Original Article
Inflammatory thoracic aortic aneurysm (lymphoplasmacytic thoracic aortitis): a 13-year-experience at a German Heart Center with emphasis on possible role of IgG4

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Abstract: Background & aim: Aortic aneurysms represent one of the major causes of cardiovascular surgery. Their etiology varies greatly based on patient's age and other clinicopathologic determinants. In addition to common atherosclerotic vascular diseases, an inflammatory etiology, in particular IgG4-related disease (IgG4-RD) has increasingly emerged as a cause of dissecting inflammatory aortic aneurysms (IAA). Methods: To assess the frequency and types of IAA, we reviewed all cases of aortic aneurysms resected at our Erlangen Heart Center during 2000-2013. Results: 376 patients underwent resection of aortic aneurysms in the study period. These are further categorized as ascending aortic aneurysms (45%), aortic arch aneurysm (2%), descending aortic aneurysm (3%), type A dissection (46%) and type B dissection (4%). Fifteen cases (4%) showed variable lymphoplasmacytic inflammation thus qualifying as IAA. Affected were 9 females and 6 males (female to male ratio = 1.5:1; age range: 52-80 yrs; mean: 70 yrs; median: 72 yrs). None was known to have IgG4-RD and serum IgG4 and/or IgG levels (known in 6 cases) were normal. Variable sclerosing lymphoplasmacytic inflammation was seen either confined to the adventitia (periaortitis; mainly in males) or extending through all layers (mainly in females). A wide range of IgG4 plasma cells (range: 3-182/HPF; mean: 51/HPF) and IgG4: IgG ratios (range: 0.02 to 0.91; mean: 0.37) were detected. All but one of the cases with at least focally transmural inflammation showed a higher IgG4: IgG ratios in excess of 0.3 (range, 0.32-0.91; median, 0.62). Lymphoid follicle and variable fibrosis were common but obliterative phlebitis was not seen. Conclusion: IgG4-rich sclerosing lymphoplasmacytic thoracic aortitis is a constant histological feature of thoracic IAA. Normal serum IgG4 in most patients, predilection for women and absence of other features of IgG4-RD all suggest a tissue-specific localized autoimmunological process and argue against a systemic disorder. The relationship (if any) of IgG4-rich lymphoplasmacytic thoracic aortitis in those patients with IAA lacking other organ manifestations or an elevated serum IgG4 level to systemic IgG4-RD remains unclear and merit further studies.

Keywords: Inflammatory aortic aneurysms, lymphoplasmacytic thoracic aortitis, aortic dissection, IgG4, IgG4-related disease, periaortitis

Introduction

According to the Stanford classification aortic dissections were divided into two groups based on presence (type A) or absence (type B) of involvement of the ascending aorta. In type A the aortic arch and occasionally the descending aorta may be affected in addition to ascending aorta. In type B dissection the descending aorta or the aortic arch distal to the right subclavian artery is involved with sparing of the ascending aorta [1, 2]. Nowadays, this Stanford classification replaced worldwide the former

DeBakey classification [3, 4] as it is more practicable in guiding clinical decision. Type A ascending aortic dissections generally require primary surgical treatment whereas type B dissections are treated conservatively or via radiological stenting with cardiac surgery reserved for further complications.

The etiopathogenesis of dissecting and non-dissecting aortic aneurysms varied greatly based on patient's age as well as other clinicopathologic factors; atherosclerotic and hypertensive cardiovascular diseases being the main

factors implicated. Other uncommon causes of aortic aneurysms include hereditary connective tissue diseases (Marfan syndrome), non-hereditary connective tissue disorder associated with degenerative changes of the tunica media (idiopathic or cystic media necrosis of Erdheim-Gsell type) as well as inflammatory conditions that may result in destruction of the elastin fibers of the media with the consequent development of aortic dilatation and/or dissection [5].

Immunoglobulin G subclass 4 (IgG4)-related disease (hereafter referred to as IgG4-RD) is a recently recognized still emerging heterogeneous systemic disease entity with diverse organ manifestations (autoimmune pancreatitis, sclerosing cholangitis, sclerosing sialadenitis/Küttner tumor, dacryocystitis/ocular disease, retroperitoneal fibrosis/Ormond disease, IgG4-related renal disease, IgG4-related lymphadenopathy and IgG4-related sclerosing inflammatory pseudotumors involving mediastinum, lung, gastrointestinal tract and soft tissue) [6, 7]. The disorder is characterized by common multifocal or multiorgan involvement, usually accompanied by elevated serum IgG4 level in 75% of affected patients [6, 7]. Histological hallmarks of the disease are: extensive tissue infiltration by lymphoplasmacytic cells rich in IgG4-positive plasma cells with formation of lymphoid follicles, prominent usually storiform fibrosclerosis, mild to moderate tissue eosinophilia, and variable degrees of obliterative phlebitis [6, 7]. Histological diagnosis relies on presence of all or most of these features. Histological findings should be interpreted in the appropriate clinical settings.

