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Thoracic aorta involvement in giant cell arteritis: a case-control analysis of morphological data at diagnosis

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ABSTRACT

Objective. *Giant cell arteritis (GCA) is a cause of potentially fatal aortic aneurysms. Descriptive data on thoracic aorta measurements at the beginning of the disease are lacking. We aimed to compare aortic diameters between a recently diagnosed GCA population and an age- and sex-matched control group.*

Methods. *Patients with GCA and with an available thoracic CT concomitant with diagnosis were included. Controls were patients matched for age and sex and hospitalised in the same care centre for pneumonia. The main criteria were the anteroposterior and lateral diameters of the ascending thoracic aorta, which were measured by a blinded evaluator.*

Results. *90 cases and 90 controls were included. Each group comprised 30 males and 60 females for a mean age of 75.1±9 and 75.7±10.1 years old. At the time of GCA diagnosis no difference was found between the two groups (anteroposterior diameter 37.1±5 mm for cases vs. 36.7±5 mm for controls, p=0.6; lateral diameter 36.6±5 mm for cases vs. 35.9±4 mm for controls, p=0.3). Thoracic aorta diameter was not significantly higher in patients with aortitis at diagnosis (n=44) than in cases without aortitis (n=46).*

Conclusion. *Morphologic comparison of thoracic aorta at diagnosis of GCA with an age- and sex-matched control population showed no significant difference. Morphologic evaluation of aorta cannot predict accurately the occurrence of aortic aneurysm. Systematic follow-up according to current recommendations is thus justified.*

Introduction

Giant cell arteritis (GCA) is the most frequent large-vessel vasculitis after 50 years. Aortic aneurysms develop in 6 to 20% of GCA patients (1-3), especially in the ascendant thoracic portion, and lead to a significant mortality increase (standardised mortality ratio 2.83) (4). Aneurysms can be present at diagnosis (5) but may also appear during the follow-up. In an observational study of 204 GCA patients, median time from diagnosis to aneurysm development was 5.4 years (4). Current guidelines advocate regular thoracic aorta follow-up by chest ultrasound or CT (1, 6), although Prieto-Gonzalez *et al*. found no new aortic dilatations after diagnosis in their cohorts of GCA patients (5, 7).

Pathophysiology for ascending aorta aneurysms in GCA is incompletely understood. Giant cell granulomas have been found on ruptured vessels walls in necropsy studies (3). The definition of risk factors for aneurysm development is controversial. Although the series with the highest number of patients found hypertension and polymyalgia rheumatica symptoms to be moderately strong risk factors (1), these findings were not replicated in other observational studies (2-4). Elevated ESR or CRP, diagnosis delay or corticoids cumulative dose are unable to discriminate patients with and without aortic aneurysm (1-4). The impact of traditional aortic aneurysm risk factors other than hypertension (age, smoking, dyslipidaemia, diabetes) is not significant or discordant between studies in patients with GCA (1-4).

Recent imaging techniques enable clinicians to detect aortic inflammation. Aortitis is radiologically defined as a thickening of the vessel wall bigger than 3 mm, or as a significant uptake of FDG in a PET (8). Three series have evaluated aortitis or large-vessel involvement as a risk factor for subsequent thoracic aneurysm in populations exclusively comprising GCA patients and found PET-proven aortitis or large-vessel fixation to be positively correlated with thoracic aneurysm development (3-9-10).

Since pathologic processes underlying thoracic aorta dilatation can be detected with PET-CT at the time of diagnosis, our working hypothesis was that aortic dilatation could already be present at that moment, all the more so as diagnostic delay is frequent in GCA. Showing a difference in aortic morphology between GCA patients and general population could strengthen the link between vasculitis and vessel aneurysm. Moreover, patients already having a dilated aorta at diagnosis could have a higher risk for evolution to thoracic aneurysm. Only one study has compared aortic morphology in 64 GCA patients at di-

agnosis with an age- and sex-matched control population but with the objective of finding radiological diagnostic criteria. Compared to controls, aortic wall thickness was greater in the GCA group with no differences in aortic diameter or atheroma (11).

We then conducted a study on a larger group comparing thoracic ascending aorta diameters of recently diagnosed GCA patients with age- and sex-matched controls.

Material and methods

We performed a retrospective case-control study from 2010 to 2017 in a university hospital in France. To be included as cases, patients had to present GCA proven by 1990 ACR criteria (12) or a positive temporal biopsy, as well as a chest CT at the diagnosis: chest CT or FDG PET/CT, with or without iodine contrast product injection. The delay between CT and diagnosis had to be of less than 3 months. To be included as controls, patients had to be diagnosed with a chest CT for assessing pneumonia. Controls were matched for sex and age (no more than 2 years of difference) with cases. Patients with aortic insufficiency were excluded.

