

Sporadic Balkan Endemic Nephropathy (BEN) beyond the known regions of BEN

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Abstract

There is an very old opinion that we diagnose only most prominent BEN cases and miss latent and mild ones, that unrecognized BEN is possible in endemic villages and the number of such cases, their characteristics, and origin are unknown.

From 1955 to 1998 year we evaluated 1235 patients with histologically proven upper urothelial tumors, who underwent surgery. The diagnosis of sporadic BEN, was made after exclusion of other known nephropathies.

In the analyzed region, BEN was present in 170 of 808 settlements, and in 104 of them, 534 cases of UUT were reported. In 66 possible BEN settlements, there were no UUT cases. In the next 457 of 808 settlements (56.6%) neither BEN, or UUT were registered.

Sporadic BEN is an atypical, mild clinical variety of BEN, with simultaneous presence of UUT. Both sexes were equally affected, with the majority of patients in sixth and seventh decade of. The presence of sporadic BEN cases gives a possibility to speculate that the existence of BEN without familiar aggregations is possible elsewhere, not only in Balkans.

Key words: Balkan Endemic Nephropathy, familiar aggregations, distribution

Introduction

The idea of »ice berg phenomenon«, (1,2) suggesting that we diagnose only most prominent BEN cases and miss latent and mild ones, is very old. There is a similar opinion, that unrecognized BEN is possible in endemic villages (in »healthy« families), and in the neighborhood of BEN areas, (3) but the number of such cases, their characteristics, and origin are unknown. Territorial distribution of cases with upper urothelial tumors (UUT) in Serbia is much wider than distribution of BEN (4, 5), suggesting the similar distribution of BEN.

The diagnosis of sporadic BEN, presented as non-familial, non-endemic disease (6), is hardly possible with standard criteria, because two main criteria for the diagnosis are missing.

Patients and methods

From 1955 to 1998 year, 1235 patients with histologically proven UUT, underwent surgery. Data collected from

urologists and patients from Serbia came from the region of 31 communities with 808 settlements, with total of 1.162.225 inhabitants (5).

The diagnosis of sporadic BEN, was made in patients that underwent surgery because of UUT, after exclusion of other known nephropathies. The presence of UUT in all such cases, enables the diagnosis, knowing that other nephropathies followed by UUT (CHN, AN etc.) are extremely rare in Serbia. The data source of territorial distribution of BEN, was standard one (7).

Non-endemic villages with sporadic BEN cases were divided into three groups, according to the number of cases (more than 3, 2, or 1 case) in settlement, during four decades of observation. The first group of settlements with sporadic BEN (≥ 3 cases) from non-endemic settlements is shown on the map, compared to 104 villages from BEN register, with simultaneous UUT presence.

Results

In the analyzed region, BEN was present in 170 of 808 settlements (7), and in 104 of them, 534 cases of UUT were reported. In 66 possible BEN settlements, there were no UUT cases. In the next 457 of 808 settlements (56.6%) neither BEN, or UUT were registered (Table 1).

Table 1. The presence of BEN and the number of UUT in the analyzed region villages, according to BEN register (1955- 1998 year)

BEN	Villages	UUT cases	Tumors per village
BEN present	40	301	7,5
BEN possible	64	233	3,6
No BEN	33	145	4,39
No BEN	36	72	2
No BEN	95	95	1
No BEN	457	0	0
BEN possible	66	0	0

The UUT was registered in 285 of 808 settlements. The UUT cases from 16 cities (182 pts.) and Belgrade (207 pts.), with no autochthonous BEN cases, were excluded from the study.

We found 312 sporadic BEN cases, with concomitant UUT, in 164 non-endemic settlements. The both sexes were equally affected: 140 males with average age of 61.06 years, and 172 females with an average age of 64.99 years.

Table 2. The number and sex distribution of sporadic BEN cases in settlements

	Settlement	Community	Sporadic BEN	Males	Females	Inhabitants
1	Orljevo	Petrovac	3	3	-	546
2	Srpce	Kučevo	3	2	1	293
3	Rakinac	Vel.Plana	3	-	3	1404
4	Kula	M.Crniće	3	-	3	908
5	Kličevac	Požarevac	3	2	1	2084
6	Nemenikuće	Sopot	3	2	1	1933
7	Brzohode	Žabari	3	-	3	1225
8	Bošnjak	Petrovac	3	2	1	696
9	V.Crniće	M.Crniće	3	-	3	926
10	Čirikovac	Požarevac	3	1	2	1645
11	Kučevo	Kučevo	3	1	2	4846
12	Živica	Požarevac	3	-	3	914
13	Sopot	Sopot	3	-	3	1720
14	M.Ivanča	Sopot	3	1	2	1857
15	Vranić	Barajevo	3	1	2	3288
16	Golubac	Golubac	3	1	2	1995
17	Viteževo	Žabari	4	2	2	1402
18	Voluja	Kučevo	4	1	3	1318
19	Vel.Selo	M.Crniće	4	2	2	694
20	Brgule	Ub	4	2	2	1356
21	Selevac	Sm.Palanka	4	2	2	4618
22	Dubravica	Požarevac	4	1	3	1521
23	Boževac	M.Crniće	5	1	4	2480
24	Toponica	M.Crniće	5	3	2	1374
25	Vel.Laole	Petrovac	5	1	4	2694
26	Mala Krsna	Smederevo	5	2	3	1829
27	Carevac	V.Gradište	5	2	3	1102
28	Rabrovo	Kučevo	5	2	3	1441
29	Ranovac	Petrovac	6	1	5	2787
30	Vrčin	Grocka	8	6	2	8034
31	Dragovac	Požarevac	8	2	6	1166
32	Barajevo	Barajevo	10	6	4	6243
33	Porodin	Žabari	11	6	5	3454
			145	59	86	69793

