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Renal comorbidity in psoriatic arthritis patients

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ABSTRACT
Introduction. Psoriatic arthritis (PA) is a multi-system inflammatory disorder that involves both musculoskeletal structures (joints, enthesis, tendons) and the skin and nails (psoriasis). Clinical manifestations can be varied from clinically asymptomatic disease to arthritis mutilans and invalidating forms.
Purpose. Identification of renal disease in patients with psoriatic arthritis depending on the degree of activity and severity of skin and joint disease.
Material and Methods. We conducted a retrospective study of 89 patients diagnosed with psoriatic arthritis in the Rheumatology Department of Clinical Emergency Hospital "Sf. Andrei" in Constanta. We collected demographic and behavioural data (age, sex, ethnicity, smoking), clinical and biological elements of joint and skin disease activity (number of painful and swollen joints, joint pain score - VAS, PASI score, ESR, CRP) and evaluation of renal function (serum creatinine, serum uric acid, urinalysis examination for proteinuria and hematuria). Chronic kidney disease was staged by calculating the value of glomerular filtration rate (GFR) with CKD-EPI 2009 equation.
Results. 49 patients have full screening of renal function, especially in disease onset or in case of therapy switch. Proteinuria was found in a significant percentage of patients (32.65%), vary widely between 10-500 mg/dL. Chronic kidney disease (CKD) was commonly found in our patients (42.85%), mostly in women (66.6%). Most cases of CKD were in stage 2 (12.4%). We observed a significant correlation between age and levels of serum creatinine ($p = 0.041$), caucasians developing more frequently CKD ($p < 0.0001$). The presence of skin psoriasis did not interfere with renal function decline in PA patients, but its severity, measured with PASI score, was correlated with cronic kidney failure stages ($p = 0.05$) and proteinuria ($p = 0.044$). The severity of joint pain (TJC, VAS) is directly related to kidney disease ($p < 0.0001$, respectively $p = 0.05$). The majority of patients with extensive joint erosions also had renal impairment (p = NS) and it can be seen a direct correlation between erosive joint disease and serum creatinine ($p = 0.029$).
Conclusions: Both the severity of psoriasis and articular disease may be involved in worsening of renal function, probably due to the chronic systemic inflammation and to an aggressive therapy imposed by the disease evolution.

Keywords: psoriatic arthritis, renal impairment, proteinuria, chronic kidney disease, inflammation

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Introduction

Psoriatic arthritis (PA) is a chronic multi-system inflammatory disorder, part of the seronegative spondylarthropathies group, that occur in 10-30% of patients with psoriasis. The disease may involves variously joints, enthesis, tendons, nails and skin sometimes with an severe and deforming progression.

The most common comorbidities described in the literature are the cardiovascular, metabolic, ophthalmologic and psychological, but the risk of malignancy, osteoporosis, renal impairment, neurological or pulmonary impairment is equally

important, those being less studied and with contradictory data[1]. Comorbid diseases and extra-articular manifestations can deeply influence the quality of life and further therapeutic options in this patient group.

The involvement of autoimmunity and chronic inflammatory process via T cell activation can cause structural damage in the glomerular basement membrane and renal capillaries which evolves with proteinuria, hematuria and/or increase of serum creatinine.

Microalbuminuria is considered by nephrologists a marker of glomerular disorder, the main glomerulopathies present in patients with PA being IgA nephropathy, secondary renal amyloidosis, membranous and membranous-proliferative glomerulonephritis. PA is associated with systemic atherosclerosis, hyperuricemia being considered a marker for subclinical atherosclerosis[2]. Some studies have found a direct relationship between hyperuricemia, hypercholesterolemia and kidney damage[3].

The reported prevalence in literature on urinary abnormalities is found in 0.53-23,3% of the pacients (4-6), depending on the criteria used for identification. GRAPPA (Group of Research and Assessment of Psoriasis and Psoriatic Arthritis) recently published a report which stated that 16% of seronegative arthritis patients, including PA, suffer a decline in glomerular filtration rate, similar percentage also found in rheumatoid arthritis (19%)[7].

Alenius has noticed a correlation between the decline of renal function and / or presence of proteinuria and patient age, duration and degree of activity of joint disease[6]. Other factors involved in development of renal lesions are the nephrotoxicity of NSAIDs and DMARDs[8] and the severity of psoriasis - measured according to PASI (Psoriasis Area and Severity Index) score[9,10].

