AB0755

INVESTIGATING CYTOGLOBIN IN GIANT CELL ARTERITIS: ITS ROLE IN THE PATHOGENESIS AND POTENTIAL AS A BIOMARKER

Keywords: Diagnostic tests, Biomarkers, Vasculitis

L. Farrukh[1], M. Felix[2], A. Ibrahim[3], R. Peredo-Wende[4], D. Jourd'heuil[5], F. Jourd'heuil[5]. [1]*Albany Medical Center, Internal Medicine, Albany, United States of America*; [2]*Yale School of Medicine, Rheumatology, New Haven, United States of America*; [3]*Albany Medical Center, Pathology, Albany, United States of America*; [4]*Albany Stratton VA Medical Center, Rheumatology, Albany, United States of America*; [5]*Albany Medical College, Department of Molecular and Cellular Physiology, Albany, United States of America*

Background: Cytoglobin (CYBG) is a non-erythroid globin that is found in medial smooth muscle cells (SMCs) of human vessels. Recent studies have postulated that CYGB act as a pro-survival factor during conditions associated with increased oxidative stress, by upregulating anti-apoptotic factors and antioxidant pathways. In this study, we hypothesized that CYGB regulates the inflammatory and antioxidant response associated with GCA pathogenesis.
Objectives: The purpose of this study is to evaluate giant cell arteritis (GCA) vascular lesions for the expression of CYGB and its association with specific molecular markers of cellular damage. We would also like to investigate the association of CYGB with GCA pathogenesis, symptomatology, degree of systemic inflammation, patient demographics, and response to treatment.
Methods: We obtained 29 temporal artery biopsy samples, 14-biopsy positive and 15-biopsy negative, from patients who underwent temporal artery biopsy for GCA diagnosis **(Table 1)**. Inclusion criteria for the experimental group included patients over the age of 18 who had histologic evidence of GCA and met the ACR 1990 classification criteria. The control group included patients who were biopsy negative for GCA. Immunofluorescence staining for CYGB will be done on all samples to assess differential expression across the experimental and control groups. Proximity ligation assays (PLA) will be done to assess binding between cytoglobin and known pro-inflammatory markers to establish mechanistic insights for CYGB in the pathogenesis of GCA. We will also obtain clinical data including signs and symptoms at presentation, levels of serum inflammatory markers, treatment, clinical course, and outcomes.
Results: We are currently conducting validation studies of the immunofluorescence and PLA staining for specific molecular markers on temporal artery biopsy samples. Thus far, we were able to validate the immunofluorescence staining for CYGB **(Figure 1)** and the PLA for CYGB and HMGB2. Once we have established robust and reliable staining protocols for other markers, we will implement these protocols in our control and GCA groups and move forward with the analysis.
Conclusion: We previously demonstrated that overexpressing CYGB in human cardiac stem/progenitor cells (HCPCS) led to an increase in cell survival in response to oxidative stress. Whereas, silencing of CYGB in these cells, increased the rate of cell death. Similarly in rat and mouse models, it was found that CYGB contributes to vascular remodeling following injury, and the absence of CYGB led to accelerated cell death and inhibition of neointima formation. Based on these studies, we hypothesized that CYGB may play a role in the pathogenesis of different vasculitis including GCA. Once we develop this correlation, we will use this data to identify cellular and serum markers for the diagnosis of GCA. [1,2]

Table 1. Demographic and clinical features of patients who underwent temporal artery biopsy

DIAGNOSIS	GCA, 14	Non-GCA, 15
Sex (F/M)	11 F/3 M	9 F/6 M
Age (avg. years)	77.1	73.1
Ethnicity		
Caucasian	13	14
African American	0	1
Asian	1	0
CLINICAL FEAUTURES		
Abnormal visual changes	12	5
New Onset Headaches	9	8
Temporal Tenderness	4	5
Jaw Claudication	3	1
Fever (◦C)	14	1
PMR symptoms	1	0
Initial CRP (Avg.)(<8.0mg/L)	46.2	43.7
ESR (Avg.)(0-25 mm/h)	57	40.4
THERAPY		
Steroid therapy	13	5
Tocilizumab therapy	5	0
Methotrexate therapy	1	2

REFERENCES:
[1] Jourd'heuil, Frances L., et al. "The hemoglobin homolog cytoglobin in smooth muscle inhibits apoptosis and regulates vascular remodeling." Arteriosclerosis, thrombosis, and vascular biology 37.10 (2017): 1944-1955.
[2] Amdahl, Matthew B., et al. "Cytoglobin at the crossroads of vascular remodeling." *Arteriosclerosis, thrombosis, and vascular biology* 37.10 (2017): 1803-1805.