Cardiovascular manifestations of IgG4-RD are uncommon. They mainly encompass idiopathic retroperitoneal (periaortic) fibrosis, inflammatory aortic aneurysm (IAA), inflammatory periarteritis, and inflammatory pericarditis [8]. The disease shows a predilection for older men. The term *chronic periaortitis* has been used for the combined involvement of the abdominal aorta (IAA) and the surrounding retroperitoneal soft tissue (retroperitoneal fibrosis) [8]. These manifestations may occur in isolation or concurrent with other cardiovascular or non-cardiovascular manifestations of the disorder. The aortic adventitia is the main layer most often involved by inflammation. Disruption of the

elastic fibers in the media may be complicated by aneurysm formation and/or dissection [9]. The frequency of lymphoplasmacytic aortitis (IAA) was 4% in a previous series of 125 thoracic aortic aneurysms [10]. However, given the recent nature and rarity of this disease and limited familiarity with its diverse manifestations, cardiovascular manifestations of IgG4-RD are still significantly under-recognized [11]. Therefore, reporting of additional cases is contributory to further characterization of its histological spectrum.

Materials and methods

All cases of aortic aneurysms resected at the University Heart Center Erlangen, Germany, from 2000-2013 were retrieved from the Archival records and reviewed for the purpose of this study. The pathology reports have been searched for specimens with variable inflammation for retrospective assessment of the histological slides. Cases without inflammatory changes according to the detailed pathology reports were not examined further. All relevant cases have been screened by one of the authors (A.A.). Pattern of inflammation (adventitial versus transmural), constitution of the inflammatory infiltrate (lymphocytic and plasma cell components, lymphoid follicle, eosinophils), obliterative phlebitis, presence or absence of prominent sclerosis and/or granulomas were recorded. Tissue samples were originally fixed in buffered formalin overnight and embedded routinely in paraffin for histological evaluation using standard hematoxylin and eosin (HE), Elastica van Gieson (EvG) and alcian blue stains. Immunohistochemistry was carried out on 3 μm sections using a Ventana automated system (Vantage) according to the manufacturer's instructions. IgG was detected using a Rabbit polyclonal antibody against human IgG (1:2000, DAKO, Denmark, pretreament with Pronase) and IgG4 with a mouse monoclonal antibody against human IgG4 (clone MCA2098G, 1:100, SeroTec, UK, pretreatment with citrate buffer). The absolute number of IgG4 and IgG expressing plasma cells were determined in 3 high power fields (HPF) containing the highest numbers of these cells. The three counts were then used to determine the average value per HPF as previously described [12]. One HPF corresponded to an area of 0.238 mm^2. The ratios of IgG4: IgG positive
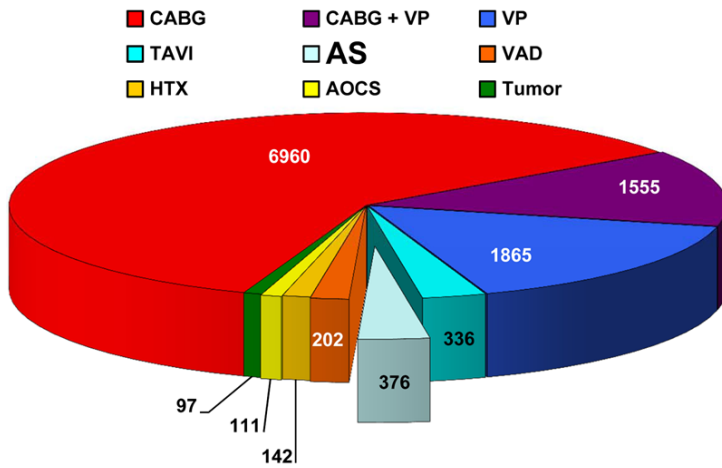
Figure 1. Cardiac Surgery at the University of Erlangen between January 2000 and January 2013. CABG = Coronary Artery Bypass Grafting; VP = Valve Procedures; TAVI = Transcatheter Aortic Valve Implantation; AS = Aortic Surgery; VAD = Ventricular Assist Device; HTX = Heart Transplantation; AOCS = Any Other Cardiac Surgery.
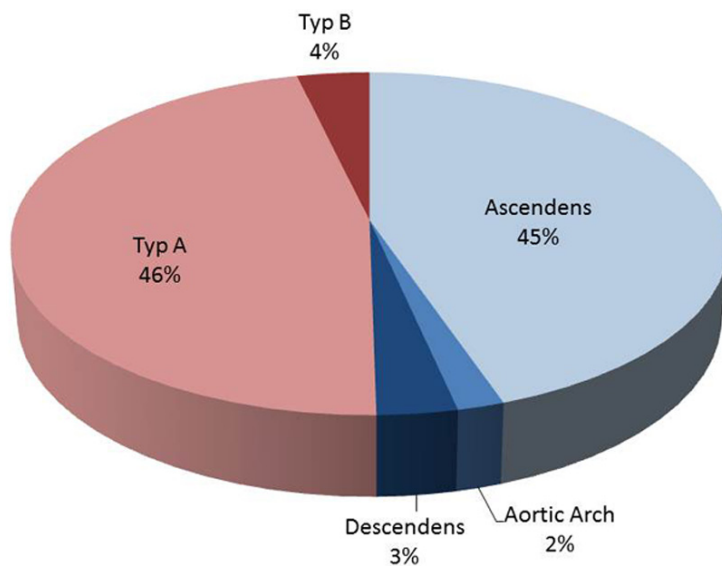

Figure 2. Distribution of underlying reasons for Aortic Surgery. Type A = Type A Dissection; Type B = Type B Dissection; Ascendens = Ascending Aortic Aneurysm; Aortic Arch = Aortic Arch Aneurysm; Descendens = Descending Aortic Aneurysm.

the adventitia or around small vessels; these were considered non-specific finings and were not analyzed further.