In the current study we evaluated the prevalence and types of changes in renal function in psoriatic arthritis patients, in relation to the severity of joint and skin damage, in order to determine the impact of an aggressive joint disease on kidney function.

Material and method

We performed a retrospective study that included 89 patients diagnosed with psoriatic arthritis - according to CASPAR (Classification Criteria for Psoriatic Arthritis) criteria - between 2008-2012. Patients were assessed by rheumatologist in the Rheumatology Departament of Clinical Emergency Hospital "Sf Apostol Andrei" in Constanta. Exclusion criteria was: the presence of any type of urinary anomaly prior to PA diagnosis, concomitant autoimmune diseases which can cause kidney damage (SLE, hepatitis B, C, hemolytic uremic syndrome, multiple myeloma) or patients in a program for dialysis or kidney transplant.

Data was collected from the patients medical records and the database of the hospital integrated laboratory and aimed demographic and behavioral characters (age, sex, ethnicity, smoking, alcohol consumption), history for joint and skin disease duration, age at onset, family history of psoriasis / seronegative arthropathy.

We also noted the main elements of clinical examination at the time of that assessment: the psoriatic arthritis types, presence of skin psoriasis and/or nail psoriasis, PASI score, the presence of activity and severity degree of joint disease (number of painful and swollen joints, number of deformed and ankylosed joints, the score for articular pain - VAS, dactylitis, enthesitis, sacroiliitis) and functional status (HAQ, BASFI).

Laboratory data monitored biological inflammatory syndrome (ESR, CRP) and evaluation of renal function (serum creatinine, serum uric acid, urinalysis examination for proteinuria and hematuria, proteinuria/24 hours). We also noted radiological joint damage and kidney ultrasound where they were mentioned.

Chronic kidney disease was staged after the calculation of glomerular filtration rate with CKD-EPI 2009 on line formula (http://www.qxmd.com/calculate-online/nephrology/ckd-epi-egfr) which accurately stratify the degree of impairment, especially for high values of the eGFR (over 60 mL/

min/1.73 m2).

Two patients who had nephrotic syndrome benefited from renal biopsy, the collected specimens were analyzed by specific staining light microscopy and direct immunofluorescence.

Statistical analysis. We create a database using SPSS version 20 for Windows (SPSS Inc., Chicago, USA) with collected data. It has been calculated for nominal values mean ± standard deviation (SD). Comparing the data was made according to Mann-Withney equations for the independent variables and the Student t-test for means. Categorical variables were analyzed using Chi – square test, and Spearman test was used to correlate proteinuria, hematuria and PASI score. P coefficient value of< 0.05 was considered statistically significant.

Table I. The main demographic and clinical

Demographic, clinical and biological data for selected patients (n = 49)	
Age (mean ± SD) (years)	57.92 ± 9.704
Disease duration (mean ± SD) (years)	13.23 ± 11.444
Total male: female	10:27
Age of onset AP (mean ± SD) (years)	44.89 ± 13.345
Erosive disease (%, No cases)	69.4% ,34
SJC (mean ± SD, min/max)	1.57 ± 2.722 (0/13)
TJC(mean ± SD, min/max)	6.76 ± 7.821 (0/30)
VAS (mean ± SD, min/max)	54.78 ± 26.225 (0/100)
PASI (mean ± SD)	4.047 ± 5.116
ESR (mean ± SD) (mm/1h, min/max)	25.75 ± 14.057 (6/58)
CRP (mean ± SD) (mg/dl, min/max)	0.869 ± 0.936 (0.08 / 3.67)
Serum creatinine (mean±SD)(mg/dl,min/max)	0.934 ± 0.584 (0.4 / 3.8)
Urinary protein (mean ± SD) (mg / dl)	45.71 ± 106.610
eGFR (mean ± SD) mL/min/1.73 m2 (min /max)	101 787 ± 40 614 (28.6 / 184.9)
NSAIDs (%, no cases)	69.4% (n = 34)
Corticosteroids (% ,no cases)	16.3% (n = 8)
DMARDS (%, no cases)	75.5% (n = 37)
Biological therapy (%, no cases)	18.4% (n = 9)

Results

Of the entire group of patients with PA, only in 49 cases (mean age ± SD = 57.92 ± 9,704 years, ratio M: F = 1: 1.23) was performed a full screening of renal function, particularly in disease onset or in case of clinical worsening or treatment change. 4 patients (8.3%) were diagnosed with nephrolithiasis, and 21 (23.6%) with CKD.

