

INVESTIGATION OF BALCAN ENDEMIC NEPHROPATHY IN MEMBERS OF ENDEMIC FAMILIES IN THE ENDEMIC VILLAGE MORAVAC

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The village Moravac, situated on the left bank of the River South Morava, has been known as endemic area for fifty years. The highest prevalence of Balcan Endemic Nephropathy (BEN) was noted during the seventh and eight decade in the last century, and after that period, permanent decreasing has been shown. The present study involved fifty members of endemic families. In all investigated subjects, clinical observations included anamnesis, physical examinations and urinalysis. In twelve (24%) subjects, urinary abnormalities were proven (proteinuria, microhaematuria, leucocyturia). These subjects further underwent the additional functional and morphological examinations at the Clinic of Nephrology, Clinical Centre Nis. In 11 (22%) subjects, clinical examinations showed different forms of renal diseases, but BEN was proven in four (one of them suffered from BEN since 2004 and he was treated by haemodialyses, while the others were diagnosed during the investigation). Other renal diseases in the examined patients were: cystic kidney disease (6%), nephrolithiasis (4%), diabetic nephropathy (2%), obstructive nephropathy (4%) and tumours of kidney (2%). In our opinion, based on this investigation, BEN showed the rising tendency. Our retrograde study on the incidence of the upper urinary tract urothelial cancer in the endemic village Moravac showed the highest frequency, like BEN, in the seventh and eight decade in the last century. Despite encouraging results, further detailed and larger investigations are needed along the River South Morava, because a number of studies suggested lower progression and middle clinical course of disease, and also a rare appearance of the upper urinary tract cancer, which is why the patients seldom visit the health institutions, mostly in advanced stage of renal insufficiency. The aim of further investigations is to detect such subjects in the initial, early phase of disease, when prevention of progressive course and therapy are more successful. *Acta Medica Medianae* 2009;48(2):5-7.

Key words: *Balkanid Endemic Nephropathy, familial nephropathy*

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Introduction

Endemic nephropathy, because of its clinical and scientific importance, is the priority goal of research in medical sciences (1).

Modern study of immune-pathogenic mechanisms and changes in cellular and subcellular level will introduce us to important changes presented from numerous aspects of this important clinical entity (1,2).

Endemic nephropathy is a provisory name, even though there are many contemporary researches conducted in well-known nephrology centers which suggest that glomerular injury and not tubulointerstitial nephritis is the primary finding, as a group of authors postulates, without valid medical documentation based on the principles of modern research in nephrology (2).

Integrated scientific and professional researches will provide conditions for effective use of results in detection, prevention, treatment, and successful rehabilitation, with the aim of improving the quality of life and significant reduction in mortality of patients with endemic nephropathy (2,3).

Lately, in South Serbia, there has been a decrease in the occurrence of endemic nephropathy. However, the results of previous researches have shown that, at this stage, it could not be said with certainty that endemic nephropathy is in complete regression, primarily because during the routine tests, modern diagnostic methods have not been used (4-6).

In order to detect the initial phase of endemic nephropathy, it is necessary to do the kidney biopsy and other modern laboratory methods, which are performed only in large, modern centers. Exploration of the occurrence of initial phase of endemic nephropathy and tumor urothelium will be enabled by continuous monitoring of modern diagnostic methods (7). Endemic nephropathy starts much earlier than many authors think. Our youngest patient was 6 years old. Although the rural population is mainly affected, we had the oppo-

rtunity to detect cases of endemic nephropathy among the urban population (8).

The criteria proposed by some authors (Dani- lović, Stefanović et al.) (9) are not adequate for the research of the initial phase of endemic nephropathy; instead, it corresponds to its advanced phase, when the diagnosis can be established by means of epidemiological and clinical findings which do not differ from other glomerulopathies in their manifest renal failure (10).

The aim of this study was to examine the members of the families affected with endemic nephropathy, living in the hyperendemic village Moravac, 25 years after the last extensive field testing of this significant socio-medical disorder (8,11).

Examinees and methods

The village Moravac is situated on the left bank of the river South Morava. It has been known for Balkan Endemic Nephropathy (BEN) for the last five decades, which classifies this village among the first places where endemic nephropathy was discovered. The highest prevalence of disease was recorded during the seventh and eighth decade of last century, after which the period of decrease in the occurrence of endemic nephropathy followed. It should be emphasized that endemic nephropathy usually manifested periodically.

The ongoing field investigation included fifty members of the families in which there were several patients with BEN. The investigation was conducted in September in 2007 in the village Moravac. Besides taking detailed anamnesis, the investigation included physical examination and complete analysis of the first morning urine. For testing of urine, urinary strips were used (Chroma 10) with all parameters on the bar. In this way, the subjects with previously diagnosed renal and urinary tract diseases were registered, as well as the subjects with pathological findings in urine.

Supplemental clinical examination included 12 patients with pathological urine findings. It was conducted at the Nephrology Clinic, Niš, immediately after completion of field work. Clinical examination included complete hemogram, general urine analysis, assessment of functional kidney condition, determining creatinine clearance and analysis of macroscopic properties (echosonographic, radiology, etc.) (8,11,12).