Results

Clinical and demographic features of the whole cohort

A total of 376 surgical resections of aneurysms of the thoracic aorta have been performed during the observation period 2000-2013, i.e., 3.2% of the total number (n=11644) of all surgical operations in that period (**Figure 1**). The distribution of underlying reasons for the aortic surgery is demonstrated in **Figure 2**. The majority of patients had ascending aortic aneurysm (n=168, 45%) or a type A dissection (n=175, 46%). The remainder had aortic arch aneurysm (n=7, 2%), descending aortic aneurysm (n=12, 3%) or a type B dissection (n=14, 4%), respectively. Patient characteristics are summarized in **Table 1**. Notably, the majority of the 376 patients were men (n=268, 71.3%), whereas there was no gender specific significance concerning age, body mass index, EuroScore (additive and logistic), creatinine or 30 days lethality (**Table 1**). Furthermore, there were no significant differences between the underlying causes for aneurysm or dissection concerning the patient characteristics. The 30 days lethality in all male and female patients with type A or B dissection was significant higher than in the other groups with aortic aneurysm. All aortic aneurysms or dissections were diagnosed either by transthoracic (TTE) or transesophageal (TEE) echocardiography (**Figure 3A**) followed by computer tomography (CT, **Figure 3B**). Typical intraoperative photographs of a huge aneurysm of the ascending aorta and a dissec-

plasma cells were then calculated. Only cells with clear-cut strong cytoplasmic reactivity were considered positive. One patient with giant cell arthritis (Horton disease) and aortic involvement (IAA) has been reported previously [13]. This case was not included in further analysis of IAA. Atherosclerotic cases occasionally showed mild degree of non-specific mononuclear cell aggregates confined to small areas of

Table 1. Patient Characteristics

Patient Characteristics	Aorta Ascendens Aneurysm (n=168)	Aortic Arch Aneurysm (n=7)	Aorta Descendens Aneurysm (n=12)	Type A Dissection (n=175)	Type B Dissection (n=14)
male/female	111/57	6/1	7/5	132/43	12/2
Age male (mean ± SD)	60.6 ± 12.2	55.4 ± 17.7	53.6 ± 10.2	54.3 ± 12.6	52.5 ± 11.9
Age female (mean ± SD)	67.9 ± 10.9	37.5 ± 0	53.2 ± 19.1	64.8 ± 12.4	57.9 ± 12.2
Body Mass Index (BMI) male (mean ± SD)	27.2 ± 4.2	28.1 ± 2.9	26.0 ± 2.9	28.9 ± 5.7	28.0 ± 3.5
Body Mass Index (BMI) female (mean ± SD)	28.3 ± 5.4	23.0 ± 0	23.6 ± 3.6	26.1 ± 4.3	25.6 ± 3.0
EuroScore male additive (mean ± SD)	8.2 ± 2.7	6.7 ± 1.0	8.3 ± 1.4	10.4 ± 3.2	8.8 ± 2.6
logistic (mean ± SD)	2.7 ± 0.9	2.3 ± 0.3	2.8 ± 0.4	3.5 ± 1.0	3.0 ± 0.8
EuroScore female additive (mean ± SD)	10.4 ± 2.9	8.0 ± 0	8.8 ± 2.8	13.1 ± 3.0	10.0 ± 2.8
logistic (mean ± SD)	3.4 ± 1.0	2.8 ± 0	3.0 ± 1.0	4.3 ± 1.0	3.3 ± 0.8
Creatinine (mg/dl) male (mean ± SD)	1.2 ± 0.4	1.0 ± 0.1	1.3 ± 0.5	1.3 ± 0.6	1.1 ± 0.5
Creatinine (mg/dl) female (mean ± SD)	1.0 ± 0.4	0.9 ± 0	1.2 ± 0.4	1.0 ± 0.5	0.8 ± 0.3
30 days Lethality male (n/% of subgroup)	2/1.8	1/16.7	0/0	26/19.7	4/33.3
30 days Lethality female (n/% of subgroup)	5/8.8	0/0	0/0	12/27.9	1/50.0

Table 2. Pattern of inflammation and IgG4/IgG values in inflammatory thoracic aortic aneurysms

