Spectrum of Aortic Disease in the Giant Cell Arteritis Population

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We report the spectrum of aortic involvement in patients with giant cell arteritis (GCA) following review of medical records of 4,006 patients including those with imaging studies. A total of 1,450 patients (36%) had a confirmed diagnosis of GCA. Of these, 974 had aortic imaging. Of the 974 patients with imaging, 435 (45%) had an identified aortopathy. The most common aortopathy was aneurysm/dilation (69%). Overall, an annual aneurysmal growth rate of 1.5 mm/y was calculated. In patients with aneurysm/dilation, aortic dissection occurred in 18 patients (6%), and these patients had a significantly higher aneurysmal growth rate compared with those without dissection (4.5 vs 1.4 mm/y, p = 0.005). The median size of the aorta at the time of dissection was 51 mm, with 7 (39%) occurring with a maximal aortic aneurysm/dilation <50 mm. In conclusion, our findings indicate higher aneurysmal growth rate in GCA compared with that reported for degenerative aortic disease. Moreover, patients who develop dissection had a significantly higher growth rate than those without dissection with over a third of these patients suffering dissection at a caliber <50 mm. **(Am J Cardiol 2017;■■:■■–■■)**

Background

Well over a century has passed since Sir Hutchinson first introduced giant cell arteritis (GCA) to the medical literature[1] which is the most common type of vasculitis in people over 50 years of age.[2] It has a predilection for the female gender[3] and represents the most common form of aortitis.[4] The histopathologic hallmark is granulomatous inflammation[5] and diagnosis is established by clinical, radiologic, and histopathologic findings. Current treatment guidelines for aneurysmal aortic disease apply to degenerative and genetically mediated diseases rather than to inflammatory aortopathies. Moreover, for inflammatory aortic disease, the role of screening to predict aortic complications remains unclear; some advocate specific imaging surveillance[4]; others recommend delaying routine screening until signs and/or symptoms of aortic involvement develop.[6,7] This divergence in recommendations clearly highlights the absence of evidence to support a particular strategy of care. Our objective is to report the spectrum of aortic abnormalities in GCA and identify those with complications, including aneurysm, dissection, or rupture. Additionally, those without defined aortic disease at baseline were identified retrospectively and followed longitudinally to determine the frequency of development of aneurysm/dilation.

Methods

The study was approved by the Mayo Clinic Institutional Review Board. Consecutive patients who underwent clinical evaluation at a single large tertiary referral center (Mayo Clinic, Rochester, Minnesota) between 1996 and 2012 were identified by a database search for the diagnosis of "giant cell arteritis" or "temporal arteritis." All charts were manually reviewed by 2 of the authors (DK and JB). Patients were included if they (1) had biopsy proven evidence of GCA or (2) met American College of Rheumatology classification criteria for clinical diagnosis of GCA.[8,9] Demographic, clinical, and imaging data were abstracted on all patients. Discrepant findings were adjudicated by a senior author (NSA). Imaging studies ordered by the clinician, regardless of the reasoning for the study, were included and reviewed by either a cardiologist or chest radiologist at the study institution (Mayo Clinic Rochester). Imaging includes transthoracic/transesophageal echocardiography, computed tomography (CT)/computed tomography angiography, magnetic resonance imaging (MRI)/magnetic resonance angiography, and/or positron emission tomography (PET) scan. The aorta was assessed as either normal or demonstrating 1 or more of the following abnormalities as described in the clinical reports: (1) ectasia, (2) aneurysm/dilation, (3) dissection, or (4) inflammation. Maximum aortic size at each location (ascending, arch, descending, and abdominal) was recorded when available. Imaging studies were included if they were obtained within 6 months before official diagnosis of GCA and

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extending to the last date of known follow-up. For patients who had no initial aortopathy, testing preceding and following the diagnosis of GCA were reviewed to assess duration in which they remained without aortic disease.

The group demonstrating aortopathy was further stratified based on aneurysm size, location of aortopathy, and development of complications, and were longitudinally followed for 3 years to determine aortic growth rate as well as incidence of dissection. Aortic size at the time of dissection events was also recorded. The group with normal aortic findings at baseline imaging was also longitudinally followed to their last available imaging procedure to determine their incidence of aortopathy.

Data regarding patient's medical history, including, but not limited to, smoking status, hypertension, hyperlipidemia, diabetes mellitus, coronary artery disease, and polymyalgia rheumatica were obtained from the medical record. Medication history was obtained from either a patient-filled questionnaire or the electronic medical record at the time of clinical encounter. Aortic locations were defined according to widely accepted guidelines.