Smokers and nonsmokers ratio was 9/39 (18.4% / 79.6%), but 17 patients in the group claim they are former smokers (not smoking for at least 6 months). 7 patients said that they consume alcohol daily , and 8 (16.3%) gave up alcohol for over 6 months at the time of assessement. Smoking or alcohol consumption did not affect renal disease in this group (p = NS).

Although the disease duration is relatively short (13.23 ± 11,444 years), more than half of the cases had an aggressive evolution and severe joint disease (69.4%) with the appearance of erosive radiological lesions (Table I).

PASI score, which estimates the severity of skin psoriasis, if it is present in more than 10% of the body surface, was 4.047 ± 5.116 on average, but 7 (14.9%) patients had a score ≥ 10 (severe psoriasis), noting a direct relationship with the renal disease (p = 0.048). Although the presence of cutaneous psoriasis not seems to influence renal function decline in patients with PA (p = NS), PASI score correlates with the degree of renal failure (p = 0.05), and other manifestations of renal impairment (p = 0.044). Nail psoriasis correlate well with CKD stages (p = 0.013) and with urinary sediment abnormalities (p <0.0001).

Almost a quarter of the investigated patients (23.6%) had varying degrees of chronic renal failure (Figure 1), although serum creatinine was apparently framed within normal limits (mean ± SD = 0.934 ± 0.584 mg / dL). Chronic kidney disease has particularly affected women (14 cases, 66.6%), most patients being in Stage 2 (8 cases, 52.38%) (Figure 1). Pearson test applied to compare the data obtained revealed a significant correlation between age and levels of creatinine (p = 0.041), caucasians developing CKD more frequent (p <0.0001). Moreover, we found that the number of painful joints (TJC), and pain intensity (VAS) are directly related to kidney disease (p <0.0001, p = 0.05) demonstrating the link between joint disease activity and kidney structures damage.

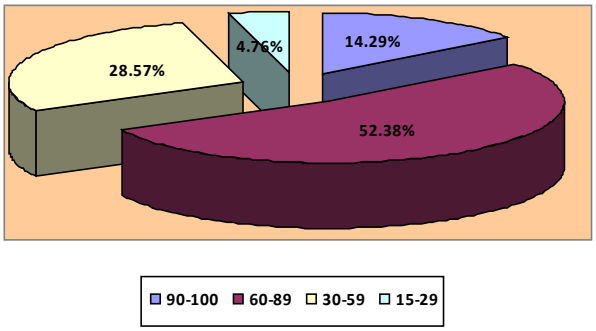

Figure 1. Distribution of chronic kidney disease based on eGFR (estimated Glomerular Filtration Rate) in patients with psoriatic arthritis

Severe impairment of peripheral joints, quantified by the number of deformed and ankylosing joints, are closely related with kidney disease (p = 0.001, respectively p = 0.002), possibly due to the persistent chronic inflammation and aggressive treatment. Still, we have not found an association between the mean severity scores calculated for peripheral joints (Health Assessment Questionnaire-HAQ) or axial segment (Bath Ankylosing Spondylitis Functional Index- BASFI) (p = NS).

Proteinuria was noted in 32.65% of evaluated cases, 4% (2 patients) with nephrotic syndrome had renal biopsy and required specific treatment. We noticed that proteinuria ≥ 30 mg/dL was associated only with age at onset of skin psoriasis (p = 0.042) and psoriasis duration (p = 0.014), without achieving correlation with other articular or cutaneous severity parameter.

It is notable that patients with urinary abnormalities and/or CKD had a mean PASI score higher (6,275 versus 4,723, p = 0.044), more swollen joints (3.5 versus 1.59, P = NS) and painful (12.25 versus 7.04, p <0.001) and increased levels of ESR (45,75mm/1h than 26,69 mm/1h, p <0.001) and CRP (1.86 mg/dL than 1.01 mg/dL, p = 0.032) compared with those without any change of renal impairment (Figure 2).

The majority of patients with extensive joint erosions had renal impairment (p = NS), obtaining a direct correlation between erosive joint disease and serum creatinine (p = 0.029). We noted that other joint activity parameters such as dactylitis, enthesitis and axial BASDAI activity score did not influence the renal function (p = NS).

