Rheumatology, Taiyuan, China; ³Brigham and Women's Hospital, Harvard Medical School, Pathology, Boston, United States of America

Background: Antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV) are recognized as a small-vessel vasculitis of autoimmune origin characterized by inflammation and the presence of circulating ANCA with the major target antigens identified as proteinase 3 (PR3) and myeloperoxidase (MPO). A very minor T cell subpopulation which lacks both CD4 and CD8 markers, known as CD4-CD8- double negative (DN) represents less than 5% of the total peripheral blood (PB) T cells in healthy individuals and plays a vital role in the pathogenesis of autoimmune disorders.

Objectives: To investigate whether DN T cells and cytokine (IFN- γ , IL-4 and IL-17) are involved in the pathogenesis of AAV and to verify whether DN T cells are associated with kidney damage.

Methods: Nineteen healthy controls (HCs) and 40 active patients with AAV were enrolled in this study. Peripheral blood mononuclear cells from AAV patients and controls were isolated by magnetic bead separation, and phenotypic characterization of mononuclear cells were determined via flow cytometry. The diagnostic value for DN T subsets was evaluated by the areas under the receiver operating characteristic curves (AUC).

Results: The percentage ($p<0.001$) and absolute numbers ($p=0.028$) of DN T cells were found to be significantly higher in patients with AAV as compared with controls. Less the percentage of DN T cells from patients with AAV were of CD62L+CD45RO+ ($p=0.024$) phenotype than was found in HCs, and the percentage of CD62L-CD45RO- ($p=0.043$) was higher. The percentage of DN T cells expressing IFN- γ ($p=0.032$), IL-4 ($p=0.039$) and IL-17 ($p=0.042$) increased in AAV patients. In AAV with renal damage, the percentage of DN T cells was expanded ($p=0.016$) than those patients without renal damage. After conventional methylprednisolone treatment, the percentage of DN T cells in patients with remission was significantly lower than those active patients ($p=0.028$). The ROC curve analysis showed that the ratios of CD4+ T cells to DN T cells and CD8+ T cells to DN T cells were useful in diagnosing AAV patients. The AUCs were 0.967 (95% confidence interval [CI] 0.922-1.000; $p<0.001$) and 0.879 (95%CI 0.789-0.969; $p<0.001$), respectively.

Conclusion: DN T cells represent an inflammatory T cell subset that produces inflammatory cytokines (IFN- γ , IL-4 and IL-17) in AAV patients. Suppression of DN T cells may be new specific treatment in autoimmune disorder such as AAV.

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THU0318

PATTERNS OF CLINICAL PRESENTATION IN TAKAYASU'S ARTERITIS

K. A. Quinn¹, K. B. Gibbons¹, S. Carette², D. Cuthbertson², N. Khalidi², C. Koenig², C. Langford², C. Mclellan², P. Monach², L. Moreland², C. Pagnoux², P. Seo², A. Sreih², K. J. Warrington², S. R. Ytterberg², E. Novakovich¹, P. A. Merkel², P. Grayson¹. ¹National Institutes of Health, Bethesda, United States of America; ²Vasculitis Clinical Research Consortium, Philadelphia, United States of America

Background: Takayasu's arteritis (TAK) is a clinically heterogeneous disease. Patterns of clinical presentation in TAK at diagnosis have not been well described, and a "triphasic pattern" of constitutional symptoms evolving into vascular inflammation and fibrosis has been reported but never systematically evaluated.

Objectives: To describe patterns of clinical presentation in TAK at diagnosis and evaluate the presence of an antecedent triphasic disease pattern in patients with TAK who presented with a major ischemic event at diagnosis.

Methods: Patients with TAK were prospectively recruited from the National Institutes of Health (NIH) and the Vasculitis Clinical Research Consortium (VCRC). All patients fulfilled the 1990 American College of Rheumatology (ACR) Classification Criteria for TAK. Based on clinical presentation at diagnosis, patients were divided into five groups from the different stages of the triphasic pattern of disease as follows: 1) constitutional symptoms (phase I), 2) carotidynia (phase II), 3) other vascular-associated symptoms (phase II), 4) major ischemic event (phase III) defined as CVA or TIA, retinal ischemia, MI, renovascular hypertension, or mesenteric ischemia, or 5) asymptomatic. Phase II was divided into two separate groups because patients with carotidynia reportedly have a higher rate of relapsing disease.

