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Vasculitis

Aortic and coronary calcifications in Takayasu arteritis ☆

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ABSTRACT

Objectives: Atherosclerosis is well recognized in Takayasu arteritis (TAK) and the associated plaques tend to be more common in areas of arteritis. We now report arterial wall calcification in a large group of TAK patients and controls. We hypothesized that the degree of coronary artery calcification would point to a systemic effect of inflammation while that in the thoracic aorta more of local inflammation.
Methods: A total of 47 patients with TAK, 43 patients with SLE and 70 healthy controls (HC) were studied. The presence of coronary artery and thoracic aorta calcifications (ToAC) was investigated by multi-detector computed tomography (MDCT). Atherosclerotic plaques in the carotid arteries were screened using B mode ultrasound.
Results: The frequency of coronary artery calcification was significantly increased among patients with SLE as compared to the healthy controls while the increase in TAK did not reach statistical significance. There were more TAK patients with ToAC among the TAK as compared to the SLE patients [21/47 (45%) vs 10/43 (23%), $P = 0.033$]. In addition, a circumferential type of calcification, vs a punctuate or linear type, was the more common type in 67% of patients with TAK whereas only the linear or punctuate type was seen in SLE patients and HC. SLE and TAK patients were found to have increased risk for carotid artery plaques. Among TAK patients, coronary artery calcification, ToAC and carotid artery plaques tend to be at sites of primary vasculitic involvement.
Conclusions: There is increased atherosclerosis in TAK and SLE. Vessel wall inflammation seems to be also important in the atherosclerosis associated with TAK.

Introduction

Takayasu arteritis (TAK) is a chronic, idiopathic, inflammatory disease that causes occlusions or stenosis in the aorta and its primary branches [1–3]. The disease is prevalent in Asia and in the Far-East [1–3]. Features of atherosclerosis, along with characteristic arterial wall changes of the disease itself are described in imaging studies of patients with TAK [4–8]. Furthermore, there are case reports of both atherosclerotic and vasculitic changes in young patients with TAK [9–12]. We and others had previously shown that, similar to patients with systemic lupus erythematosus (SLE), patients with TAK had significantly more atherosclerotic plaques in the carotid arteries compared to the healthy controls [13,14]. Moreover, we had observed that atherosclerotic plaques were more common in areas where the primary vessel disease was prominent [13]. We thus reasoned that local inflammation most probably also contributed to the atherosclerosis observed in TAK.

Calcification in arteries appears to correlate with the extent of atherosclerosis. Multi-detector computed tomography (MDCT) allows noninvasive detection of arterial calcification. In this study, we initially had aimed to investigate the presence of coronary artery calcification and had started MDCT imaging for this purpose in patients with TAK and SLE and healthy controls (HC). However, as the study progressed we became aware of the intense aortic calcification among TAK patients and decided to also formally look at the presence of thoracic aorta calcification (ToAC). We reasoned that the degree of coronary artery calcification both in TAK and SLE would be more indicative of a systemic effect of increased inflammation and that in the thoracic aorta more of local vascular inflammation.

Patients and methods

We studied consecutive female patients with TAK and SLE seen in the rheumatology outpatient clinic at the Cerrahpasa Medical Faculty, at the University of Istanbul between July 2007

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and July 2008. Seventeen patients with TAK and 12 with SLE were included in our previous study in which we had investigated only carotid artery plaques [13]. Apparently healthy members of the hospital staff who volunteered to participate in the study were also included as HC. Patients and controls were all aged ≤ 50 years. Patients with TAK fulfilled the ACR 1990 criteria [15] and patients with SLE fulfilled the revised 1997 ACR criteria [16]. Patients with chronic renal failure (serum creatinine > 1.4 mg/dL) were not included because of the increased tendency for arterial calcification.

Data about disease duration, clinical characteristics, immunosuppressives and corticosteroids use were obtained from patient's charts. Disease duration was defined as the time from initial diagnosis in both TAK and SLE. Entire aorta and primary branch vessels angiograms were available in all patients with TAK at the time of diagnosis. For the purpose of the current study, data on anatomical localizations associated with TAK were based on the latest vascular imaging available. These were conventional angiography covering complete aorta and all branch vessels in 26 patients, thoracic and abdominal MR angiographies in 17 and thoracal and abdominal CT angiographies in 4. The median time that had elapsed between the last imaging study and the current work was 15 months [IQR: 5-39].

Traditional cardiovascular risk factors were assessed as previously described [13]. Briefly, these were body mass index (BMI), waist circumference, familial history of cardiovascular disease, diabetes mellitus, hypertension, hyperlipidemia and smoking. Among patients with TAK, arterial blood pressure could be measured only from the lower extremities in 4 (9%) and could not be measured at all on either extremity in 3 (6%) patients. Additionally, angina pectoris and history of myocardial infarction were assessed with the help of a questionnaire.

