AB0561 B CELL THERAPY IN REFRACTORY/ RELAPSED ANCA ASSOCIATED VASCULITIS- A SINGLE CENTRE PROSPECTIVE OBSERVATIONAL STUDY

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Background: Rituximab (Rtx), a novel biological, having B cell depletion mechanism is an anti- CD 20 antibody and is found to be useful in patients of ANCA associated vasculitis. In AAV the disease activity correlates with increased circulating B cells. Rituximab has been found to be useful in depleting these B cells. According to the RAVE study, Rituximab was shown to be non-inferior to Cyclophosphamide in inducing remission. It also showed that the regimen (Rtx) may be superior to the standard regimen of Cyclophosphamide and glucocorticoids for remission induction in severe relapsing ANCA-associated vasculitis.
In our study, B cell therapy was given in those patients only who had persistent disease activity or relapse.
Objectives: To assess response of Rtx in relapsed /refractory cases of AAV and show that it is a good therapeutic stratergy in such cases.
Methods: In our cohort there were 49 patients of ANCA associated vasculitis, diagnosed by clinical and serological criteria, (by both ELISA and IFA) classified according to ACR criteria and supported, wherever possible, by biopsy. In this prospective study, patients were seen during January 2012 to January 2017. A total of 15 patients received Rituximab for various reasons. Rituximab (Rtx) was given as 1 gram infusion on day 1 and day 15 as induction therapy and subsequently 6 monthly maintenance doses of 500 mg were administered. No other immunosuppression other than steroids were given.
Results: Median follow up was 22 months. All patients had recieved Cyclophosphamide (median dose 6 grams) and 1mg/kg glucorticoids at onset. Among the patients who received Rituximab, all had anti PR3 antibody positive & all were GPA clinically. 14 patients (93.33%) had lung involvement, renal involvement was seen in 7 (46.6%) patients, 13 (86.6%) patients had upper respiratory tract involvement, 6 (40%) had ophthalmic involvement. Nervous system involvement was seen in 5 (33.3%) and myocarditis was seen in 3 (20%) each. 3 (20%) patients had gangrene.
Indications for receiving Rtx were heterogenous. It was given for involvement of lung, renal, ophthalmic, upper respiratory and nervous system in 6 (40%), 3 (20%), 3 (20%), 1 (6.66%) and 1 (6.66%) respectively. Whereas 1 (6.66%) patient received Rtx for persistent disease activity.
12 out of 15 patients (80%) achieved remission at mean follow up of 3 months while one achieved at 6 months follow up & all maintained continued remission. 1 patient was due for 3-month follow up. 1 patient died due to lung infection during the course. 4 patients had permanent morbidities/organ damage which they already had before starting Rtx. Only one patient had infusion reaction at the end of 1st induction however she remained in remission after the first dose itself.
Conclusions: 86.6% patients achieved remission after Rtx and remained in continous remission at median follow up of 22 months. Rtx is a very good therapeutic strategy for refractory/relapsed especially PR3+ AAV also it can be used as a maintenance regimen for long term.
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AB0562 CLASSIFICATION OF ANCA ASSOCIATED VASCULITIS BASED ON PR3 AND MPO SEROLOGY & THEIR OUTCOME: A SINGLE CENTRE PROSPECTIVE STUDY

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Background: It is often difficult to classify small vessel vasculitis, especially AAV, as Granulomatosis polyangitis [GPA], Microscopic polyangitis [MPA], Eosinophilic granulomatosis polyangitis [EGPA] & Idiopathic cresentic glomerulonephritis. But with the discovery of ANCA, rheumatologists divide this as ANCA positive or negative vasculitis.
Objectives: To classify AAV as anti-proteinase 3 (PR3) antibody+ or anti-myeloperoxidase (MPO) antibody + & compare their clinical presentation & outcome.
Methods: 49 patients were included in our study from August 2011 till January 2017. Patients were classified according to PR3 and MPO serology [based on ELISA].
Results: Median follow up was 18 months. PR3 + were 38 and 11 patients were MPO+. GPA was significantly higher in PR3 Group vs MPO group [36 (94.7%) vs 1 (9.1%) p<0.0001*] while MPA was significantly lower in PR3 group as compared to MPO (2 [5.3%] vs 5 [45.45%] p=0.001*). All EGPAs were MP0+ (4 [36.35%]). 48 fulfilled ACR clinical criteria for GPA/MPA or EGPA. 1 patient with arteritic anterior ischemic optic neuropathy without any other major organ involvement had significantly higher titres of MPO antibodies & was sorted as unclassified AAV. None were idiopathic crescentic glomerulonephritis in our cohort. 18 were biopsy proven [15 PR3+vs 3 MPO+]. Lung involvement was significantly higher in PR3 group than MPO group (32 [84.2%] vs 6 [54.5%] p=0.037*).Kidney involvement was also more in PR3 group but was not statistically significant (20 [52.6%] vs 4 [36.4%] p=0.341). Upper respiratory involvement was significantly higher in PR3 group (26 [68.4%] vs 3 [27.3%] p=0.014*).
Comparision between manifestations of ophthalmic, cardiac, peripheral vascular system & nervous systems of PR3+ & MPO+ groups was not statistically significant.
Complete remission without permanent organ damage was seen in 16 (42%) vs 6 (54.5%) in PR3 and MPO groups respectively (p=0.465). Frequency of relapse/refractory disease, though higher in PR3 group, was not statistically significant (PR3 vs MPO, 10 [26.3%] vs 1 [9.1%] p=0.228). Rates of morbidity & mortality were not significant statistically between PR3 & MPO groups (11 [28.9%] vs 2 [18.2%] p=0.476 & 3 [7.9%] vs 1 [9.1%] p=0.899 respectively). Similar comparisons were made between those who were classified clinically as GPA, MPA & EGPA with respect to remission, relapse, morbidity and mortality. All EGPAs achieved remission. Comparison between groups when divided as GPA & PR3 and MPA & MPO did not show statistical significance. 15 patients (all clinically GPA & PR3+) of the cohort [39.5%] received rituximab for relapse/refractory disease during/after initial induction therapy with cyclophosphamide & steroids.
Conclusions: In this study, we did not find any advantage of clinical classification over serological. Wrongly diagnosing patients when disease is still evolving & inter-clinician bias are eliminated when classifying patients according to serology. Classification as PR3 & MPO is simpler and universal.
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AB0563 RITUXIMAB IN PATIENTS WITH TAKAYASU ARTERITIS: A SEVEN PATIENTS EXPERIENCE

