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Extra-cranial giant cell arteritis and Takayasu arteritis: How similar are they?

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ABSTRACT

Objective: To compare clinical and imaging characteristics of patients with giant cell arteritis (GCA) and upper extremity (UE) arterial involvement to patients with Takayasu arteritis (TAK).
Methods: A cohort of patients seen at the Mayo Clinic with TAK diagnosed between 1984 and 2009 and a cohort of patients with GCA and UE arterial involvement diagnosed between 1999 and 2008 were studied.
Results: The TAK cohort consisted of 125 patients (91% female); the mean age (±SD) at diagnosis was 30.9 (±10) years. The cohort of patients with GCA and UE involvement comprised of 120 patients (80% female); the mean age (±SD) at diagnosis was 67.8 (±7.5) years. The mean time from onset of symptoms to diagnosis was significantly longer in TAK (3.2 years) than GCA (0.5 years), $p < 0.001$. UE claudication was reported in 40% with TAK and 53% with GCA, $p = 0.04$. UE blood pressure discrepancy was present in 65% with TAK versus 28% with GCA, $p < 0.001$. Involvement of the thoracic aorta, abdominal aorta, carotid arteries, innominate artery, mesenteric artery, and left renal artery was more frequently observed in TAK ($p < 0.05$). Among patients with luminal changes of the thoracic aorta, stenotic/occlusive lesions were predominant in TAK (81% compared to 0% in GCA), whereas aneurysmal disease was more common in GCA (100% compared with 19% in TAK, $p < 0.001$).
Conclusion: Patients with GCA and UE involvement differ from patients with TAK in clinical and imaging characteristics. Aortic aneurysms were more common in GCA, while stenotic changes of the aorta were more common in TAK, suggesting different pathophysiologic mechanisms or vascular response to injury.

Introduction

Giant cell arteritis (GCA) and Takayasu arteritis (TAK) are both granulomatous large-vessel vasculitides that share many clinical and radiographic features that can make it challenging to classify patients [1–3]. In routine clinical practice, age is often used to distinguish between the two conditions. In a study, age at disease onset ≤40 years was the single most discriminatory variable in classifying patients with TAK versus GCA [3]. Age at onset of ≥50 years is one of the American College of Rheumatology (ACR) classification criterion for GCA [4]. However, patients with large-vessel vasculitis who fall in the age group of 41–49 years are not included in the classification criteria for either condition. Other variables that may allow for the correct classification of GCA are Caucasian race, temporal artery abnormalities, and shoulder stiffness [3]. Conversely, aortic or renal abnormalities, upper extremity systolic blood pressure difference of >10 mmHg, and aortic or subclavian bruits were associated with TAK compared to GCA [3].

While cranial manifestations of GCA are well-recognized, it has been increasingly appreciated that GCA is a systemic disease that extends beyond the superficial temporal arteries and can cause manifestations including large-artery stenoses or aortic involvement (aortitis, aneurysm formation, and dissection) [5–9]. Several prospective imaging studies in patients with newly diagnosed GCA have shown that a majority of patients with GCA have subclinical inflammation of the aorta and its branches [10–16].

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Table 1
The 1990 American College of Rheumatology classification criteria for giant cell arteritis [4][a] and Takayasu arteritis [21][b]

Age, ≥ 50 years	Age at disease onset, < 40 years
New localized headache	Claudication of extremities
Temporal artery abnormality (tenderness to palpation and decreased or absent pulses)	Decreased brachial artery pulse
Erythrocyte sedimentation rate ≥ 50 mm/hr by Westergren method	Blood pressure difference > 10 mmHg
	Bruit over subclavian arteries or aorta
Abnormal temporal artery biopsy showing vasculitis with predominance of mononuclear cell infiltration or granulomatous inflammation	Arteriogram abnormality (narrowing/occlusion of the aorta, primary branches, and large arteries in the proximal, upper, and lower extremities not due to another cause)

[a] Presence of 3 or more of the criteria listed above has a sensitivity of 94% and specificity of 91% for diagnosis of GCA.
[b] Presence of 3 or more of the above criteria has a sensitivity of 90.5% and specificity of 97.8% for the diagnosis of Takayasu arteritis.