CT was performed using a Philips Diamond Select Brilliance CT 64-slice CT mm. PET- 18FDG was performed with a MCT Flow Siemens device.

Our main criterion was the CT measure of ascending thoracic aorta, *i.e.* anteroposterior and lateral diameters on axial slice at the level of pulmonary artery (Fig. 1A).

We also measured CT diameters of aorta at the following levels: ascendant aorta on sagittal slices, aortic cross and descending portion of aorta in a frontal plane (Fig. 1B).

Presence of aortitis was evaluated. Aortitis was defined by an aortic wall thickening more than 3 mm on CT when contrast injection was done, or by increased (superior to the liver uptake) and circumferential FDG uptake when a FDG PET/CT was available (8).

Our definition of the aorta segments was the one used in previous radiological studies (13). A list of mixed cases and controls was generated by a senior physician with access to clinical data. Measures were made by a blinded medical evaluator unknowing of the patients' medical histories.

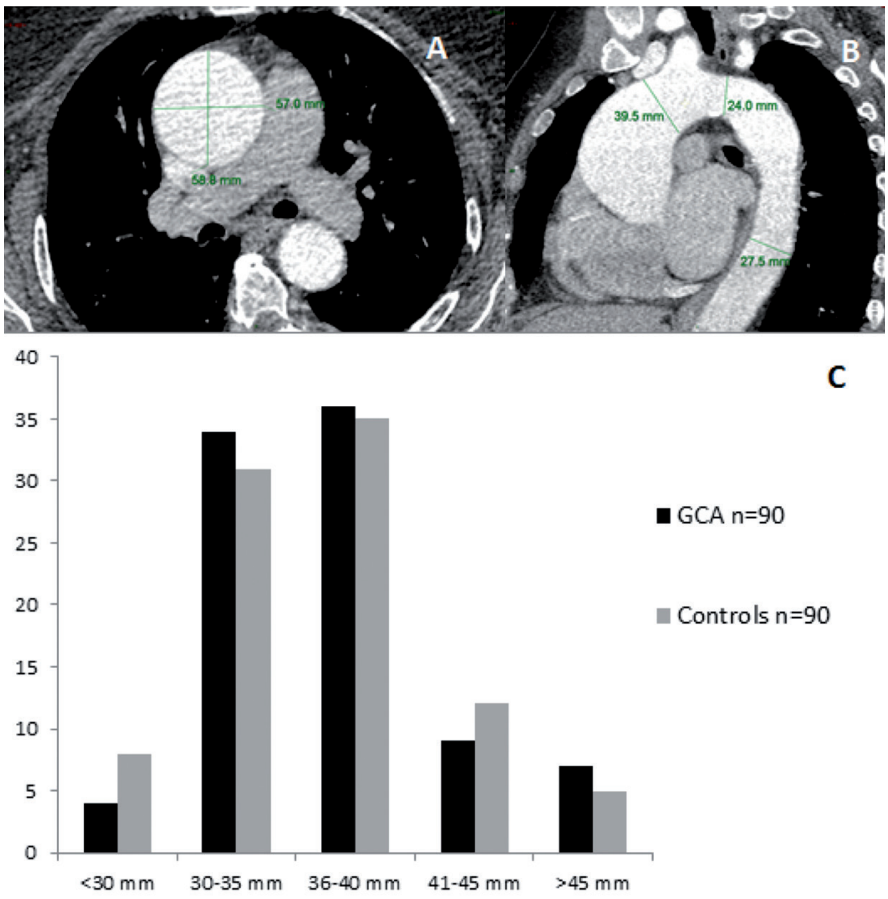

Fig. 1. **A**: measurement of anteroposterior and lateral aorta diameters, on axial CT.
B: measurement of 3 aorta segments, arch, cross and descending on this frontal CT
C: repartition of anteroposterior aorta diameters in GCA and controls.

Table I. ACR 1990 GCA criteria.

1.	Age at onset ≥50 years
2.	A new headache
3.	Temporal artery abnormality such as tenderness to palpation or decreased pulsation
4.	Erythrocyte sedimentation rate ≥50 mm/h
5.	Abnormal artery biopsy showing vasculitis with mononuclear cell or granulomatous inflammation, usually with giant cell infiltrates

Table II. Mean ascendant thoracic aortic diameters in GCA and controls, evaluated on CT at diagnosis.