No.	Age	Sex	Diagnosis	Serum IgG (mg/dl)*	Serum IgG4 (mg/dl)**	IgG4/1hpf	IgG/1hpf	IgG4/IgG Ratio	Chronic inflammation pattern
1.	74	M	Aneurysm, ascending aorta	NA	664	155	250	0.62	Adventitia + transmural, elastic fiber degeneration
2.	72	W	Type A dissection	NA	197	45	190	0.24	Mild adventitia + mild transmural
3.	70	W	Aneurysm, ascending aorta	611	269	17	84	0.2	Adventitia, fokal transmural, LFs
4.	73	W	Aneurysm, ascending aorta	NA	NA	90	100	0.9	Adventitia, LFs
5.	76	W	Aneurysm, ascending aorta	NA	NA	42	60	0.7	Transmural, porminent LFs
6.	67	W	Type A dissection	NA	NA	182	200	0.91	Transmural, porminent LFs
7.	79	W	Aneurysm, ascending aorta	NA	NA	43	148	0.29	Adventitia, LFs
8.	70	W	Aneurysm, ascending aorta	NA	NA	20	62	0.32	Transmural
9.	80	M	Aneurysm, ascending aorta	NA	NA	12	64	0.18	Adventitia
10.	62	M	Type B dissection	NA	NA	8	102	0.07	Adventitia
11.	74	M	Type A dissection	NA	NA	3	135	0.02	Adventitia
12.	74	W	Aneurysm, ascending aorta	NA	NA	13	44	0.29	Adventitia, focal transmural, LFs
13.	61	W	Aneurysm, ascending aorta	1190	961	120	240	0.5	Transmural, foci of necrosis, giant cells
14.	67	M	Type A dissection	735	369	10	60	0.16	Adventitia
15.	52	M	Type A dissection	635	257	11	60	0.18	Focal intramural

NA = not available; hpf = high power field; LFs = lymphoid follicles. *Reference values: 751-1560 mg/dl. **Reference values: 52-1250 mg/dl.
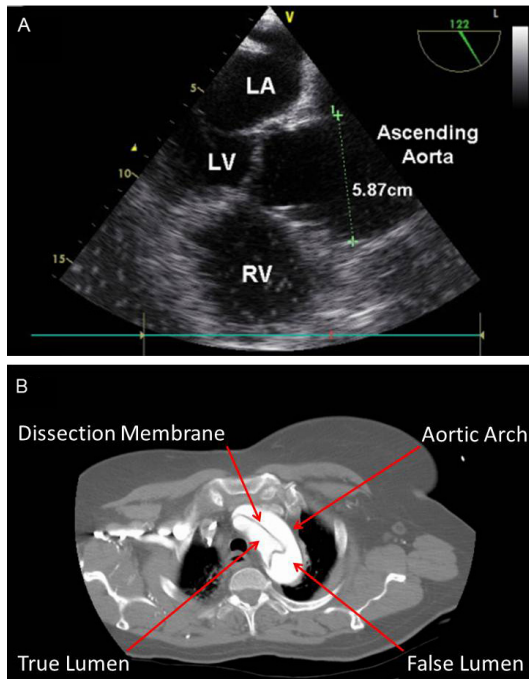
Figure 3. A: Transesophageal echocardiogram (TEE): Longitudinal scan of the aortic root revealed a huge aneurysm of the ascending aorta with a maximum diameter of 5.87 cm. The aortic valve was not involved. LV indicates left ventricle; LA, left atrium; RV, right ventricle. B: Contrast-enhanced electrocardiogram-gated computed tomography (CT) demonstrated a dissection of the complete thoracic aorta. The entry was just at the level of the aortic root and extended via the large ascending aorta and the aortic arch to the descending aorta down to the arteria mesenterica superior.

tion of the complete thoracic aorta are demonstrated in **Figure 4A** and **4B**.

Clinical features of inflammatory aortic aneurysms (lymphoplasmacytic sclerosing thoracic aortitis)

The clinicopathologic features of the 15 patients with IAA are summarized in **Table 2**. Patients were 9 females and 6 males (female to male ratio = 1.5:1) aged 52-80 yrs (mean, 70 yrs; median, 72 yrs). Underlying diseases/indications for surgery were ascending aortic aneurysms (n=9), type A dissection (n=5) and type B dissection (n=1). Serum IgG and IgG4 levels were available for 4 patients and only IgG4 for another two: all were within normal levels. In addition, serum IgG and/or IgG4 were determined in another 16 patients without inflammation (control group without IAA) and all showed normal values (data not shown).
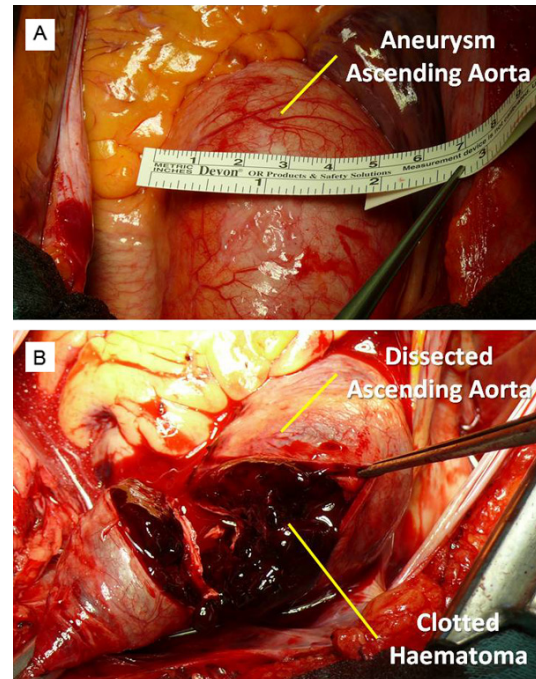

Figure 4. A: Intraoperative photograph showing a gross specimen from a huge aneurysm of the ascending aorta. B: Intraoperative photograph from another example taken after opening of the ascending aorta, showed extensive dissection with clotted blood in the aortic wall.

