Features of the Onset of Takayasu’s Arteritis According to Gender

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Abstract

Background: Although there are various published epidemiological studies regarding Takayasu’s arteritis (TA), none have analyzed the influence of gender on the clinical and laboratory manifestations or vascular alterations at disease onset.

Objectives: To analyze the influence of gender on clinical and laboratory manifestations and variations in vascular imaging at TA onset.

Methods: A retrospective, unicentric cohort study that evaluated 55 consecutive TA patients between 1982 and 2012. All available clinical data and laboratory test results related to the onset of the disease were analyzed. We included only patients aged 12-35 years at diagnosis to exclude age-related factors.

Results: We analyzed 17 men and 38 women, mostly Caucasian, with a comparable mean age between genders. There was no gender difference regarding the clinical or laboratory characteristics, comorbidities, or smoking habit, except for abdominal pain, which was more common in men. Regarding vascular lesions, the presence of ascending aortic aneurysms was significantly more frequent in males. Male gender represented an independent risk factor for the occurrence of abdominal pain and ascending aortic aneurysms in TA patients.

Conclusion: Abdominal pain and ascending aortic aneurysms occurred more frequently in men with TA, suggesting a more severe disease profile in males. (Arq Bras Cardiol. 2013;101(4):359-363)

Keywords: Takayasu Arteritis / epidemiology; Male; Female; Cohort Studies; Aortic Aneurysm, Abdominal; Abdominal Pain.

Introduction

Takayasu’s arteritis (TA) is a type of primary systemic vasculitis that affects medium and large arteries, including the aorta and its main branches, as well as the pulmonary and coronary arteries. The pathophysiology of TA is characterized by vessel wall inflammation, leading to thickening, stenosis, dilatation, and/or aneurysm formation of the affected vessels. The signs and symptoms that reflect the context of the systemic inflammation or ischemia of an organ or limb include the presence of claudication, angiodynia, peripheral pulselessness, murmurs, severe systemic arterial hypertension, myocardium infarction, and ischemic stroke, among others.

In general, systemic autoimmune diseases affect more women than men, by a ratio of 2–10:1. Systemic lupus erythematosus and Sjögren's syndrome, for example, have ratios of 7–10:1, whereas rheumatoid arthritis and systemic sclerosis have ratios of 2–3:1, while TA also tends to affect women more often, with a ratio of 1.2–29:1.

Although there have been various epidemiological studies regarding TA, none have reported the influence of gender on the clinical and laboratory manifestations and the vascular alterations at the onset of the TA. Although Sharma and Jain studied a possible role of sex in the distribution of the vascular lesions in TA and found a tendency for greater involvement of the abdominal aorta in men and the aortic arch and its branches in women, they did not specify whether their findings were cumulative or related to disease onset.

Thus, in the present study, we evaluated the initial clinical manifestations and the vascular alterations at the onset of TA according to gender.

Methods

We evaluated 55 consecutive TA patients (17 men and 38 women) treated at the vasculitis unit of our tertiary facility between 1982 and 2012. We included only patients who were aged between 12 and 35 years at TA diagnosis and who met at least three of the six American College of Rheumatology classification criteria (1990). The study protocol was approved by our local ethics committee.

Demographic data, clinical manifestations, and vascular images were obtained through a systematic review of the patients’ medical records. The follow parameters were analyzed: (A) clinical manifestations: constitutional symptoms (weight loss, fever, fatigue), headache, dizziness, visual
impairment (blindness), seizures, carotidynia, claudication, abdominal pain, chest pain, dyspnea, articular manifestations (arthritis/arthralgia), and erythema nodosum; (B) laboratory findings: C-reactive protein (CRP) (reference value: < 5 mg/L) and erythrocyte sedimentation rate (ESR) (reference value: < 19 mm/1st hour); (C) comorbidities: myocardium infarction, ischemic stroke, systemic arterial hypertension, heart failure, type 2 diabetes mellitus, and dyslipidemia; (D) habit: smoking; and (E) echocardiography: aortic insufficiency.

All vascular images were obtained via angiography or computed tomography angiography, in which we evaluated the following parameters: stenosis/occlusion, aneurysm/vascular ectasia, and the anatomical location of these lesions.

The results were expressed as the means ± standard deviation (SD) or as percentages. We used the Student’s t-test to analyze the parametric data and the Mann-Whitney U-test for the nonparametric data. The 95% confidence intervals (95% CI) of the percentages were calculated by binomial distribution. All calculations were performed using STATA ver. 7.0 statistical software (Stata Corp., College Station, TX, USA). A p-value < 0.05 was considered statistically significant.