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Background: Takayasu arteritis (TAK) is a large vessel vasculitis involving the aorta and its major branches in patients younger than 40 years. Glucocorticoids (GCs) are the mainstay of treatment for TAK, but relapses and GC dependence are seen in more than two-thirds of patients. Increasing evidence supports a role for B cells in the pathogenesis of TAK. Circulating plasmablasts and memory B cells are increased, while naive B cells are decreased in patients with active TAK as compared with inactive and control patients [1]. These findings suggest a potential role for B cell depleting therapy in TAK.
Objectives: Our aim was to assess the efficacy and safety of Rituximab (RTX) in a series of 7 patients with TAK.
Methods: We conducted an open-label study on 7 TAK patients (5 followed prospectively, 2 retrospective cases) treated with RTX. All patients satisfied the American college of Rheumatology classification criteria for TAK. Six of the 7 patients had a disease refractory to high dose GCs and conventional immunosuppressive (IS) and/or biologic agents. One newly diagnosed, treatment naïve TAK patient refused GCs and received RTX alone. RTX was administered according to rheumatoid arthritis scheme (2 infusions of 1.000 mg, 15 days apart). Clinical evaluation, laboratory tests (full blood count, ESR, CRP) and imaging modalities (CTA or MRA, and PET/CT) were performed at first RTX administration and every 6 months thereafter. Disease activity was assessed using Kerr index. Radiographic disease progression was defined as new or worsening lesions at follow-up CTA or MRA. PET/CT was considered positive for active disease if two or more large vessels showed grade 2 FDG uptake or higher.
Results: Seven patients (6 females) were included in the study. Mean (SD) age was 32.4 (±16.1) years. At first RTX administration, all patients had active disease

Table 1. Parameters of disease activity before and after Rituximab treatment

Case	Age/Sex	Disease duration (yr)	Previous therapy	ESR/CRP at first RTX (mm/h, mg/dl)	PDN dose at first RTX (mg/day)	Concomitant IS therapy	RTX cycles	ESR/CRP 6 months after last RTX (mm/h, mg/dl)	Imaging (CTA/MRA) 6 months after last RTX	PET/CT 6 months after last RTX	Kerr index 6 months after last RTX	Outcome 6 months after last RTX	PDN 6 months after last RTX	Therapeutic changes	Follow-up (m)
1	20/F	2y	MTX	38/6.2	25g	MTX 20 mg weekly	2g	6/4.7	No disease progression	Positive	Positive	Active disease	5g	Stop RTX, start ADA	12g
2	32/F	0m	None	48/4.6	0m	None	1g	6/3.4	Disease progression	Positive	Positive	Disease progression	12.5g	Stop RTX, start PDN+TCZ	12g
3	21/F	1y	MMF	12/2.7	50g	MMF 2 gr day	1g	16/2.8	Disease progression	Positive	Positive	Disease progression	5g	Stop RTX, start ADA	12g
4	60/M	20y	MTX, MMF, ADA, IFX	66/2.0	25g	MMF 2 gr day	2g	18/0.5	No disease progression	Negative	Negative	Remission	7.5g	PDN tapering, No changes	36g
5	19/F	3y	MTX, AZA, TCZ, IFX, ADA	98/11.5	50g	None	2g	78/4.0	Disease progression	Positive	Positive	Disease progression	10.75g	Stop RTX, start MMF	24g
6	22/F	1y	AZA, MTX	MD/4.5	10g	None	1g	MD/0.3	No disease progression	ND	Negative	Remission	2.5g	No changes	72g
7	54/F	3y	MTX, AZA, TCZ	MD/1.10	15g	None	3g	MD/0.20	No disease progression	ND	Negative	Remission	10g	PDN tapering, No changes	60g

ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; RTX = rituximab; PDN = prednisone; IS = immunosuppressive; CTA = Computerized Tomography Angiography; MRA = Magnetic Resonance Angiography; PET/CT = positron emission tomography/computerized tomography; MTX = methotrexate; ADA = adalimumab; TCZ = tocilizumab; MMF = mycophenolate mofetil; IFX = infliximab; AZA = azathioprine; MD = missing data; ND = not done.