Pathological features of inflammatory aortic aneurysms

The resection specimens usually comprised multiple tissue pieces of the aortic wall. Gross examination showed intramural bleeding associated with dissection in most of cases of dissecting aneurysms. Variable degrees of adventitial inflammation were seen in all cases, occasionally with a band like-submesothelial pattern (**Figure 5A**). This is commonly associated with significant thickening of the adventitia which seems then to merge with the media imperceptively (**Figure 5B**) with associated prominent storiform hyaline sclerosis (**Figure 5C**). The sclerosis was usually bordered by heavy plasma cell aggregates (**Figure 5D**). In addition, 5 cases showed at least focal unequivocal lymphoplasmacytic infiltrates within the substance of the tunica media (**Figure 6A** and **6B**). Intramural inflammation was associated with evidence of elastic fiber damage in 2 cases; one of them showed in addition to fragmentation also foci of necrosis and isolated multinucleated giant cells (**Figure 6C** and **6D**).
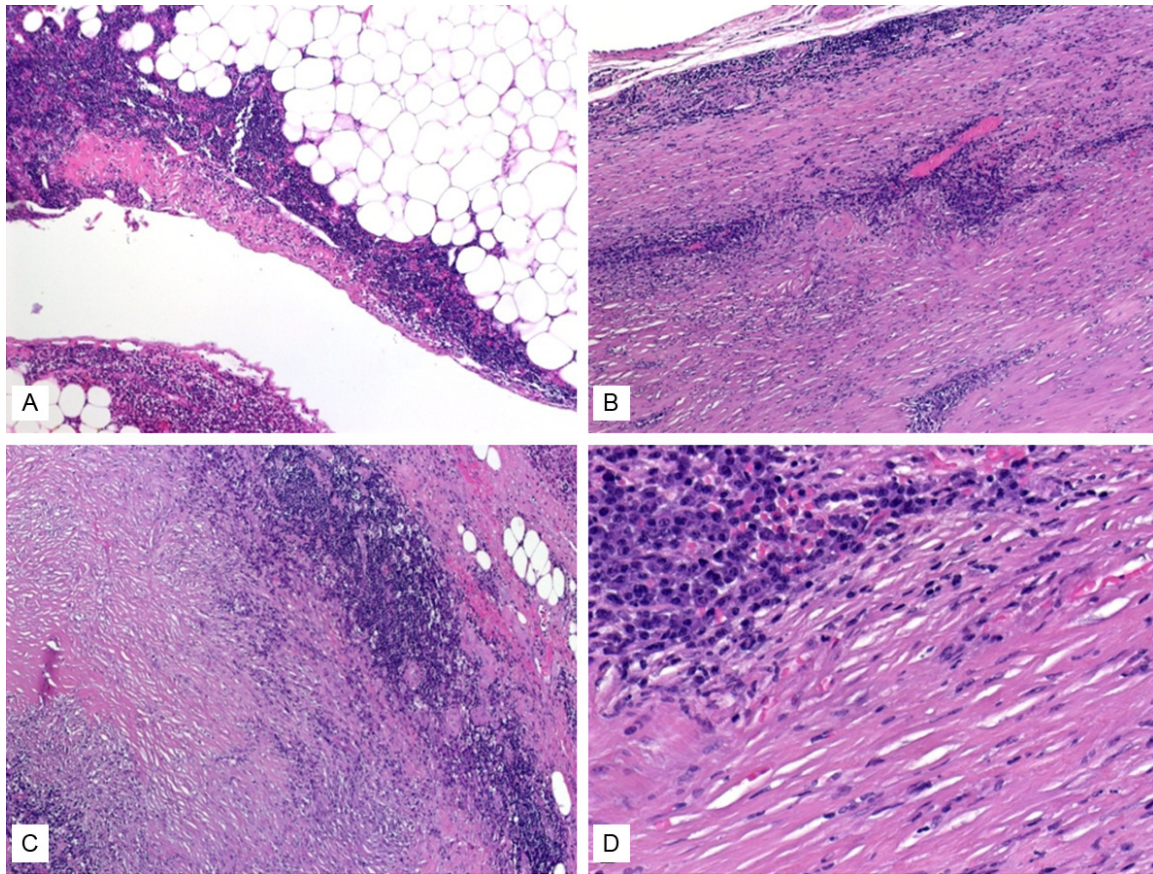
Figure 5. Representative examples of the inflammatory pattern in lymphoplasmacytic thoracic aortitis. A: Diffuse adventitial lymphoplasmacytic infiltration extending into adjacent fat (in other areas infiltrating the aortic wall). B: Inflammatory aggregates interrupted by prominent sclerosis. C: Transition from storiform hyaline sclerosis (upper left) to plasma cell-dominated inflammation bordered by lymphoid follicles. D: Higher magnification showed plasma cell aggregates with hyaline basket-wave fibrosis.