Results

We analyzed records of 17 men and 38 women with TA, who were mostly Caucasian and had a comparable mean age between genders (Table 1). The clinical and

| Features                  | Male (n = 17) | Female (n = 38) | P   |
|---------------------------|--------------|-----------------|-----|
| Age at disease onset ± SD (years) | 23.5 ± 7.6   | 25.3 ± 5.5      | 0.371 |
| Ethnicity: white (%)      | 9 (52.9)     | 28 (73.7)       | 0.130 |

### Clinical onset manifestations

| Feature                   | Male (%) | Female (%) | P   |
|---------------------------|----------|------------|-----|
| Weight loss (%)           | 8 (47.1) | 9 (23.7)   | 0.083 |
| Fever (%)                 | 7 (41.2) | 10 (26.3)  | 0.270 |
| Fatigue (%)               | 2 (11.8) | 6 (15.8)   | 0.696 |
| Headache (%)              | 1 (5.9)  | 6 (15.8)   | 0.308 |
| Dizziness (%)             | 0        | 2 (5.3)    | 0.335 |
| Visual disturbances (%)   | 1 (5.9)  | 2 (5.3)    | 0.926 |
| Amaurosis (%)             | 1 (5.9)  | 0          | 0.131 |
| Convulsions (%)           | 1 (5.9)  | 0          | 0.131 |
| Carotidynia (%)           | 3 (17.6) | 8 (21.1)   | 0.770 |
| Upper limb claudication (%)| 5 (29.4) | 16 (42.1)  | 0.371 |
| Lower limb claudication (%)| 2 (11.8) | 12 (31.6)  | 0.119 |
| Abdominal pain (%)        | 6 (35.3) | 2 (5.3)    | 0.004 |
| Chest pain (%)            | 0        | 6 (15.8)   | 0.083 |
| Dyspnea (%)               | 1 (5.9)  | 6 (15.8)   | 0.308 |
| Articular manifestations (%)| 1 (5.9) | 4 (10.5)   | 0.165 |
| Erythema (%)              | 1 (5.9)  | 4 (10.5)   | 0.580 |
| Elevated ESR and/or CRP (%)| 6 (35.3) | 23 (60.5)  | 0.613 |
| Aortic insufficiency (%)  | 3 (17.6) | 6 (15.8)   | 0.863 |

### Comorbidities

| Feature                  | Male (%) | Female (%) | P   |
|--------------------------|----------|------------|-----|
| Ischemic stroke (%)      | 1 (5.9)  | 10 (26.3)  | 0.143 |
| Systemic arterial hypertension (%)| 10 (58.8) | 20 (52.6)  | 0.370 |
| Cardiac insufficiency (%)| 0        | 1 (2.6)    | 0.500 |
| Myocardium infarction (%)| 0        | 1 (2.6)    | 0.500 |
| Diabetes mellitus (%)    | 0        | 2 (5.3)    | 0.335 |
| Dyslipidemia (%)         | 2 (11.8) | 12 (31.6)  | 0.119 |
| Smokers (%)              | 2 (11.8) | 4 (10.5)   | 0.892 |

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; SD: standard deviation.
laboratory characteristics and comorbidities of patients at disease onset are shown in Table 1. There was no gender difference regarding the distribution of signs and symptoms, except for abdominal pain (35.3% vs. 5.3%, p = 0.004, in men and women, respectively). The presence of aortic insufficiency, elevation of ESR and CRP, comorbidities, and habit (smoking) were also similar between genders.

Regarding vascular lesions found in the first imaging for each patient, we observed that there was no gender difference in the frequency or the location of the stenoses/occlusions, which were more common in the carotid and subclavian arteries in women than men (Table 2). However, the presence of ascending aortic aneurysms was significantly more frequent in men (35.3 vs. 10.5%, p = 0.028), although other aneurysm locations did not differ between genders.

Multivariate analysis showed that male gender was a risk factor for the occurrence of abdominal pain (OR, 18.75; 95% CI, 2.89–121.54) and aortic aneurysm (OR, 9.51; 95% CI, 1.94–46.70) (Table 3).

### Discussion

To our knowledge, the present study is the first to analyze the presentation of TA in terms of clinical manifestations and vascular imaging alterations according to gender. Compared to women, men had a higher prevalence of abdominal pain and ascending aortic aneurysm at diagnosis of TA.

Despite the existence of various epidemiological series regarding TA patients, none have compared disease presentation between men and women. In this study, all of the parameters refer clearly to the onset of symptoms before any drug or surgical treatment is initiated. Furthermore, we evaluated only patients aged between 12 and 35 years to exclude clinical manifestations, comorbidities, or vascular changes that could be related to advanced age rather than to TA alone.

