Clinical and vascular features of Takayasu arteritis at the time of ischemic stroke

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ABSTRACT

Objectives: Takayasus arteritis (TA) is a systemic vasculitis whose clinical presentation varies from asymptomatic to serious neurovascular events, including stroke. However, few studies are currently available assessing stroke in TA. Thus, we described the clinical and laboratory characteristics and vascular imaging features in patients with TA at the time of stroke.

Materials and Methods: This is a single center retrospective cohort study investigating the clinical and demographic data of 18 (15.0%) patients with a history of stroke confirmed by imaging methods, among 120 patients with TA, assessed in the 1985-2012 period.

Results: The mean age of the 18 patients at the time of stroke was 29.4±10.9 years, with 94.4% female and 88.9% Caucasian. Of these patients, 14 (77.8%) had previous stroke at diagnosis of TA, while in four cases the stroke occurred after confirmed TA diagnosis. Regarding the clinical course, 12 (66.7%) had peripheral neurological sequelae and one patient died as a result of cerebral hyperperfusion syndrome after carotid revascularization.

Conclusions: Our results showed a high prevalence of stroke in TA and revealed most of these events occurred concomitantly with diagnosed TA. Moreover, although four patients had strokes after diagnosis of TA, these occurred at a young age, demonstrating they were most likely the result of vascular changes secondary to TA.

Keywords: Neurological manifestations; Stroke; Systemic vasculitis; Takayasus arteritis.

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INTRODUCTION

Takayasu's arteritis (TA) is a rare idiopathic systemic vasculitis that affects the large vessels, such as the aorta and its main branches[1].

Concerning pathogenesis, TA causes inflammation of the vascular wall, leading to thickening, stenosis, dilation and/or aneurysm formation within affected vessels[2]. Moreover, occlusion of carotid and/or vertebral vessels and also severe or uncontrolled arterial hypertension can lead to neurovascular events, such as stroke and transient ischemic attack (TIA)[3].

The prevalence of neurovascular events in TA varies from 5 to 17%[4-10], contributing to high morbidity and mortality in this population. A French study, for example, found 6.6% and 15.9% neurovascular events as the first presenting features of TA and during follow-up, respectively8, whereas Sato et al.[10] observed 8% and 19% neurovascular events as the initial manifestation of TA and during follow-up. However, these studies did not report details of stroke events such as neurological manifestations.

Therefore, the aim of the present study was to analyze the demographic, laboratory and vascular features of TA patients at the time of stroke along with the features of this neurological event.

MATERIALS AND METHODS

A single-center retrospective study was performed of 120 consecutive TA patients followed at our tertiary service between 1985 and 2012. All patients fulfilled at least three of the six American College of Rheumatology (ACR) criteria for the classification of TA[11]. Eighteen (15.0%) out of 120 TA patients had a history of stroke which was defined as an episode of sudden-onset lateralized neurological deficit confirmed by objective evidence of ischemia on computed tomography brain scan.

TABLE I. NEUROLOGICAL, CLINICAL AND LABORATORY FEATURES OF PATIENTS WITH TAKAYASU'S ARTERITIS AT STROKE ONSET

Features	
Hemiparesis (%)	14 (77.8)
Headache (%)	5 (27.8)
Dizziness (%)	4 (22.2)
Seizures (%)	2 (11.1)
Visual changes (%)	2 (11.1)
Aphasia (%)	2 (11.1)
Syncope (%)	2 (11.1)
Constitutional symptoms (%)	1 (5.6)
Limb claudication (%)	14 (77.8)
CRP (mg/L)	3.9 [2.2-6.3]
ESR (mm/1st hour)	12 [6.0-25.5]

C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) expressed as median [interquartile range].

TABLE II. ARTERIOGRAPHIC CLASSIFICATION OF PATIENTS WITH TAKAYASU'S ARTERITIS AT STROKE ONSET

Typology of vascular involvement*	
Type I (%)	10 (55.6)
Type IIa (%)	1 (5.6)
Type IIb (%)	1 (5.6)
Type III (%)	0
Type IV (%)	0
Type V (%)	6 (33.3)

*According to classification proposed by Hata et al.12. Type I: involvement of branches of aortic arch; Type IIa: involvement of ascending aorta, aortic arch and its branches; Type IIb: type IIa plus involvement of thoracic descending aorta; Type III: involvement of thoracic descending aorta, abdominal aorta and/or renal arteries; Type IV: involvement of abdominal aorta and/or renal arteries; Type V: type IIb plus type IV.

Patient data were obtained from a systematic review of patient charts. All parameters analyzed pertained to stroke onset: patient demographic data; neurological manifestations (hemiparesis, headache, dizziness, seizures, visual changes, aphasia, syncope; clinical and laboratory [C-reactive protein (CRP): reference value: < 5 mg/L, erythrocyte sedimentation rate (ESR): reference value: < 19 mm / 1st hour] features; TA angiographic classification[12]; comorbidities (arterial hypertension, diabetes mellitus, dyslipidemia); habit (smoking).

Statistical analysis: Continuous variables were expressed as mean ± standard deviations (SD), median [interquatile range] or as percentages (%).

RESULTS

The mean age ± SD of the 18 patients at the stroke event was 29.4 ± 10.9 years, with 94.4% female gender and 88.9% white ethnicity. The clinical and neurological features were: hemiparesis (77.8%), limb claudication (77.8%), headache (27.8%) and dizziness (22.2%). Constitutional symptoms such as fever, fatigue and weight loss were found in only one patient (5.6%). All neurological, clinical and laboratory features of the TA patients at stroke onset are shown in Table I.