Discussion

The diagnosis of BEN is not absolutely accurate, just very possible (8). The similar situation is with sporadic BEN cases, where simultaneous occurrence of UUT, after exclusion of all other nephropathies, makes a diagnosis more accurate. Both sexes were affected equally, the patients were in sixth or seventh decade of life, with mild to moderate degree of renal failure in 39,4%. In the most endemic BEN areas, the patients with BEN and UUT, had renal failure in 60% (9). The cases with BEN and UUT, presented without the signs of renal damage at the time of surgery for UUT, developed renal failure later on.

The distribution of 312 sporadic BEN cases in 164 non-endemic settlements was: 33 villages with ≥ 3 cases (4.39 per settlement), 36 villages with two, and 95 with only one case. Like in our previous report (5), the territorial distribution of villages with various UUT incidence had a concentric, rather than mosaic pattern. The endemic villages with highest incidence, were situated in central and the lowest parts of the river valleys, and less endemic, in their surroundings and higher altitudes. These 33 villages with sporadic BEN, were located like a ring, around groups of BEN villages. The same pattern existed in the valleys of rivers Kolubara, Morava and Mlava. The villages with two and one sporadic BEN cases, were located over wider territory.

The basic differences between BEN and sporadic BEN, are that there are no young sporadic BEN cases with very small kidneys and severe renal failure, and there is no familiar occurrence of the disease. The incidence of sporadic cases in the settlements, during 40 years of observation, was one case every 10, 20 or 40 years.

One can speculate that sporadic BEN is the result of low concentration of ethiological agent in nature and therefore the incidence is minimal, the age of onset is high, and the renal failure is not severe, with normal or slightly smaller kidneys.

Here documented territory, endangered with BEN, including sporadic BEN cases, is actually much larger, which means that the distribution of ethiologic agent in the nature is not limited only in known endemic or hypoendemic areas.

Conclusions

Sporadic BEN is an atypical, mild clinical variety of BEN, with simultaneous presence of UUT, characterized with very low incidence in the non-endemic areas and without familiar agglomeration, which are the crucial characteristics of BEN. The number of sporadic BEN cases without UUT, remains undetected, because of rigidity in diagnostic criteria and the absence of specific findings.

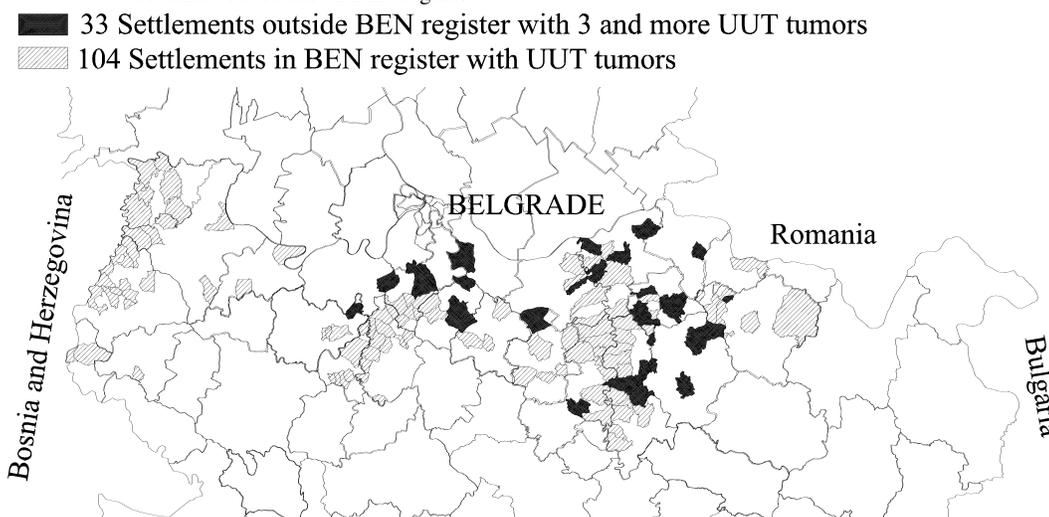
We found 312 sporadic BEN cases in 164 non-endemic villages.

Both sexes were equally affected, with the majority of patients in sixth and seventh decade of life (male average age was 61.06, and female average age was 64.99 years). Moderate or mild renal failure was found in 39.4%.

The 33 villages with ≥ 3 sporadic BEN, were located in the circle around the known BEN zones, certifying the diagnosis of BEN. The rest of villages were spread over wider territory.

The presence of sporadic BEN cases gives a possibility to speculate that the existence of BEN without familiar aggregations, with low incidence in the settlement (one case per few decades) is possible elsewhere, not only in Balkans, but it is still impossible to detect sporadic BEN using the standard diagnostic procedures.

Map 1. Territorial distribution of 33 settlements with sporadic BEN cases associated with UUT cases, localized out of known BEN regions.



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