Associated clinical characteristics were evaluated in each group and differences among groups were assessed by chi square test and Kruskal-Wallis test, as appropriate. Preceding symptoms were also assessed to determine the presence of a triphasic disease pattern.

Results: A total of 275 patients with TAK were included (VCRC=208; NIH=67). Similar heterogeneity of clinical presentation was identified in each cohort: constitutional symptoms (8%), carotidynia (13-15%), other vascular symptoms (43-47%), major ischemic event (28-30%), and asymptomatic (2-6%). Frequency of male gender was more common in patients who presented with constitutional symptoms or were asymptomatic at diagnosis ($p<0.01$). Patients who presented with constitutional symptoms and major ischemic events were youngest at diagnosis. Patients in the asymptomatic group were oldest at diagnosis and often were not treated ($p<0.01$). Involvement of the abdominal vasculature was associated with major ischemic events and asymptomatic presentations. Major ischemic events after diagnosis were infrequent in the groups who did not present with a major ischemic event, occurring in 10-20% cases. Relapse ($p<0.01$) and recurrent pharyngitis preceding diagnosis ($p<0.01$) was most frequent in patients who presented with carotidynia.

A total of 79 patients [VCRC=59 patients, NIH=20 patients] presented with a major ischemic event. The majority of these patients (53%) reported symptoms of active disease prior to the major ischemic event. Few patients (19%) who presented with a major ischemic event reported a triphasic pattern of disease.

Conclusion: There is heterogeneity in clinical presentation at the time of diagnosis in TAK and this heterogeneity can be used to group patients according to pattern of disease presentation. Patients do not necessarily progress sequentially through phases of disease, but the majority of patients presenting with a major ischemic event report some preceding symptoms. Data from this study demonstrate distinct subgroups within TAK and supports the concept that TAK is possibly a heterogeneous collection of multiple diseases.

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THU0319

DEVELOPMENT AND OUTCOME OF AORTIC COMPLICATIONS DURING TOCILIZUMAB TREATMENT OF GCA AND HISTOPATHOLOGIC EVIDENCE OF RESIDUAL INFLAMMATION-A CASE SERIES.

A. Rubbert-Roth¹, P. K. Bode², T. Langenegger³, C. Pfofe⁴, T. Neumann¹, O. C. H. Kim⁵, J. Von Kempis¹. ¹Rheumatology Clinic, Cantonal Hospital St Gallen, St Gallen, Switzerland; ²Institute of Pathology and Molecular Pathology, University Hospital of Zurich, Zurich, Switzerland; ³Rheumatology Clinic, Cantonal Hospital Zug, Baar, Switzerland; ⁴Pathology Institute Triemli, Triemli Hospital, Zurich, Switzerland; ⁵Radiology Clinic, Cantonal Hospital St Gallen, St Gallen, Switzerland

Background: Giant cell arteritis (GCA) may affect the aorta and the large aortic branches and lead to dissections and aortic aneurysms. Tocilizumab (TCZ) treatment has the capacity to control aortic inflammation as has been demonstrated by CRP normalization and imaging data. However, limited data are available on the histopathological findings obtained from patients who underwent surgery because of aortic complications during TCZ treatment.

Objectives: We report on 5 patients with aortitis who were treated with TCZ and developed aortic complications.

Methods: We describe a retrospective case series of patients with GCA treated with TCZ, who presented in our clinic between 2011 and 2019. Three patients underwent surgery. Histopathologic examination was performed in specimen from all of them.

Results: Five female patients were diagnosed with GCA (4/5) or Takayasu arteritis (1/5) involving the aorta, all them diagnosed by MR angiography and/or FDG PET CT scan. Three patients (one with aortic aneurysm, one with dissection) underwent surgery after having been treated with TCZ for seven weeks, nine months and four years, respectively. Imaging before surgery showed remission on MRI and/or PET-CT in all cases. At the time of surgery, all patients showed normalized CRP and ESR values. Histopathological evaluation of the aortic wall revealed infiltrates, consisting predominantly of CD3+CD4+ T cells. Enlargement of pre-existing aneurysms was observed in the other two patients 10 weeks and 4 months after discontinuation of TCZ, respectively. Both patients were not eligible for surgical intervention and died during follow-up.

Conclusion: Our case series suggests that during treatment with TCZ, regular imaging is necessary in this patient population to detect development of structural changes such as aneurysms or dissections. Despite treatment, residual inflammation might persist which could contribute to eventual aortic complications.

