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Original Article

Course and Prognosis of Primary Systemic Vasculitidies (PSV) with Renal Lesions

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Abstract

Background. Vasculitidies represents heterogeneous group of diseases characterised with the destructive inflammation in and around blood vessel wall which can cause ischemia of tissues and organs supplied by the affected vessels.

Methods. We conducted prospective-retrospective study in which we included 62 patients. Thirty two patients have had primary systemic vasculitis (PSV) with renal lesions. Sixteen of them were ANCA positive and 16 were ANCA negative. We also followed 30 patients with PSV without renal lesions. The follow up of patients was two years from the time of diagnosis of PSV. We followed serum creatinine, creatinine clearence, 24h-proteinuria, as well as erythorocyte sedimentation rate (ESR), C-reactive protein (CRP) and fibrinogen. We also scored the activity of vasculitis with Birmingham Vasculitis Activity Score (BVAS). The diagnosis of PSV was established on the basis of Chapell Hill international consensus criteria.

Results. After two years of follow up patients with PSV without renal lesions showed better course and prognosis than patients with PSV with renal lesions. This was largely due to statistically lower number of affected organs in the former group. We didn`t found any significant difference in the course and prognosis beetween ANCA positive and ANCA negative patients with vasculitis and renal lesions. Patients with PSV and renal lesions that had more than 50% of crescents on kidney biopsy specimens had significantly worse kidney function at the begining and at the end of follow up, as well as a higher value of persistent activity index (BVAS.2) of vasculitis at the end of follow up comparing with the patients who had less than 50% crescents or no crescents at all at the kidney biopsy material. Patients with P-ANCA positive vasculitidies have had significantly higher degree of BVAS.1 at the begining of follow up and significantly higher degree of BVAS.2 at the end of follow up.

Conclusions. The prognosis of vasculitis is largely connected with the number of the affected organs with the vasculitis process. Percutaneous kidney biopsy have tremendous prognostic importance in the vasculitis with renal lesions. Patients with pANCA positive vasculitidies had higher levels of activity according to BVAS probably because of the smoldering type of their disease.

Key words: glomerulonephritis, kidney diseases, prognosis, severity of illness index, vasculitis

Introduction

Vasculitidies represents heterogeneous group of diseases characterised with destructive inflammation in and around blood vessel walls. As a consequence of this inflammatory process lumen of the blood vessels can become compromised which can lead to ishemia of the dependent tissues and/or organs. Etiopathogenesis of different forms of vasculitides is incompletely understood with combined effects of genetic and environmental factors. Clinical presentation of vasculitidies varies, in large part due to the diameter of the involved blood vessel. Respectively, involvement of the large blood vessel can be presented with claudication of the extremities, murmurs over the involved vessel, aortic dilatation, assimetric blood pressure, etc.; involvement of the medium sized blood vessels can be presented with skin nodules, skin ulcerations, mononeuritis multiplex, gangrene of the digits, while involvement of the small blood vessels (arterioles, capilaries and venules) can be presented with purpura, glomerulonephritis, alveolar hemorrhage, uveitis, etc. Prognosis of the vasculitidies depends on the type of vasculitis, the spectrum of the involved organs, the time elapsed from the first simptoms of the disease to the correct diagnosis and on the treatment. Nowadays, the treatment pallette is very wide, with corticosteroids and cyclophospha-mide that serves as a standard immunosupressive therapy for more than 30 years [1,2] through drugs like azatioprine and methotrexate to the whole new generation of drugs that first found their place in solid organ transplantation and hematology/oncology such as mycophenolat mofetil, etanercept [3], deoxipergualin [4] and rituximab [5-7].
The aims of the study were to determine difference between the course and prognosis of patients with PSV with renal lesions and those patients with PSV without renal lesions, also to determine difference in course and prognosis of ANCA positive and ANCA negative patients with PSV and renal lesions, and finally to explore the difference between the two groups of patients according to type of ANCA (pANCA or cANCA).