TA was diagnosed in 14 (77.8%) patients immediately after the stroke event, whereas four (22.3%) out of 18 patients developed strokes after confirmed TA diagnosis: two cases at one year after TA (at the age of 27 and 50), one case at five years after (at the age of 27) and one case at 8 years post diagnosis (at the age of 29).

Considering the classification of vascular involvement proposed by Hata et al.[12], ten (55.6%) TA patients had type I lesions (involvement of branches of aortic arch), one (5.6%) type IIa (involvement of ascending aorta, aortic arch, and its branches), one (5.6%) type IIb (type IIa plus involvement of thoracic descending aorta) and six (33.3%) had type V (all aorta and its branches) as shown in Table II.

During follow up, twelve (66.7%) patients developed neurological sequelae. One patient died as a result of cerebral hyperperfusion syndrome after carotid revascularization surgery. TA was in remission in 15 (83.3%) cases.

Concerning comorbidities and habits, seven (38.9%) patients had arterial hypertension, six (33.3%) had dyslipidemia, one (5.6%) was a current smoker, while five (27.8%) were ex-smokers at stroke onset.

DISCUSSION

In the present study, the neurological and vascular features of patients with TA at the stroke onset were analyzed. A high prevalence of stroke was observed in this population.

Whereas other available studies[4-10] described 5 - 7% neurovascular events in TA, this neurological manifestation was noted in 15% of our patients. Neurologic involvement is a frequent occurrence and may often be the first presenting feature of the disease process. Occlusion of the vertebral or carotid arteries can cause ischemic stroke and patients may present with headache, syncope, and blurred vision. The main neurological findings in our patients with stroke were hemiparesis, followed by headache, vertigo, seizures, visual changes, aphasia and syncope.

Moreover, the main clinical manifestations of the TA patients at stroke onset were presence of limb claudication, hemiparesis, diminished pulse and blood pressure asymmetry. Regarding constitutional symptoms occurred in only one case. In a Chinese study involving 125 patients the most common symptom was reduced pulse (89%), followed by limb claudication (55%) and constitutional symptoms (one third of patients)[13].

In general, the initial manifestations of TA included constitutional symptoms, limb claudication, decreased arterial pulse, heart murmurs, arterial hypertension and blood pressure asymmetry[4-9]. Nonspecific signs and symptoms indicative of inflammatory disease are more frequent at the early stages of the disease, such as elevated inflammatory activity, anemia and leukocytosis[6]. However, many of these changes can go unnoticed at the beginning of the disease and many patients are asymptomatic during the early stage. Furthermore, cardiovascular and neurological manifestations increase with disease progression in parallel with increased vascular lesions[6]. Consequently, some patients may not have classical TA manifestations, instead exhibiting isolated neurovascular events[14] as was the case in our patients.

Four out of the 18 patients analyzed in the present study had strokes after the confirmed TA diagnosis. However, these strokes occurred in younger patients, reinforcing the hypothesis that the course was probably the result of vascular changes secondary to TA. A French study found 6.6% and 15.9% neurovascular events as the first presenting features of TA and during follow-up, respectively8, whereas Sato et al.[10] observed 8% and 19% neurovascular events as the initial manifestation of TA and during follow-up.

Concerning follow up, two thirds of patients developed neurological sequelae, whereas one patient died as a result of cerebral hyperperfusion syndrome after carotid revascularization.

In this study, the prevalence of arterial hypertension was 38.9%, dyslipidemia 33.3%, smoking history 33.3%, whereas no cases of diabetes mellitus were found. Some studies have shown that patients with TA have an elevated number of factors known to be associated with cardiovascular risk such as hypertension and hypertriglyceridemia compared with healthy controls[15]. Although patients with TA have other risk factors for stroke, we found that, even in patients whose neurological manifestations occurred after diagnosis of TA, these occurred at a young age and were therefore probably due to vascular inflammation of the disease.

Angiographic findings tend to vary widely among studies conducted in different parts of the world. Japanese studies for example, show involvement of the aortic arch (types I and II of angiographic criteria)[12] in approximately 50% of patients, where our study showed similar results with 55.6% representing type I[16-18]. In other studies, such as those in India, Thailand and Brazil, the prevalence of patients classified as type I and II was lower, while type V patients predominated[7,19]. This variation in the pattern of vascular involvement suggests a role of ethnicity in the pathophysiology of TA, and likewise in the prevalence of cerebrovascular events. The finding of a higher prevalence of patients with angiographic classification Type I (55.6%) affecting the aortic arch branches, justifies the neurovascular events found in our patients.

Our study is limited by being a retrospective study, with the typical problems inherent to this type of cohort. Furthermore, the data collected were dependent on the medical records. Although all of the variables are related to the time of diagnosis (TA or stroke), it is not known whether they accurately reflect events at the beginning of the disease. Moreover, this study includes the characteristics of the study population from a tertiary care center and likely represents a more severe disease spectrum. Consequently, the frequency of TA and stroke in TA might have been under- or overestimated.

CONCLUSION

In summary, the neurological features of patients with TA at stroke onset are variable and correlate to vascular anatomic abnormalities. Moreover, a high prevalence of stroke and defined TA diagnosis at stroke event was observed in our TA patients.

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