclophosphamide; MTX: methotrexate.
*More common findings in paediatric-onset Takayasu's arteritis patients.**More common findings in adult-onset Takayasu's arteritis patients.

cardiographic data analysis revealed that systemic hypertension (23.1% *vs*. 53.3%, p=0.049), ascending aortic dilatation (3.7% *vs*. 50%, p=0.001) and left ventricular hypertrophy (25% *vs*. 60%, p=0.036) were more frequent in paediatric-onset TAK patients. There was no difference between groups in terms of ventricular geometry changes. Twenty-two percent of adult patients and 53% of paediatric patients had moderate-to-severe valvular insufficiency at the time of diagnosis (p=0.045). It was observed that moderate-severe aortic insufficiency was statistically more frequent in paediatric onset TAK patients (46.7% *vs*. 11.1%, p=0.020) and there was no difference between the groups in terms of other valve insufficiencies.

Comorbidities

As far as comorbidities are concerned, hypertension was more commonly encountered during the follow-up period in the paediatric TAK patients (54.2% *vs*. 29.9; p=0.019). On the other hand, cerebrovascular disease was more common in adult patients (0 *vs*. 14.2; p=0.048). Although the rest of the comorbidities were more common in adults, the differences have not reached the statistical significance. Eight of the patients with TAK died during the follow-up period due to infectious causes (6 adult and 1 paediatric case) and heart failure (1 paediatric case) (Table I).

Treatment choices

Corticosteroids which is the main therapeutic agent of TAK management, were given to all of the patients (not shown in the table). The total dose of corticosteroids used were lower in the paediatric group. Cyclophosphamide and all biological therapies were more commonly used in patients with paediatric-onset TAK than adult-onset disease. Although not significant, endovascular interventions were more common in the adult group whereas vascular surgery was more common in the paediatric group (Table III).

Discussion

In this study, we aimed to highlight the differences between the paediatric and adult onset TAK in terms of clinical characteristics, laboratory findings, distribution of the vascular involvement sites and differences in treatment approaches. This retrospective data is sourced from a large cohort of a single tertiary referral centre in Turkey.

We reported a higher ratio of female in adults, although not statistically significant. A similar result was found in the other studies comparing adult and paediatric TAK patients (15-17).

This study suggested that paediatric-onset TAK was a more inflammatory disease as compared to the adult-onset disease. In children the clinical presentation, though insidious, tended to be more inflammatory. This was reflected in their complaints, high acute phase reactants and extent of vascular involvement according to the Numano classification and activity index. Clinically, most of the paediatric patients were more ill, with the fatigue and the severe pain they were experiencing in the target area. They tended to have high acute phase reactants. Szugye *et a*l. had also reported that constitutional symptoms (weight loss, fatigue, and anorexia) were the most common complaints in children with TAK and that all of the pa-

tients had elevated ESR levels at presentation.(18) However, acute phase reactants have not been previously reported to be significantly higher in children compared to adults (Table V) (15-17).

We also noted that hypertension was more frequent among paediatric-onset TAK patients, which was attributed to increased renal artery involvement in children. The high rate of hypertension is feature has been highlighted in other childhood TAK series as well and has been the reason for including it as a criterion in the paediatric Ankara 2008 criteria. (7, 19-21) Furthermore the cardiac examination revealed that increase in left ventricular mass index, ascendan aortic dilation and significant aortic regurgitation was statistically more frequent in children during diagnosis period which reflects the severity of the disease in children. In addition, although it is not statistically significant, systolic dysfunction is more common in paediatric patients (20% *vs*. 7.4%, p=0.329). These findings might have occurred due to hypertension caused by renal artery involvement. Monti *et al*. reported the association between renal artery involvement and severe cardiac and renal dysfunction (22). On the other hand the adults display a more subtle disease with lower acute phase reactants.

There were differences in vessel involvement as well. In this largest study, which the novel disease classification tree is applied for both paediatric and adult TAK patients, the involvement of the abdominal aorta and its branches was more frequent among paediatric onset patients. On the other hand, subclavian artery and the upper aorta was more frequently attacked in the adult-onset patients. A similar pattern of vascular involvement was also observed in patients reported from Canada and Brazil (15-16). This was reflected in more pronounced difference between pulses and blood pressures in adult patients whereas hypertension was more frequent among the paediatric patients. Type 1 disease was more common among adults whereas type 4 and 5 were more common among children. Type V disease was reported to be the most common presentation in two other childhood series, as well (19-20). It is tempting to suggest that this also reflects more severe disease in children. The distribution of vessel involvement is in accordance to the previously published multicentre Turkish series of adult TAK patients. Bicakcigil *et al*. reported type 1 and 5 disease to be 32% and 51% respectively among their adult TAK Turkish patients (2), and in the other cohorts type I disease was reported 0-32% and type 5 disease was reported 29-67% (23-26). Similarly, in the previously published adult series, left subclavian artery involvement was 56.8% and right subclavian artery involvement was 44.9% (10).

The activity indices in TAK are still not validated in children. BVAS and PVAS are known to not perform well. According to the ITAS-2010 and ITAS-A activity index, the median scores of childhood-onset disease, was 8 and 11 respectively which means the patients were active at the time of TAK diagnosis.

In the presented series, the use of immunosuppressive drugs was more common in children. The need for additional immunosuppressive on top of steroids has been previously highlighted as well. Although it was reported that remission could be achieved in 60% of adult patients with only steroids, only 2 of the 25 paediatric patients were reported to respond to steroid treatment and they required immunosuppressive agents (18, 27). The increased usage of immunosuppressive drugs in the paediatric group is partially due to more severe vessel involvement, with both the thoracic and abdominal aorta and branches being involved, and partially due to the desire to use less steroids in this adolescent age group. The introduction of biologics will probably decrease the use of cyclophosphamide in the coming years.

The diagnosis of TAK, especially in children is challenging. There are no pathognomonic laboratory tests, unless an angiogram is performed. Most patients will have hypertension or a specific ischaemic pain to guide the paediatrician in the diagnosis. However, the differential diagnosis includes many diseases. For example, one of the patients had been followed for months with work-up for renal tests and ankylosing spondylitis for her back pain. Another patient was followed by neurologists as a case of "atypical epilepsy" or Munchausen syndrome. Since children can present with atypical symptoms, the diagnosis may be delayed for longer periods (22). Blood pressure should be measured form both arms in any patient with an unexplained pain and high acute phase response.

The comorbidities were as expected in this disease. Similar comorbidities have been previously reported in the largest Turkish cohort as well such as hypertension (43%), cerebrovascular accidents (18%), spondyloarthropathy, psoriasis and inflammatory bowel disease (2).

The main limitation of this study is its retrospective design, with missing data due to its retrospective nature. We do not have the results of the objective scales for treatment response and damage. Also, cumulative dose and usage period for corticosteroids and the other first-line anti-rheumatic drugs is not known. Discrepancy for the distribution of vascular involvement and inflammatory conditions suggest that these groups may have different disease course and treatment response. A prospective study would have allowed better assessment of the activity and follow-up of the patients.

In conclusion, we suggest that TAK should be taken into account in the differential diagnosis for all patients presenting with inflammatory symptoms. Our data suggests that the disease tends to be more severe with abdominal symptoms predominantly in childhood-onset patients, whereas aortic arch involvement is dominant in the adult group. Further multicentre and multinational collaborative studies are needed to demonstrate and confirm the differences in age of onset for TAK.

Competing interests

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