	GCA n=90	Controls n=90	*p*-value
Female/Male	60/30	60/30	
Mean age (SD)	75.1 (9)	75.7 (10.1)	0.7
Mean (SD) anteroposterior diameter	37.1 (5.1)	36.7 (5.0)	0.6
Mean (SD) lateral diameter	36.6 (5.2)	35.9 (3.9)	0.3
Mean (SD) Anteroposterior diameter in female (n=60)	36.5 (5.4)	35.7 (5.5)	0.4
Mean (SD) Anteroposterior diameter in male (n=30)	38.3 (5.2)	38.6 (5.4)	0.8

Statistical analyses were made through the StatView programme. Mean and standard deviation of variables are given. Paired test *t*-was used to com-

pare parametric variables. A *p*-value <0.05 was required for statistical significance.

Results

We included 90 patients with GCA and 90 controls, mean age was respectively 75.1±9 and 75.7±10.1 years old. The sex ratio was 30 males, 60 females. 72% of cases had a temporal arteritis biopsy diagnostic positive for GCA.

There was no significant difference in anteroposterior or lateral diameters between cases and controls (Table I). Upper limits of anteroposterior diameters confidence intervals were similar to those found in the literature for the general population. There was no difference in aortic diameters between GCA and controls separating female and males (Table I).

Repartition of aortic anteroposterior diameters in GCA and controls is given in Figure 1C.

There was no significant difference when comparing the other segments of aorta, between cases and controls on proximal transverse arch (GCA 33.3±7 mm, controls 33.9±4 mm; p=0.7), on aortic cross (GCA 33.3±7 mm, controls 33.9±4 mm; p=0.7; and descending aorta (GCA 29.5±4 mm; controls 30.6± 4 mm; p=0.9).

Aortitis was present at diagnosis in 49% (44/90) of the cases and never observed in controls. There was no significant difference on the aorta diameters between patients with or without aortitis, in the total population (aortitis 37.9±5.1 mm, no aortitis 36.4±4.8 mm, p=0.6), and in women or men analysed separately (data not shown).

Discussion

Our study showed no difference in thoracic aorta measurements between GCA patients at diagnosis and age- and sex-matched controls, at diagnosis. Aortitis is now more frequently detected with recent imaging techniques, which broadens the spectrum of GCA to patients without typical cranial symptoms (13-14). Interestingly, aortic diameters were not be affected by the presence of aortitis in our study group. This suggests that the inflammatory process leading to dilatation could take place over months and years, all the more so as radiological inflammation can persist in clinically cured patients.

Characteristics of our patients are comparable to previous data, given mean aorta diameter is age, sex and index body surface dependent. In a French study including younger patients at risk for cardiovascular disease (mean age 56), the mean aortic diameter was 34.4 mm (15). Our results are concordant with the recent study by Berthod *et al*. showing no differences in aortic diameters between patients with GCA and controls (mean diameters respectively 35.9 mm and 35.2 mm) (11). A previous study investigating diameters of the aorta in 46 patients with GCA on FDG PET/CT had also showed very close results: mean ascending aorta diameters were respectively 38.7 mm and 38.6 mm in male and in female patients (10).

The main strength of our study lies in its statistical power. Using a sample size estimation equation setting power at 90% and alpha risk at 5%, we evaluate that a 1.7 mm difference between the two groups could have been detected. However, as our study is retrospective, we cannot eliminate residual bias between GCA and age- and sex-matched controls. We also did not compare aortic walls parallelism loss between the two groups. Finally, our subgroup analysis of patients with or without aortitis or according to sex may be underpowered.

As for clinical implications, our study highlights the unpredictability of thoracic aorta aneurysms in GCA. We have shown that a normal thoracic aorta in the time of diagnosis is in no way reassuring, aortic lesions appear later in the follow-up, then systematic follow-up of thoracic aorta size, by ultrasonography or by chest CT, is relevant. Actually, neither classical risk factors for thoracic aorta aneurysm (2-4), neither clinical nor biological courses can predict the development of an aneurysm, with the possible exceptions of hypertension and PMR symptoms (1). In de Boysson's recent series, large-vessel fixation on PET-scanner predicted aortic dilatation, although a significant number of patients (7%) without large-vessel involvement still developed aortic dilatation at 17 months (9).

In conclusion, aortic enlargement is frequent in the course of GCA, but at diagnosis, there is no difference between patient and controls, justifying the strong follow-up recommended by current guidelines (6).

Key messages

- Giant cell arteritis can cause fatal aortic aneurysms several years after diagnosis.
- We found no difference in aortic diameters between patients recently diagnosed with GCA and controls.
- Systematic follow-up of the thoracic aorta is justified during GCA follow-up.

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