Blood samples were collected after overnight fasting to measure total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, glucose, creatinine, erythrocyte sedimentation rate (ESR) and high sensitive C-reactive protein (hsCRP) levels.

Assessment of coronary and aortic calcification

All subjects underwent multi detector computed tomography (MDCT) imaging with a SOMATOM Sensation 16 Cardiac (Siemens AG, Erlangen, Germany). Data acquisition parameters were 120 kV; 133 mAs; slice collimation, 1.5 mm; slice width, 3.0 mm; rotation time, 0.42 s; and table feed, 5.6 mm. Thirty to 40 slices were obtained during a single breath-holding period. Images were reconstructed with retrospective electrocardiogram gating to a 512-pixel matrix using a medium body filter. All images were examined by a radiologist (C.A.) blinded to the clinical data. Coronary artery calcification scores were calculated according to the Agatston method [17] using Syngo VB 10B (Siemens AG) software. Individual scores were calculated for the left main coronary artery, descending branch of the left coronary artery, circumflex branch of the left coronary artery, and right coronary artery. These scores were summed to calculate a total core score for each subject. The presence of coronary artery calcification was defined as a calcification score > 0. The same MDCT images served to detect calcification in the thoracic aorta which included ascending, arcus and descending regions. Another radiologist (D.C.O.) again blinded to the clinical data, examined the scans and described the calcification as circumferential if the entire vessel wall was affected, or punctuate or linear when the vessel wall was partially involved and absent when there was no radiological evidence of calcification. The radiologist also defined the anatomic location of the calcification. A third radiologist (O.T.), who was blinded to the hypothesis and who had not evaluated coronary artery calcification or ToAC in the previous images re-examined all 161 images to assess inter-observer variability. Kappa value was 0.90 for the presence or absence of thoracic aorta calcification, 0.88 for circumferential type of calcification and 1.0 for the punctuate or linear type of calcification. Kappa value ranged between 0.64 and 0.70 for the anatomical site of the ToAC.

Assessment of carotid artery atherosclerosis

B-mode carotid artery ultrasonography (USG) was done as described before [13]. A USG device (Esaote, Mylab 70, Italy) equipped with a 7.5–15 MHz linear array imaging probe was used. The right and left common, internal and external carotids and carotid bulb were scanned for atherosclerotic plaques in all patients and controls. All carotid USG studies were done by the same physician (E.S.). Also intima media thickness (IMT) of far walls of right and left common carotids was measured in Takayasu patients. The highest value on either side was taken into consideration. Cut-off levels which define diffuse increase in IMT was set as ≥ 0.9 mm (a value calculated as lower limit of 95% CI, in our previous study) [13].

All participants gave informed consent and the local ethic committee of Cerrahpasa Medical School approved the study.

Statistical analysis

Continuous data were given as the mean and standard deviation (SD). Comparisons between groups were made by one-way ANOVA followed by post hoc Tukey correction for continuous variables. The categorical variables were compared by the chi-square test or the Fisher exact test. Comparisons between subjects with and without coronary artery calcification, ToAC and carotid artery plaques were made by the independent sample *t*-test and by the chi-square test or the Fisher exact test. Those variables, which were associated with plaque or calcification were later analyzed by multiple logistic regression tests.

The odds ratios and 95% confidence intervals (CIs) for coronary artery calcification, ToAC and carotid artery plaques prevalence were calculated by binary logistic regression models. Healthy controls were accepted as the reference group. In the first model unadjusted analyses were done. In the second model, adjustment for age only was done. All tests were performed using SPSS for Windows, version 17.0, software (SPSS Inc, Chicago, IL).

Results

There were 47 patients with TAK (mean age: 37.4 $\pm$ 8.0 years), 43 patients with SLE (mean age: 39.3 $\pm$ 8.1 years) and 70 HC (mean age: 40.2 $\pm$ 5.2 years). The mean disease duration was 9.5 $\pm$ 6.8 years in TAK and 11.0 $\pm$ 4.6 years in SLE.

Clinical characteristics of Takayasu patients

At the time of the study, 9 patients were free of symptoms. In the remaining one or more symptoms were observed. These were fever ($n = 2$), fatigue or malaise ($n = 7$), upper extremity claudication ($n = 21$), lower extremity claudication ($n = 12$), carotidynia ($n = 8$), headache ($n = 18$), vertigo ($n = 10$), visual disturbances ($n = 4$), tinnitus ($n = 2$), syncope ($n = 2$), stroke ($n = 2$), dyspnea ($n = 3$), hemoptysis ($n = 1$), palpitation ($n = 1$), episcleritis ($n = 1$), erythema nodosum ($n = 2$) and artralgia and