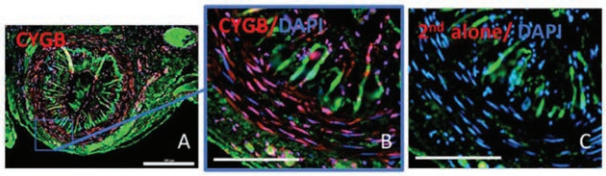


Figure 1. Validation of the immunofluorescence staining for cytoglobin (CYGB) on temporal artery biopsy specimen

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.358

AB0756

IDENTIFICATION OF HISTOPATHOLOGIC FINDINGS OF PATIENTS WITH GIANT CELL ARTERITIS: A MULTICENTRE STUDY IN THE ERA OF 2022 ACR/ EULAR CLASSIFICATION CRITERIA FOR GCA

Keywords: Diagnostic tests, Validation, Vasculitis

G. Sandal Uzun[1,2], O. Gokoz[3], A. Heper[4], B. Cimer Oğut[5], S. Güresci[6], A. Omma[7], M. A. Oztürk[8], A. Ateş[9], L. Kılıç[1,2], O. Karadag[1,2]. [1]*Hacettepe Univercity Faculty of Medicine, Department of Internal Medicine Division of Rheumatology, Hacettepe University Medical Faculty, Ankara, Turkey, Ankara, Turkey*; [2]*Hacettepe Univercity Faculty of Medicine, Hacettepe University Vasculitis Research Centre, Ankara, Turkey*; [3]*Hacettepe Univercity Faculty of Medicine, Department of Pathology, Hacettepe University, Faculty of Medicine, Ankara, Turkey*; [4]*Ankara University Faculty of Medicine, Ankara, Turkey., Department of Pathology, Ankara, Turkey*; [5]*Gazi University Faculty of Medicine, Ankara, Turkey., Department of Pathology, Ankara, Turkey*; [6]*Ministry of Health Ankara City Hospital, Ankara, Turkey., Department of Pathology, Ankara, Turkey*; [7]*Ankara City Hospital, Ankara, Türkiye., Clinic of Rheumatology, Ankara, Turkey*; [8]*Gazi University Faculty of Medicine, Ankara, Turkey., Division of Rheumatology, Department of Internal Medicine, Ankara, Turkey*; [9]*Ankara University Faculty of Medicine Ankara, Turkey., Division of Rheumatology, Department of Internal Medicine, Ankara, Turkey*

Background: Although temporal artery biopsy (TAB) is the gold standard in the diagnosis of giant cell arteritis (GCA), the specific histopathological findings and their relationship with clinical diagnosis have not been well discussed. In recent 2022 ACR/EULAR GCA classification criteria, the presence of giant cells, predominantly mononuclear cell infiltration, and fragmentation in the internal elastic lamina have been defined for the interpretation of definitive vasculitis. [1]
Objectives: To re-evaluate TAB histopathological findings of patients with GCA recruited from 4 tertiary centres in Ankara according to the2022 ACR/EULAR Classification criteria and compare frequencies of these items with DCVAS study [2].
Methods: TAB reports of patients with GCA from 4 tertiary centres between March 2004 and February 2022 were retrospectively reviewed according to the histopathological items defined in the updated criteria. TAB reports were classified by the local physicians as normal, nondiagnostic, consistent with vasculitis but not definite, and definite vasculitis.
Results: Totally, TAB histopathologic reports of 88 patients with GCA were reviewed. The mean age of the patients at the time of TAB was 69.7(±8.5) years and 46(52.2%) were female. Twenty-eight reports without microscopic details were excluded and reports of 60 patients were reanalysed. Of the 60 patients,

Ann Rheum Dis: first published as 10.1136/annrheumdis-2023-eular.1935 on 30 May 2023. Downloaded from http://ard.bmj.com/ on September 29, 2024 at Gazi Universitesi. Protected by copyright.

46 (76.6%) met one of the defined histopathological findings of updated criteria (Figure 1). Histopathological findings of all patients with microscopic findings were detailed in the Table 1. 17(28.3%) patients had at least two histopathological findings.