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THU0320

RENAL TRANSPLANTATION DUE TO RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (RPGN) AND SYSTEMIC AUTOIMMUNE DISORDERS. STUDY OF 42 PATIENTS FROM A SINGLE CENTER.

L. Sanchez-Bilbao¹, M. De Cos-Gómez², J. C. Ruiz-San Millán², M. A. González-Gay¹, R. Blanco¹. ¹H.U. Marqués de Valdecilla, Rheumatology, Santander, Spain; ²H.U. Marqués de Valdecilla, Nephrology, Santander, Spain

Background: Rapidly Progressive Glomerulonephritis (RPGN) is characterized by a rapid and severe decline in kidney function that may lead to a kidney transplantation. RPGN is classified in three groups: **a)** Type I or associated to anti-glomerular basement membrane antibodies (RPGN-GBMa), **b)** Type II or associated to immunocomplexes (RPGN-immunocomplexes), and **c)** Type III or pauci-immune (RPGN-pauci-immune). RPGN can be primary, without extra-renal involvement (RPGN-renal-limited), or secondary to systemic autoimmune disorders (RPGN-SAD), infectious diseases or drugs. Kidney transplantation in RPGN-SAD may be associated to a worse outcome.

Objectives: To assess **a)** clinical features of the three types of RPGN, **b)** comparison of post-transplant survival and graft survival between these three types.

Methods: We studied three groups of patients according to renal biopsy: **a)** RPGN-GBMa (n = 11), **b)** RPGN-immunocomplexes (n = 2) and **c)** RPGN-pauci-immune (n=29). All these patients were transplanted in a single reference University Hospital. The main outcome variables were **a)** graft survival up to 15 years

and patient survival up to 30 years and **b)** evolution of renal function (serum creatinine and proteinuria) in the first 5 years of follow-up.

Results: We included a total of 42 patients with renal transplant due to RPGN, mean age at diagnosis 44.87±17.01 years (48.53±17.45 at the time of the transplant). No significant differences at baseline were observed between the three RPGN groups regarding sex, age and cardiovascular risk factors. Renal biopsy had been performed in the 42 patients with RPGN: type I or RPGN-GBMa (n=11, 26.2%), type II or RPGN-immunocomplexes (n=2, 4.8%) and type III or RPGN-pauci-immune (n=29, 69.0%).

It was also reported the presence or absence of systemic autoimmune disorders (31% RPGN-SAD and 69% RPGN-renal-limited). According to the presentation and the clinical characteristics of the patients, another classification has been established: **a)** type I (18.2% (n = 2) Goodpasture-syndrome), **b)** type II (100% renal-limited), **c)** type III (13.8% (n = 4) granulomatosis with polyangiitis) and 20.70% (n = 6) microscopic polyangiitis. The evolution of serum creatinine and the proteinuria after the transplant is shown in TABLE 1 and 1.1. Neither differences were found in terms of graft and patient survival between the 3 groups (Figures 1 and 2).

Figure 1. Graft survival.

TABLE 1.

	1 Month			6 Months			1 Year		
Serum Creatinine mg/dL	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III
N	11	2	26	10	2	22	10	2	22
Mean±SD	1.78±0.8	3.85±4.03	1.64±0.67	1.59±0.73	1.45±0.77	1.99±1.31	1.55±0.62	1.50±0.70	1.77±1.10
Proteinuria mg/24 h	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III
N	9	2	23	10	1	19	10	ND	19
Mean±SD	470.00±566.85	400.00±565.68	408.22±449.00	611.87±832.20*	797.00±556.29*	362.98±323.38*	656.10±1206.68	ND	282.54±272.35

*p<0.05

TABLE 1.1

	3 Years			5 Years		
Serum Creatinine mg/dL	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III
N	11	2	20	8	2	18
Mean±SD	1.64±0.74	1.70±0.69	1.85±1.34	1.55±0.86	1.60±0.84	1.72±0.82
Proteinuria mg/24 h	RPGN-type I	RPGN-type II	RPGN-type III	RPGN-type I	RPGN-type II	RPGN-type III
N	11	2	17	8	2	16
Mean±SD	510.79±832.90	272.57±291.20	340.65±344.17	238.23±311.19	443.88±300.87	579.26±1114.5

*p<0.05