Circumferential aortic wall thickening on transthoracic/transesophageal echocardiography was considered evidence for inflammation.[10] Mural thickening and delayed contrast enhancement on CT and MRI was considered evidence of inflammation.[11,12] Increased fludeoxyglucose (^{18}F-FDG) PET uptake in the aorta was deemed consistent with inflammation.[13,14] Ectasia was defined as CT or MRI evidence of aortic dilation less than 1.5 times (50%) larger than the expected normal size of the aorta at that anatomic location.[15] Echocardiographic measurements of the thoracic aorta were made in either the right or left parasternal long-axis view, whereas short- and long-axis assessments were made of the abdominal aorta. Aortic measurements were made using the leading edge technique, described in the American Society of Echocardiography guidelines.[16] Echocardiographic diagnosis of aortic dilation or aneurysm was based upon guidelines, relating expected aortic size to body surface area and age.[16] Dilation and aneurysm were combined as a single entity, to avoid confusion between variations in clinical reporting between imaging modalities. CT and MRI required reformations of the aorta in a plane perpendicular to the flow of blood; measurements of aortic caliber utilized an inner edge to inner edge technique.[17] CT and MRI definition of proximal ascending aorta dilation was >40 mm.[18] Descending aortic dilation was considered present when the aortic measurement exceeded 30 mm.[18] Abdominal aortic aneurysm was defined as a diameter >30 mm, whereas dilation was defined as a diameter >20 mm.[19] Echocardiographic diagnosis of dissection required evidence of an intimal flap with creation of a true and false lumen.[20] Computed tomography angiography and MRI/magnetic resonance angiography findings of 2 distinct lumens (true and false) with a distinct intimal flap were considered consistent with aortic dissection.[21]

Categorical variables were summarized by count and percentage and were compared between groups using Pearson chi-square test or Fisher exact test, where appropriate. Distributions of continuous variables were examined for normality. Variables found to be approximately normally distributed were summarized by mean and standard deviation and compared between groups using 2-sample *t* test. Continuous variables found to be non-normally distributed were summarized by median and quartiles and compared between groups using nonparametric rank-sum test. Kaplan-Meier methods were used to examine the incidence of aortopathies during follow-up. For this analysis, subjects without aortopathy were censored at last known imaging date.

Growth rates were evaluated using repeated measures analysis. In this analysis, year of follow-up beyond diagnosis was considered as a categorical variable. An autoregressive correlation structure was used to model correlation between repeated measurements taken over time, and this structure assumes that observations taken closer together in time are more strongly correlated. As the primary question was to assess differences in growth rates between various groups, this difference was estimated and tested within the repeated measures framework by including an interaction term between group and time variables. SAS version 9.4 (Cary, North Carolina) was used for analyses, and 2-sided p values <0.05 were considered to be statistically significant.

Results

Of 4,006 patients identified with possible GCA, 1,450 had a confirmed diagnosis of which 974 (67%) had aortic imaging. Of the 974 patients with aortic imaging, 720 (74%) had biopsy-proven GCA. The study population was predominately female 706 (72%) with mean age of 72.8 ± 8.5 years. Figure 1 represents proportions of patients with specific imaging tests. Compared with the 476 patients not included in the study due to lack of imaging, there was no difference in age and gender distributions.

At least 1 aortic abnormality of interest was found in 435 (45%) patients. Those with aortic abnormalities were younger (71.9 ± 8.3 vs 73.5 ± 8.6, p = 0.003). Aneurysm/dilation was the most common abnormality (69%), followed by inflammation (32%), ectasia (14%), and dissection (4%) (Figure 2). The proportion of male patients was higher in those with aneurysm/dilation than in those without (37% vs 24%, p < 0.0001), whereas there was a trend toward a higher proportion of female patients in those patients with inflammatory findings versus in those without (79% vs 72%, p = 0.07). Additionally, those with inflammatory findings were younger (68.9 ± 7.9 vs 73.4 ± 8.4, p < 0.0001) compared with those without. Age and gender distribution were similar among patients with findings of either ectasia or dissection (Table 1).

There were 539 patients without evidence of aortopathy at the time of GCA diagnosis, and 246 (46%) had follow-up imaging for various reasons, including reasons unrelated to GCA. The median follow-up was 4.0 years. Ten of the 246 patients with follow-up data available developed an aortopathy and the 5- and 10-year incidence rates were estimated to be 0.9% (95% confidence interval [CI]: 0, 2.3) and 11.3% (95% CI: 3.4, 18.7), respectively (Figure 3). The median time to the detection of aortopathy was 6.9 years (interquartile range 5.3, 7.5). Of the patients who developed aortopathy, 9 (90%) developed aneurysm/dilation, whereas 1 (10%) developed aortic inflammation (Figure 4) and all occurred in the thoracic aorta (8 ascending, 2 descending aorta). The patients who developed aortopathy were of similar age (72.3 ± 5.0 vs 74.5 ± 7.7, p = 0.37) and gender (80% vs 76% female, p = 0.76) to those patients who remained disease-free. One