Other comorbidities detected in our patients were: hypertension = 58.3% obesity = 51.1%, diabetes = 29.2% coronary artery disease= 22,9%, dyslipidemia = 52.1%, but none correlate with kidney failure.

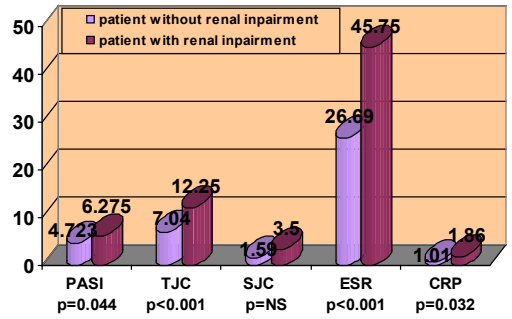

Figure 2. The relationship between kidney disease and inflammatory markers in selected patients (PASI=Psoriasis Area Severity Index; TJC= Tender Joint Count; SJC= Swollen Joint Count; ESR= Erythrocyte Sedimentation Rate; CRP= C Reactive Protein)

Discussions

Reviewing the literature in PubMed and Google Sholar we have found that this is the one of the few study that approach the kidney disease from double perspective of severity and activity of joint and skin manifestations in patients with PA.

Although most studies have focused on cardiovascular comorbidities in patients with PA, our data shows that a large number of patients have chronic kidney disease, most in the early, reversible stages. Renal inpairment (chronic hematuria, proteinuria, elevated serum creatinine) has a similar prevalence of cardio-vascular and metabolic extra-

articular manifestation in PA. These data are well above those reported in other studies. A Brazilian study performed on 271 patients with PA found a prevalence of 0.4% for renal impairment, most cases with mixed (axial and peripheral) clinical forms[11]. Another recently published study, conducted on 1230 american patients with psoriatic arthropathy with moderate-severe manifestation of cutaneous psoriasis reported a prevalence of 2%[12]. This difference may be due to the different assessment of renal function, the small number of patients studied and the absence, in a significant percentage of patients in our study, of renal function assessment.

Since CKD is currently considered an independent risk factor for cardiovascular complications[12,13], kidney disease in patients with PA should be detected and treated in the early stages, as it has been proposed for rheumatoid arthritis or lupus erythematosus[14] .

Our study revealed the major influence of chronic systemic inflammation (measured by TJC, SJC, VAS, ESR and CRP) on renal function in patients with psoriatic arthritis, witch was also reported by some previous studies[6,15]. Alenius showed that inflammatory serum markers (ESR and CRP) is a predictor for the occurrence of asymptomatic urinary abnormalities. Furthermore, severe joint disease appears to be an additional risk factor for the occurrence of kidney disease, possibly due to chronic inflammatory process and aggressive therapy used to reduce joint symptoms. This observation completes the data reported by a study conducted on a group of Asian patients with psoriasis who revealed that psoriatic arthritis can modify the evolution of CKD in psoriatic patients[17].

It is known the relationship between inflammation and accelerated atherosclerosis and thus may explain in part the association between arthritis and renal function changes.

The method used in our study was to determine proteinuria by analyzing urinalysis, but in values ≥ 500 miligrams/dL we determined proteinuria/24 hours. A significant percentage of patients in our study had varying degrees of proteinuria, two of theme being diagnosed with nephrotic syndrome and CKD. Although the presence of proteinuria does only correlate with duration and age at onset of skin psoriasis, this is a early marker for glomerular impairment and its regular monitoring is important in patients with arthritis and psoriasis.

It is difficult to compare our results with previous studies because of the methods of measuring the different biological parameters, calculating eGFR and patient profile. The limits of this study are the absence of proteinuria /24 hours in all patients and the absence of the albumin/creatinine ratio which would be assessed the microalbuminuria. However, it concluded that both CKD and proteinuria are found frequently in patients with psoriatic arthritis, especially in those with severe and active disease, linked in part to persistent chronic systemic inflammation. Based on these observations we can say that glomerular structural changes are common in patients with psoriatic arthritis and are exacerbated by aggressive evolution of skin lesions and joints damage.

Further larger studies are needed covering the whole spectrum of biological changes secondary to renal impairment to correctly assess the glomerular and tubulo-interstitial structural damage in this group of patients.

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