In this way, in the subjects with pathological urinary findings, the partial diagnostics were completed.

Results and Discussion

Urinary pathological findings recorded during the field work are shown in Table 1. Out of 20 registered pathological findings, there were 12 findings in urine; one kind of pathological finding

was found in 6 examinees, two kinds of pathological findings were found in urine of four subjects; one kind of pathological finding was found in 6 examinees; two kinds of pathological findings were reported in 4 patients, while in two patients there were three pathologic findings in the urine within several days.

Proteinuria and microhaematuria were present in the majority of subjects and were the basic finding for additional clinical research. Besides low protein values in urine, microhaematuria is one of the most important parameters in detection of early stage of endemic nephropathy.

Overall prevalence of renal patients (diagnosed earlier and during this investigation) is shown in Table 2. Four of 50 examinees, i.e. 6% suffered from BEN. In one patient the disease was diagnosed earlier, so that from 2004 he was on hemodialysis. In others, the disease was discovered during this investigation. It is certain that relatively high percentage of BEN in this study does not reflect the high prevalence of patients in the general population, as derived from a very small selected sample of family members with BEN. Moreover, it points out, at least for now, that it appears in the manifest form periodically, which is often typical of endemic nephropathy. This finding is not in agreement with the findings of some other authors, but the number of authors who have opposite results is not small either (8,11,12).

The incidence of subjects suffering from endemic nephropathy on dialysis and subjects with UUT (upper urothelial tumors) for the past 50 years is given in Table 4. Their incidence in our material was highest in the seventh and eighth decades, although is not rare in younger patients (8,11,12).

Conclusion

Results of this study indicate a decreasing trends in BEN and UUT in the locality of the village Moravac. However, as numerous recently conducted studies have pointed to very slow progression and mild clinical course of BEN as well as rare occurrence of UUT in endemic areas, it should be expected to register a smaller number of patients with this disease coming to health centers. Therefore, monitoring of these diseases and insight into their actual frequency and distribution in the valley of the river South Morava will be possible only by conducting continuous fieldwork investigations. In this way, early detection, timely prevention and treatment would be enabled. In addition, in the recent years, higher frequency of UUT has been reported in the regions not having been known for BEN.

Finally, we should bear in mind that BEN and UUT still represent serious problems in some regions of our country.

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ISPITIVANJE ČLANOVA PORODICE SA BALKANSKOM ENDEMSKOM NEFROPATIJOM U SELU MORAVAC

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Selo Moravac, smešteno na levoj obali reke Južne Morave, po oboljevanju od Balkanske endemske nefropatije (BEN) poznato je skoro pet decenija. Najviša prevalencija oboljenja zabeležana je tokom sedme i osme decenije prošlog veka, dok period nakon toga karakteriše njeno kontinuirano opadanje. Aktuelnim terenskim istraživanjima obuhvaćeno je pedeset članova porodica u kojima je bilo obolelih od BEN. Ispitivanje je podrazumevalo anamnezu, fizikalni pregled i pregled prvog jutarnjeg urina. Kod 12 (24%) ispitanika registrovane su pojedine urinarne abnormalnosti (protienurija, glicozurija, mikrohematurija, leukociturija i pozitivni nitriti). Ove osobe su potom podvrgnute dopunskom ispitivanju na Klinici za nefrologiju Kliničkog centra u Nišu koje je obuhvatilo funkcionalne i morfološke metode dijagnostike. Kod 11 (22%) ispitanika terenskim i kliničkim ispitivanjima verifikovana su različita bubrežna oboljenja, a BEN kod njih četvero (jedan je dijagnostikovao ranije i od 2004. godine je na lečenju dijalizom, a troje su dijagnostikovani tokom ovih ispitivanja). Ostala oboljenja bubrega u ispitivanoj populaciji su: cistična bolest (6%), kalkuloza (4%), dijabetesna nefropatija (2%), opstruktivna nefropatija (4%) i tumor bubrega (2%). Na osnovu dobijenih rezultata može se zaključiti da i ovo istraživanje ukazuje na opadajući trend oboljevanja od BEN.

Retrospektivna studija incidence tumora gornjeg urotelijuma u Moravcu pokazuje njihovu najveću učestalost u sedmoj i osmoj deceniji prošlog veka, a potom trend opadanja, baš kao i u slučaju BEN.

Rezultati ovog istraživanja, iako ohrabruju, nameću potrebu opsežnijih terenskih istraživanja BEN u dolini Južne Morave, s obzirom na to da brojna istraživanja ukazuju na sporiju progresiju i blaži klinički tok BEN, a takođe i znatno ređu pojavu TGU (koji su često bili udruženi sa BEN), zbog čega se bolesnici ređe obraćaju zdravstvenim ustanovama, i to mahom u odmaklim stadijumima bubrežne slabosti. To bi bio jedini način da se ustanovi stvarna učestalost i raširenost ovih oboljenja na tim prostorima i da se otkriju u ranim stadijumima i tako omogućiti njihova adekvatna prevencija. *Acta Medica Medianae* 2009;48(2):5-7.

Ključne reči: balkanska endemska nefropatija, porodična nefropatija