Patients and methods

We conducted prospective-retrospective study which included 62 patients. Thirty two patients (group 1) with primary systemic vasculitis (PSV) with renal lesions, 16

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ANCA positive (8 pANCA positive and 8 cANCA positive) and 16 ANCA negative patients, and 30 patients with PSV without renal lesions (group 2). The study included patients that were treated at the Clinical center in Novi Sad between year 2000 and 2006 and the diagnosis of PSV was established according to Chapel Hill consensus conference criteria [8]. In the group of patients with PSV with renal lesions (n=32) 8 patients were diagnosed as Wegener`s granulomatosis (WG), 11 as microscopic polyangiitis (MPA), 5 patients were diagnosed as poliarteritis nodosa (PN), 4 patients as kryoglobulinemic vasulitis (KV), 3 patients as Henoch-Schönlein purpura (HSP) and one patient was diagnosed as Churg-Strauss syndrome (CSS). In the group of patients with PSV without renal lesions (n=30) 15 patients were diagnosed as leokocytoclastic vasculitis (LCKV), 6 patients were diagnosed as having KV, and 3 patients were diagnosed as having HSP, gigantocellular vasculitis (GCV) and vasculitis of the central nervous system, respectively. The follow up of the patients was two years from the time of diagnosis.

We have followed serum creatinine, creatinine clearance, 24h-proteinuria, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and fibrinogen that was measured with standard methods. Percutaneous needle biopsy of the kidney was performed in the whole group (n=32) with renal lesions at the time of admission to our institution and established clinically visible renal impairment. The obtained material was examined with light and immunofluorescent microscopy. We also used Birmingham Vasculitis Activity Score (BVAS) and its modification for Wegener`s granulomatosis to evaluate activity of the vasculitis in every patient [9,10]. For the determination of ANCA we used "Euroimmun-Medizinische Labordiagnostika" AG commercial kits with starting titer of mentioned antibodies of 1:10.

Observed parameters were continous or discontinous variables. The categorisations of the variables are presented through average values and standard deviations. Distribution of the patients was presented with Student`s T-test. Fisher`s test was used for evaluation of the intensities of observed variables.

Results

In the overall structure of patients we have observed a slight preponderance of female gender (58,1% vs. 41,9%) that was largely due to the higher incidence of LCKV in females of our population. There was no singificant difference notified beetween the two groups according to the age of patients and the duration of simptoms of the disease before the diagnosis was established (Table 1).

Table 1. Average age of patients and average duration of simptoms before the establishment of diagnosis of vasculitis

	Nephritis + N=32	**T**	**Nephritis – N=30**
Age of patients	61,91 ± 9,8	NS	56,33 ± 15,01
Days before the diagnosis	67,31 ± 86,49	NS	38 ± 48,99

There was a significant difference in the number of the affected organs beetween the two groups favouring the group with PSV and renal lesions (4,19 ± 1,2 vs 1,3 ± 0,53; p<0,01). At the begining of our study we observed significant difference beetween the two mentioned groups (p<0,01) in all of the parameters that were followed except fibrinogen as well as at the end of the study. During the two-year course of the study we registered three deaths in the first group, two because of the cardiac arrest and one because of the acute fulminant hepatitis, while three patient in the first group commenced with chronic hemodyalisis program and none of the patients in the second group. We didn`t find any statistically significant difference beetween the subgroups with ANCA positive and ANCA negative PSV with renal lesions. We conducted a percutaneous renal biopsy in the whole group of 32 patients with PSV and renal lesions. In 9 patients we have founded more than 50% of crescents at the examined material and this group of patients had signifficantly worse (p<0,01) kidney function at the begining as well as at the end of the study compared to the group of 23 patients with less than 50% crescents or without crescent formation at all.