Gender is likely a determinant in the prognosis of several rheumatic diseases. For example, systemic lupus erythematosus tends to have a worse prognosis

### Table 2 - Angiographic characteristics of Takayasu’s arteritis according to gender

| Vessels                  | Stenosis / Occlusion | Male | Female | p    | Aneurysm / Ectasia | Male | Female | p    |
|--------------------------|----------------------|------|--------|------|---------------------|------|--------|------|
| Left coronary (%)        |                      | 0    | 1 (2.6)| 1.000|                     | 0    | 0      | 1.000|
| Right coronary (%)       |                      | 0    | 1 (2.6)| 1.000|                     | 0    | 0      | 1.000|
| Left vertebral (%)       |                      | 0    | 6 (15.8)| 0.131|                     | 1 (5.9)| 0      | 0.131|
| Right vertebral (%)      |                      | 0    | 6 (15.8)| 0.131|                     | 1 (5.9)| 0      | 0.131|
| Left carotid (%)         |                      | 7 (41.2)| 20 (52.6)| 0.487|                     | 0    | 0      | 1.000|
| Right carotid (%)        |                      | 6 (35.3)| 20 (52.6)| 0.200|                     | 0    | 0      | 1.000|
| Left subclavian (%)      |                      | 6 (35.3)| 21 (55.3)| 0.926|                     | 1 (5.9)| 2 (5.3)| 0.926|
| Right subclavian (%)     |                      | 4 (23.5)| 14 (36.8)| 0.552|                     | 1 (5.9)| 1 (2.6)| 0.552|
| Brachiocephalic trunk (%)|                      | 1 (5.9)| 5 (13.2)| 0.391|                     | 2 (11.8)| 2 (5.3)| 0.391|
| Pulmonary trunk (%)      |                      | 0    | 1 (2.6)| 0.500|                     | 0    | 1 (2.6)| 0.500|
| Aortic                   |                      |      |        |      |                     |      |        |      |
| Ascendant (%)            |                      | 1 (5.9)| 2 (5.3)| 0.926|                     | 6 (35.3)| 4 (10.5)| 0.028|
| Cross (%)                |                      | 1 (5.9)| 4 (10.5)| 0.168|                     | 2 (11.8)| 1 (2.6)| 0.168|
| Thoracic (%)             |                      | 1 (5.9)| 7 (18.4)| 0.108|                     | 4 (23.5)| 3 (7.9)| 0.108|
| Abdominal (%)            |                      | 2 (11.8)| 7 (18.4)| 0.552|                     | 1 (5.9)| 1 (2.6)| 0.552|
| Infrarenal (%)           |                      | 2 (11.8)| 8 (21.1)| 0.131|                     | 1 (5.9)| 0      | 0.131|
| Left renal (%)           |                      | 7 (41.2)| 5 (13.2)| 0.500|                     | 0    | 0      | 0.500|
| Right renal (%)          |                      | 6 (35.3)| 5 (13.2)| 0.131|                     | 1 (5.9)| 1 (2.6)| 0.131|
| Upper mesenteric (%)     |                      | 3 (17.6)| 7 (18.4)| 0.945|                     | 0    | 0      | 1.000|
| Lower mesenteric (%)     |                      | 2 (11.8)| 3 (7.9)| 0.645|                     | 0    | 0      | 1.000|
| Celiac trunk (%)         |                      | 2 (11.8)| 4 (10.5)| 0.131|                     | 1 (5.9)| 0      | 0.131|
| Left iliac (%)           |                      | 1 (5.9)| 6 (15.8)| 0.308|                     | 0    | 0      | 1.000|
| Right iliac (%)          |                      | 1 (5.9)| 5 (13.2)| 0.424|                     | 0    | 0      | 0.500|
in men, although this view remains controversial[^20-23]. In rheumatoid arthritis, female gender has been associated with higher scores of disease activity[^24] and is an established predictor of radiographic progression[^25]. Furthermore, the inflammatory response appears to be more severe in women than in men as well as the presence of giant cell arteritis and polymyalgia rheumatica[^26]. However, there are no studies that have evaluated sex as a determining factor in TA prognosis. Our results showed a strong association between the presence of aortic aneurysm and male gender, thereby correlating this gender to a poor prognostic factor.

Other factors classically associated with poor prognosis in TA include the following: retinopathy, hypertension, severe aortic regurgitation, and the presence of aortic or arterial aneurysm, as mentioned previously[^27]. Subsequently, the presence of severe functional disability and cardiac involvement were reported as predictors of either death or major events on follow-up[^28]. Sharma and Jain[^6] reported a trend toward a higher frequency of hypertension in men with TA compared with women, but this was not observed in the present study. Chugh et al[^29] studied renovascular hypertension in Indians with AT and also found no difference between genders. Aortic regurgitation was also similar in both sexes in our series, in contrast to the findings of Kobayashi and Numano[^30], who reported a higher prevalence of aortic regurgitation in women.

Our study was limited by its retrospective nature and complicated by typical problems of this type of cohort. Furthermore, the collected data were dependent on the medical records and even though all of the variables were true at the time of diagnosis, we do not know if they accurately reflected manifestations at disease onset.

### Conclusion

Abdominal pain and ascending aortic aneurysms occurred more frequently in men with TA and the male gender was an independent risk factor for such findings. Nonetheless, further studies will be needed to confirm male gender as a predictor of poor prognosis in TA.

### Author contributions

Conception and design of the research and Statistical analysis: Shinjo SK; Acquisition of data, Analysis and interpretation of the data, Writing of the manuscript and Critical revision of the manuscript for intellectual content: MontAlverne ARS, Paula LE, Shinjo SK.

### Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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### Study Association

This study is not associated with any post-graduation program.

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