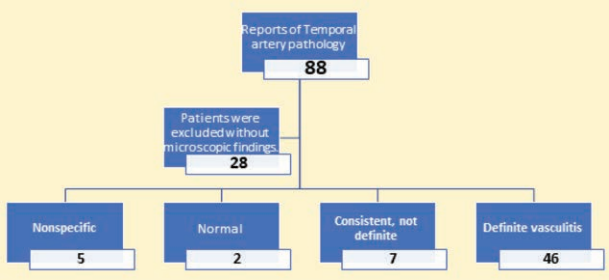


Figure 1.

Table 1. Specific histopathological findings of patients who underwent biopsy with a preliminary diagnosis of giant cell arteritis

Demographic and Histopathologic findings	DCVAS (n=705)	Our study (n=60)
Mean age,SD	73.5 ± (8.5)	69.7(±8.5)
Sex, female	**455(65)**	**46(52.2)**
Giant cells,n(%)	303(51)	18(30)
Internal elastic lamina fragmentation, n(%)	242(41)	22(36.6)
Mononuclear leukocytes (no definition of intimal/adventitial), n(%)	198193(32)	26(43.3)
Intimal thickening, n(%)	198(33)	21(35)
At least one of the defined histopathologic findings for definitive vasculitis *		46(76.6)
>=2 defined histopathologic findings for definitive vasculitis*		17(28.3%)
Vascular thrombosis, n(%)	26(4)	2(3.3)
Granuloma, n(%)	23(4)	1(1.6)
Perivascular inflammation only, n(%)	8(2)	-
Medial calcinosis, n(%)	NA	5(8.3)
Myxoid degeneration, n(%)	NA	6(10)
Adventitial mononuclear infiltration, n(%)	NA	3(5)

NA: Not applicable* defined histopathologic features are giant cells, predominantly mononuclear cell infiltration, and fragmentation in the internal elastic lamina for definitive vasculitis

Conclusion: Even giant cells were reported less in our study, updated histopathological definitions for GCA seem an excellent option to diagnose vasculitis definitively.

REFERENCES:

[1] Ponte, C., et al., *2022 American College of Rheumatology/EULAR classification criteria for giant cell arteritis.* Ann Rheum Dis, 2022. **81**(12): p. 1647-1653.

[2] Putman, M.S., et al., *Clinicopathologic Associations in a Large International Cohort of Patients With Giant Cell Arteritis.* Arthritis Care Res (Hoboken), 2022. **74**(6): p. 1013-1018.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.1935

AB0757 TAKAYASU DISEASE: ABOUT 109 CASES

Keywords: Vasculitis

H. Khibri[1], F. Ibourk El Idrissi[1], A. Meghraoui[1], M. Obtel[2], C. Yasmina[1], N. Mouatassim[1], W. Ammouri[1], M. Maamar[1], H. Harmouche[1], M. Adnaoui[1], Z. Tazi Mezalek[1]. [1]*Souissi Rabat, Department of Internal Medicine-Clinical Hematology, Rabat, Morocco*; [2]*Faculty of Medicine And Pharmacy of Rabat, Clinical Epidemiology Service, Rabat, Morocco*

Background: TAKAYASU disease is an inflammatory vasculitis of the means and large caliber, which affects th aorta and its main branches, and which leads to the formation of arterial stenosis, thromboses and aneurysms. Touching preferably young women, it may be responsible for complications severe visceral events that may be life-threatening.

Methods: We conducted a 38-year, single-centric retrospective study (1984 and 2022) in patients followed for TAKAYASU vasculitis at the department of internal medicine and the department of vascular surgery of the Ibn Sina Hospital in Rabat. Statistical data were analyzed using SPSS 20. 0 software and KHI- DEUX analytical test.