However, calcifying atherosclerotic changes within the media were uncommon; seen only in two cases. All cases with dense inflammatory infiltrates showed perineural or perivascular inflammation and lymphoid follicles were a common feature (seen in 7/15 cases). All cases were associated with variable interstitial sclerosis and this was particularly prominent in cases with transmural or intramural lymphoid follicle-containing inflammation. There was no evidence of neutrophils or abscess formation; neither were there any epithelioid granulomas. Small vessels did not show obliterative changes. Prominent eosinophils were seen in one case but a few scattered eosinophils are commonly seen in most cases. Taken by gender, 4 of the 6 males had inflammation confined to the adventitia. On the other hand, all but one of the females had evidence of transmural inflammation (**Table 2**).

The absolute number of IgG4 positive plasma cells varied greatly from 3 to 182 cells/HPF (mean: 51 cells/HPF). The IgG4: IgG ratios ranged from 0.02-0.91 (mean: 0.37). When considering specific inflammatory patterns, all but one of the cases with at least focally transmural inflammation showed a higher number of IgG4 cells (range: 20-182; mean: 104 cells/HPF) and a high IgG4: IgG ratios in excess of 0.3 (range: 0.32-0.91; mean: 0.62). The presence of lymphoid follicle was associated with a tendency towards higher IgG4 to IgG ratios (mean 0.48 versus 0.37 for the whole cohort). On the other hand, inflammation confined to the adventitia (6 cases) was associated with a lower IgG4 plasma cell counts (range: 3-90 cells/HPF; mean: 27) and a lower IgG4: IgG ratios (range: 0.02-0.90; mean: 0.27). The pattern of distribution of IgG4 positive plasma cells varied greatly from diffuse (**Figure 7A** and
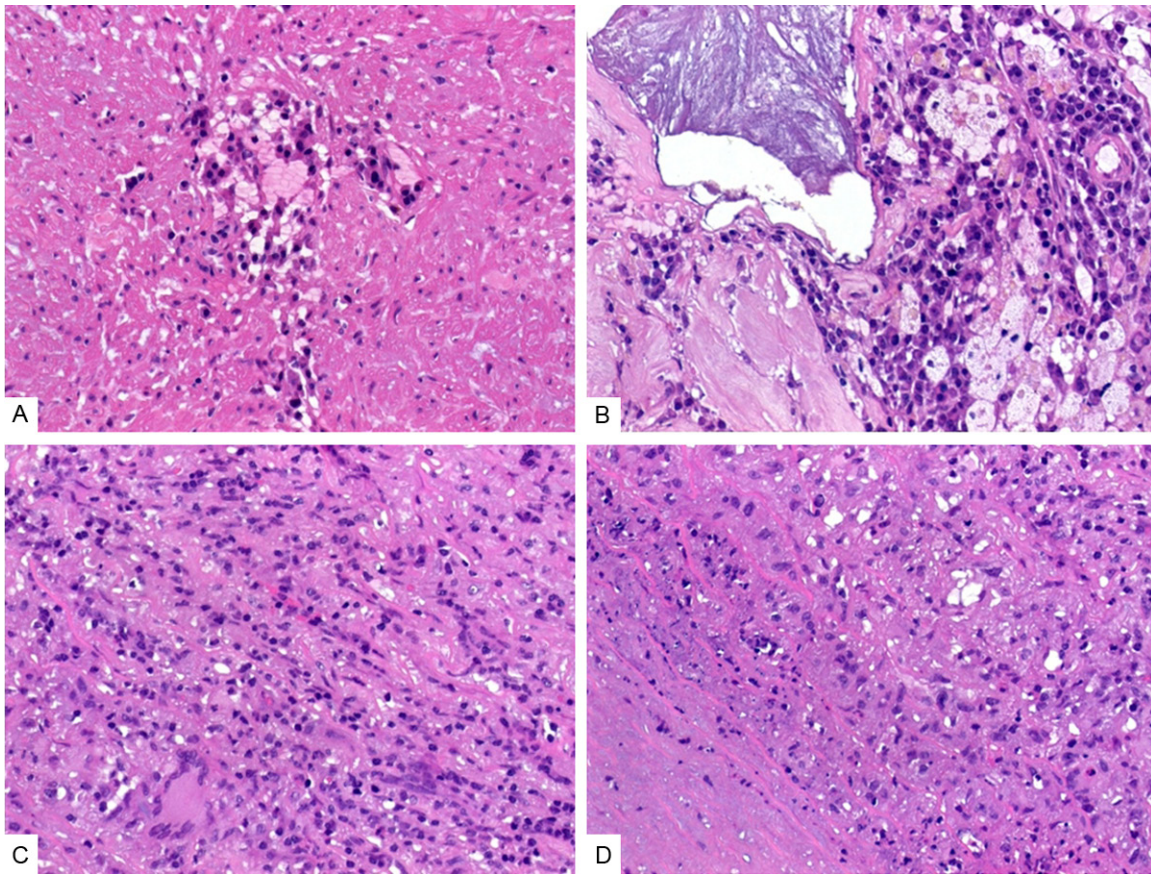
Figure 6. Pattern of elastic fiber damage in lymphoplasmacytic thoracic aortitis. A: A focus of plasma cells associated with elastic fiber loss within the media. B: This example showed dense plasma cell infiltrates abutting a focus of calcification with a few foamy histiocytes. C: This example showed parallel arrays of damaged elastic fibers, note multinucleated giant cells at lower field. D: This case showed subtotal loss of elastic tissue with prominent vacuolation and associated lymphoplasmacytic cells.