A subset of patients with GCA can present with upper extremity arterial occlusive disease that is similar to that seen in patients with TAK [11,17,18]. However, compared to patients with TAK, those with GCA are often less likely to undergo imaging even in the presence of symptoms of vascular insufficiency [3,19]. In a study, while 100% of patients with TAK had large-vessel imaging performed, only 62% of those with GCA and signs or symptoms of vascular insufficiency underwent imaging of the large vessels [2]. Therefore, peripheral arterial manifestations from GCA are likely under-recognized and under-detected.

It is still unknown whether patients with GCA who have upper extremity arterial involvement more closely resemble patients with TAK. In this study, we compared clinical and radiologic features of patients with GCA and upper extremity arterial involvement to patients with TAK. The findings of this study may advance our understanding of patterns of involvement between the two forms of large-vessel vasculitis and whether the two conditions are within a single disease spectrum or distinct entities.

Patients and Methods

This is a retrospective study that included patients from two established cohorts of patients seen at Mayo Clinic, Rochester, Minnesota: one with TAK [20] and the other with GCA with upper extremity involvement [9].

A comparison of the ACR classification criteria for the two forms of large-vessel vasculitis is given in Table 1.

TAK cohort

All patients with TAK evaluated at Mayo Clinic between January 1, 1984, and December 31, 2009, were identified using the International Classification of Disease–9th version code for TAK. All medical records were reviewed to confirm the diagnosis. Patients who met the American College of Rheumatology (ACR) criteria for TAK with the exception of the age criteria [21] were included. Patients between 41 and 50 years of age who otherwise met the TAK ACR criteria without fulfilling the ACR criteria for giant cell arteritis (GCA) [4] were also included. All patients with TAK had at least one or more of the following imaging studies at baseline: conventional angiography, computed tomography angiography (CTA), magnetic resonance angiography (MRA), ultrasonography, and/or positron emission tomography (PET).

GCA cohort

Using an electronic clinical notes search tool (Enterprise Data Trust portal), a cohort of patients with GCA and upper extremity arterial limb involvement between January 1, 1999, and December 31, 2008, evaluated at Mayo Clinic has been established [9]. The Enterprise Data Trust Portal is an electronic notes search tool that allows a search for keywords in the electronic clinical notes of all patients seen at the Mayo Clinic within the specified time frame. All patients were > 50 years old at diagnosis. Findings of upper extremity arterial involvement attributed to GCA were confirmed by CTA, MRA, conventional angiography, ultrasonography, and/or PET.

Data collection

Data were abstracted from the medical records with a preformatted questionnaire including demographic information, symptoms at diagnosis, laboratory findings, pathology reports, and imaging studies at diagnosis.

Statistical analysis

Descriptive statistics were used to summarize the data. Percentages were used for categorical data. For continuous variables with a normal distribution, we used means and standard deviation (SD). Continuous variables that were skewed were presented as medians with interquartile ranges (IQR, 25th and 75th percentiles). The Wilcoxon rank sum test was used to analyze continuous variables, and chi-square tests were used for categorical variables. Bonferroni correction for multiple comparisons is reported in the footnotes of each table to allow readers to interpret our findings with adjustment for multiple comparisons, if desired.

Results

We identified 125 patients (91% female) with a diagnosis of TAK; the mean age at diagnosis was 30.9 years (standard deviation ± 10.4 years). The GCA cohort comprised of 120 patients (80% female); the mean age was 67.8 years (standard deviation ± 7.5 years), all with involvement of upper extremity arteries confirmed by imaging.

A comparison of clinical variables and symptoms of vascular insufficiency at diagnosis is given in Table 2. Lower extremity claudication was similar between the two groups, but a higher frequency of patients with TAK had upper extremity blood pressure discrepancy, vascular bruits, or pulse abnormalities (Table 2). A greater proportion of patients with GCA had elevated acute phase reactants at diagnosis compared to patients with TAK (Table 2).

Imaging studies performed were CT angiogram in 32 patients (26%) with TAK and 61 patients (51%) with GCA; conventional angiogram in 63 patients (50%) with TAK and 35 patients (29%) with GCA; and MRA in 28 patients (22%) with TAK and 25 patients (21%) with GCA. The distribution of arterial abnormalities seen on imaging is shown in Table 2. Involvement of the thoracic aorta, abdominal aorta, carotid arteries, innominate artery, mesenteric artery, and left renal artery was more frequently observed in TAK