Results: We collected 109 files. The sex ratio (F/M) was 7. 3 (96 women/ 13 men). 11. 92% of patients were male. The mean age was 34. 8 ±11. 9 (12 – 62 years). Patients who had juvenile takayasu diagnosed before 20 years of age were 11 (10%) and patients who had late-diagnosed takayasu to over 50 years of age were 14 (12. 88%). HTA was present in 44 (40. 7%) of patients at diagnosis, 11 (10. 1) of patients were taking oral contraceptives. Inflammatory syndrome was associated in 72 (66. 1%) with no statistically significant difference with a P=0. 6. Vascular symptomatology was present in 103 (95. 4%) of the cases o vascular murmur (66. 1%), pulse suppression (62. 4%), intermittent claudication (49. 5%) and ischemia (10. 1%). Extravascular symptoms were present in 47. 6% of the patients dominated by inflammatory arthralgia (18. 3%). Only one patient had asymptomatic TAKAYASU vasculitis discovered by chance during ultrasound examination for a thyroid nodule. Cardiac involvement occurred in 36 (33%) of patients and consisted mainly of valvulopathy (20. 2%) and cardiomyopathy (17. 4%). Central neurological involvement was present in 17 patients. (15. 6%) of patients with complicated HAI in 13 patients. Renal impairment was present in 35 patients (32. 11%). Ophthalmologic involvement in 26 (23. 9%) of patients was mainly represented by retinal vasculitis and optic nerve involvement. In addition, 10 patients had 24 pregnancies, 4 patients had preeclampsia, we recorded 9 abortions and half of our patients had full term pregnancies. The type of injury in our series was mainly stenosis and was found in 73 (67%) of cases. Occlusion was recovered in 21 (19. 3%) patients. Thrombosis was found in 26 (23. 9%) of patients and aneurysms in 19 (17. 4%) of patients. TAKAYASU vasculitis was Type I in 42 (38. 5%) patients, followed by Type V in 39 (35. 8%). Type IIa was present in 7 patients (6. 4%), type IIb in 4 patients (3. 7%), type III in 2 patients (1. 8%), and type IV in 14 patients (12. 8%). Most patients 104 (95. 4%) received corticosteroids and 77 (70. 6%) received immunosuppressive therapy including one on mycophenolate mofetil. 2 patients received anti-TNF therapy (adalimumab) and 1 patient received Tocilizumab. At the surgical level; 9 (8. 3%) of patients had angioplasty; A further 6 (8. 3%) underwent cardiac surgery (5 aortic valve replacement and closed-heart commissurotomy) and 15 (13. 8%) had vascular surgery. The outcome was favourable in the majority of patients. Late relapses > 6 months were reported in 25 (23. 1%) patients. There was only one death from global heart failure. We analyzed several associations such as vascular and cardiac disease, vascular and neurological disease. None returned significant with P ranging from 0. 3 to 1.

Conclusion: The results of our study are consistent with the literature and confirm the predominance of women and the stenosing nature of this vasculitis. Early diagnosis and management of the disease significantly improves the progression profile of the disease.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.2597

AB0758 TAKAYASU DISEASE IN JUVENILE FORM: ABOUT 11 CASES

Keywords: Vasculitis

F. Ibourk El Idrissi[1], H. Khibri[1], A. Meghraoui[1], M. Obtel[2], C. Yasmina[1], N. Mouatassim[1], W. Ammouri[1], M. Maamar[1], H. Harmouche[1], M. Adnaoui[1], Z. Tazi Mezalek[1]. [1]*Souissi, Department of Internal Medicine-Clinical Hematology, Rabat, Morocco*; [2]*Faculty of Medicine And Pharmacy of Rabat, Clinical Epidemiology Service, Rabat, Morocco*

Background: Takayasu disease is a non-specific inflammatory vasculitis of the large and medium caliber arteries occurring during the 2nd or 3rd decade. Attachment before the age of 20 is rare.

Methods: This is a retrospective descriptive study including patients with aged less than 20 years with Takayasu disease out of a series of 109 patients between 1984 and 2022 in a department of internal medicine and vascular surgery at the CHU INB SINA of Rabat.

Results: We identified 11 cases of patients under 20 years of age with a Takayasu disease with a sex ratio of 1 man to 2. 6 woman (8 women/ 3 men) The mean age of patients was 17 years ±2. 8 (12 - 20 years). (45. 5%) had hypertension at diagnosis, 10 patients (90. 9%) had symptomatology type of vascular murmur (54. 5. %), pulse suppression (63. 6%), lameness. intermittent (36. 4%), no ischemia (23. 1%) and one patient had extravascular: headache, fever, altered general condition... Inflammatory syndrome was present at diagnosis in 8 of our patients (72. 7%) Aortic involvement was found in 7 patients (63. 63%) predominantly due to abdominal aorta (6 patients). We identified 4 cases (36. 36. %) of arterial damage. 3 cases of cerebral arteries (27. 27%). The most common arterial disorders stenosis (72. 7%), thickening (54. 5%), thrombosis (9. 1%) and aneurysm (9. 1%). 6 patients (54. 54%) had heart disease as part of the study. Takayasu disease dominated by cardiomyopathies (4 cases), 2 cases of valvulopathy, and 1 only case of pericarditis. Associated in two cases with rhythm disturbances. 3 patients

Ann Rheum Dis: first published as 10.1136/annrheumdis-2023-eular.1935 on 30 May 2023. Downloaded from http://ard.bmj.com/ on September 29, 2024 at Gazi Universitesi. Protected by copyright.