7B) to dense aggregates bordering areas of elastic fiber loss/necrosis (**Figure 7C**) or heavy infiltrates encasing the vasa vasora in the adventitia (**Figure 7D**). Interestingly, one specimen had a periaortic lymph node that was found (incidentally) to contain clusters of IgG4 plasma cells on immunostaining (**Figure 7D** inset).

Discussion

IAA represents an uncommon disease of different etiologies. In particular, chronic infections (syphilitic mesaortitis [14] and rare miscellaneous chronic bacterial infections [15]), autoimmune diseases (Takayasu aortitis, other large vessel diseases and aortic involvement in diverse vasculitides) [16] as well as other poorly characterized conditions have been implicated [5]. However, the etiopathogenesis and

nosological classification of a subset of IAA characterized by prominent lymphoplasmacytic tissue infiltration in the absence of other underlying infectious or autoimmune systemic diseases remain unclear and poorly characterized. Nevertheless, close similarity of histological findings in many cases of lymphoplasmacytic IAA to other organ manifestations of IgG4-RD and occurrence of IAA in patients with known IgG4-RD suggested IAA as a manifestation (component) of that systemic disorder [10, 17].

Sakata et al compared 11 cases of abdominal IAA with 12 age-matched cases of atherosclerotic abdominal aortic aneurysm. They found no difference in the incidence of risk factors between the two groups (autoimmune/fibrosing diseases were detected in only 3 patients with inflammatory, but in none with atherosclerotic abdominal aortic aneurysm). However,
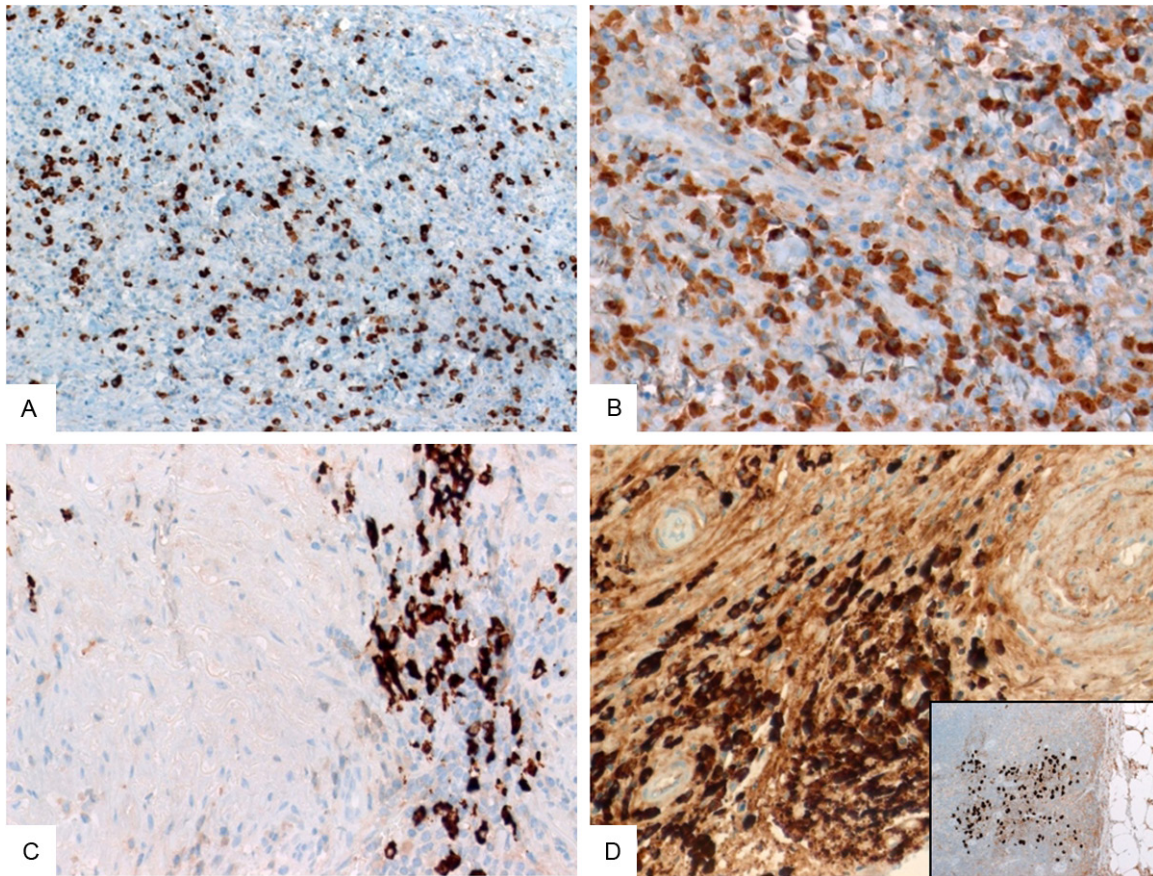
Figure 7. IgG4 immunostaining (A) in this case showed diffuse distribution that was similar to IgG pattern (B). C: Aggregates of IgG4 plasma cells (right) bordering elastic fiber loss (left). D: Dense IgG4 plasma cells encasing small adventitial vessels that lacked obliterative vasculitis. Inset: dense aggregate of IgG4-positive plasma cells in a regional lymph node.