Finally, we evaluated the group of ANCA positive vasculitis with renal lesions (n=16) which comprised of 8 pANCA positive and 8 cANCA positive patients. We found statistically significant difference beetween these groups in BVAS.1 and BVAS.2 at the begining of the study and in BVAS.2 at the end of the study. Patients with pANCA positive vasculitidies (7 with MPA and 1 with CSS) had more active disease at the aforementioned stages than patients with cANCA positive vasculitis (all with WG) (Table 2).

Table 2. Average values and standard deviations of observed parameters in groups of c-ANCA and p-ANCA positive patients at the end of the study

	p-ANCA N=8	**T**	**c-ANCA N=8**
Creatinine	249,85 ± 216,44	NS	312,25 ± 368,56
Creatinine clearance	30,42 ± 23,59	NS	49,55 ± 39,34
24h-proteinuria	645 ± 576,16	NS	483,5 ± 551,35
ESR	40,42 ± 40,84	NS	35 ± 25,41
Fibrinogen	4,38 ± 1,58	NS	3,62 ± 1,23
CRP	10,56 ± 17	NS	7,02 ± 7,5
BVAS.1	6,29 ± 8,77	NS	2,75 ± 4,4
BVAS.2	9,14 ± 2,85	<0,01	1,25 ± 0,89

Discussion

Primary systemic vasculitidies represents heterogeneous group of diseases with variable prognosis. Prognosis of PSV is quite variable with some types of vasculitidies that can completely resolve (LCKV, HSP) while some types of vasculitidies can be coupled with a serious morbidity and mortality (MPA, WG, vasculitis of the CNS). In majority of the published studies, tipical vasculitis patients are in their fifties and sixties, like in our study. Exception to this rule are patients with HSP and Kawasaki disease that are more prevalent at younger ages. Relatively long time that have elapsed from the first simptoms to the correct diagnosis can be associated with the longlasting existence of general

complaints (malaise, fatigue, loss of apetite and body weight) that sometimes make the definite diagnosis hard to establish. Statistically significant difference in the parameters of kidney function beetween the two basic groups of patients at the begining and at the end of the study was straightforward because first group was comprised of patients with PSV with renal lesions and second one of patients with PSV without renal lesions. Significant differences beetween these two groups according to the acute phase reactants and BVAS can be explained with a significantly higher number of the affected organs in the group with PSV and renal lesions in contrast to the group with PSV without renal lesions (4,19 ± 1,2 vs 1,3 ± 0,53; p<0,01). Worse prognosis of the patients with PSV and renal lesions is evident since three patients died and also three patients commenced with chronic hemodyalisis program in that particular group of patients.

Comparing the two subgroups of patients with PSV and renal lesions, first one with ANCA positive vasculitis (n=16) and second one with ANCA negative vasculitis [16], we have found statistically significant difference according to the affection of the lungs (p<0,01) and ENT region (p<0,001) in the favour of the group with ANCA positive vasculitis. There was no significant difference in the parameters of kidney function, acute phase reactants and BVAS beetween those subgroups and no significant difference in the prognosis of these patients.

The statistically significant difference in renal function (p<0,01) observed beetween the group of patients with more than 50% of crescent formation (n=9) versus the group of patients with less than 50% of crescent material or without crescents (n=23) clearly demonstrate the prognostic relevance of the percutaneous kidney biopsy.

Finally, we compared the two subgroup of patients with ANCA positive vasculitis, 8 pANCA positive and 8 cANCA positive. We didn`t found any significant difference according to the parameters of kidney function and acute phase reactants but we observed significant difference in persistent activity (BVAS.2) of the vasculitis in favour of the pANCA positive vasculitis patients. It can be explained with higher average number of affected organs in this group and also with the study of Serra *et al*. [11] about smoldering, chronically active vasculitis.

Conclusion

The prognosis of vasculitis is largely connected with the number of the affected organs with the vasculitis process. Percutaneous kidney biopsy have tremendous prognostic importance in the vasculitis with renal lesions. Patients with pANCA positive vasculitidies had higher levels of activity according to BVAS probably because of the smoldering type of their disease.

Conflict of interest statement. None declared.

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