lymphoplasmacytic cell infiltration and fibrosis were significantly more intense and extensive and lymph follicle formation and small vessel vasculitis were more frequently found in inflammatory as opposed to atherosclerotic aneurysms. Further, a significant increase in IgG4-positive plasma cells was seen in the former but not in the latter. The authors concluded that inflammatory abdominal aortic aneurysms may reflect the presence of IgG4-RD, and not a simple inflammatory aneurysm of the aorta [17]. Laco et al analyzed 11 cases of isolated thoracic aortitis of ascending aorta (9 women and two men aged 52-79 years). None had previous, concurrent or evidence of subsequent IgG4-RD or manifestations of it. Inflammation affected mainly the adventitia and media and was associated with severe medial elastic fiber damage. Adventitial obliterative phlebitis was absent. In five cases, >20 plasma cells/HPF were detected with a mean IgG4/IgG ratio of 0.55 (range: 0.07 to 0.98). All six cases with

ratios >0.50 revealed prominent adventitial fibrosis. The authors concluded that a subset of isolated thoracic aortitis may represent a manifestation of IgG4-RD [18]. Comparing 23 cases of IAA with 11 atherosclerotic cases, Raparia et al found the cut-off of >50 IgG4 positive plasma cells/HPF highly discriminating between the two etiologies (found in 57% of IAA but in none of the atherosclerotic cases) [19]. However, a lower number of IgG4 positive plasma cells was found in both groups [19]. All of their IAA patients had history of smoking, arterial hypertension or coronary artery disease and none showed other manifestations of IgG4-RD. Serum measurement of IgG4 was not done in any of the patients.

Our findings in this study are consistent with previous studies regarding frequency and pathological features of IAA. IAA represents 4% of all thoracic aortic aneurysms in the series published by Kasashima et al [10] and also in our

current series. Although mainly seen in the adventitia, we observed variable degrees of intramural extensions of lymphoplasmacytic infiltrations occasionally associated with evidence of elastic fiber damages suggesting an autoimmune response directed towards tissue derivatives of the aortic wall layers. Consistent with most of previous studies, we found no obliterative phlebitis but common perineural inflammation, frequent lymphoid follicle formation and variable sclerosis. Our series is more unique in that we determined serological values of IgG, IgG4 or both in almost have of the cases of our IAA and none showed pathological values.

However, the role of IgG4-mediated immune responses in the pathogenesis of IAA seems to be not limited to pure autoimmune mechanisms. Siddiquee et al studied the composition of inflammatory infiltrates in two cases of chronic active infectious abdominal aortitis (both caused by gram-positive bacteria) and found a high number of IgG4 plasma cells (50/hpf) which made up 50% of the IgG plasma cell population in that cases [20]. Thus caution is needed when treating or planning to treat patients with IAA by corticosteroid or immunosuppressive drugs, as an inflammatory infectious etiology must be excluded before such treatment. Indeed, some authors raised concerns regarding steroid therapy suggesting that immunosuppressive therapy might result in reduction of the vascular wall thickness and thus enhance aneurysmal complications [9].

There seems to be a significant difference in the demographic and clinicopathologic features of abdominal IAA and lymphoplasmacytic thoracic aortitis (thoracic IAA). While abdominal disease seems to be closely related to IgG4-RD as evident from involvement of periaortic retroperitoneal tissue, presence of obliterative phlebitis and predominance of old males (10:1 in the series of Sakata et al) [17], lymphoplasmacytic thoracic aortitis although sharing some histological features with abdominal IAA, seems to be a disease of old women. The female to male ratios were 4.1:1 in the series of Laco et al [18] and 1.5:1 in our current series (2.7:1 for both series). In our series, the predominance of women in the group of IAA (60%) contrasts sharply with the significant overrepresentation of males (71.3%) in the whole cohort of the 376 patients with thoracic aortic aneurysms. Interestingly, all but one of our cases with prominent extramural extension of the inflammation associated with a higher IgG4:IgG ratio were females. On the contrary, 4 of the 6 males had inflammation confined to the adventitia.

In summary, we reported our experience with 15 cases of thoracic IAA illustrating highly overlapping histological features with IgG4-RD in patients lacking other features of systemic IgG4-RD and having normal serum IgG4 levels. Uniform absence of serological and other features of IgG4-RD in our patients and the striking female predilection (in contrast to IgG4-RD which primarily affects old males) suggest a localized autoimmune process directed towards aortic wall tissue derivatives and argue against a generalized systemic disorder in these patients. The mechanism and/or causes responsible for triggering this chronic lymphoplasmacytic aortitis that would ultimately result in aneurysmal dilatation and/or dissections remains to be further studied. Histopathological evaluation of tissue specimens still represents the only clue to diagnosis of IgG4-rich lymphoplasmacytic aortitis/IAA and should alert clinicians to the possibility of an underlying systemic disorder.

Disclosure of conflict of interest

None.

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