Frequency of Alport syndrome at dialysis center "Vrsac"- Vrsac

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Abstract

Alport syndrome (AS) is a hereditary nephropathy characterized by persistent haematuria that may evolve to end stage renal disease, associated with sensorineural hearing loss, ocular abnormalities. Th aim of the study was to establish correct diagnosis and to estimate the frequency of disease.
We evauated 44 members in four generations from one Gipsy family in Vrsac county. Through the family inquiry and a review of medical records, the genealogic tree was made. The frequency of Alport syndrome in Dialysis Center Vrsac is 12.5% (5 out of 40 patients).
Considerably great frequency of AS in our dialysis center is confirmed in comparison to other centers in our country, which is probably caused by consanguinity or mutation that is not connected with X chromosome, or due to other factors that are not of genetic nature like lifestyle, diet, infections or something else.

Key words: Alport syndrome, disease frequency

Introduction

Alport syndrome (AS) is a hereditary nephropathy characterized by persistent haematuria that may evolve to end stage renal disease (ESRD). This syndrome is associated with sensorineural hearing loss, ocular abnormalities (anterior lenticonus, macular or peripheral flecks), and ultrastructural abnormalities of the glomerular basement membrane (GBM) (1). Mutation in collagen type IV genes are responsible for disorders of glomerular basement membrane, that produce broad spectrum of disease phenotypes ranging from benign haematuria to most severe forms of AS. This leads us to agglutinate different entities under the name of "collagen type IV" nephropathy (2). AS displays considerable phenotypic and genetic heterogeneity (3), and this syndrome is relatively rare. There are three genetic forms of AS exist: X-linked form (accounts for 85% cases), autosomal-recessive (responsible for approximately 10-15% of cases; and autosomal-dominant form (less than 1%), in at least some families. The estimated gene frequency ratio of AS is 1:5000 (5).
This study is implemented with the aim to establish correct diagnosis, to estimate frequency of disease, to make a genealogical tree, to collect data from epidemiological, ophthalmic, audiometric tests and to compare them with the other experiences from literature, and to confirm the type of heredity through a review the genealogic tree.

Patients and methods

A great frequency of Alport syndrome is presented in Vrsac county. There is a large percentage of this phenomenon causing end stage renal disease (ESRD) at our center and it is 12.5% (5 out of 40); and this percentage is high and is very likely to increase. All the patients are from one Gipsy family, at this moment with 44 members in four generations, and all of them live in the same village 65 km away from Belgrade. The oldest alive member is 40, and the youngest one is one-month-old baby.

Results

Through the family inquiry, as well as the review of medical records, the genealogic tree was made (Figure 1). The frequency of Alport syndrome in Dialysis Center Vrsac is 12.5% (5 out of 40 patients). AS is considered the be a cause of approximately 0.6 to 2.3% of ESRD in Europe and the United States (6,7), and from the registry 2004 in Serbia and Montenegro it is less than 1%. This proportion is probably underestimated because of the diagnostic difficulties.
Average ages when started with dialysis is 21.5 years for males and for females is 35 years (with the deceased family members). The male patients III:5, III:6, III:12 and III:13 started the dialysis at the age of 22, 21, 23 and 24 respectively, and the female patient II:2 started at the age of 34. At present, the male patients spent average 4 years and female spent on dialysis 6 years. Thus the deceased members (two female and one male patient) from the same family, started the dialysis at the age of 41 and 31(females), and 17 (male) and spent less than one month, the first, and less than two years, the other female; and less than a year for the male. All patients have had macroscopic haematuria before they started with dialysis. They should probably have started sooner, given the fact that they had come in a very bad condition, with extremely high values of serum creatinine and blood urea concentrations and had urgently started with haemodialysis. They have not consulted a doctor before, considering that they had painful haematuria, nausea, frequent vomiting, and a peripheral edema. Clinical examinations have shown a great percentage of extrarenal abnormalities with variability of signs, which is rare. All the patients who were on dialysis have progressive sensorineural deaffnes (5 out of 5), both for high and low frequencies with similar findings in the study of autosomal dominant nephropathy (8). Ocular abnormalities had 4 out of 5 patients, except a female patient. They had lenticonus anterior and retinitis pigmentosa. Two biopsies at light microscopy indicated disorders of GBM. Three out of five patients on

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dialysis had hypercholesterolaemia (total cholesterol more than 8.3, 7.1 and 6.7 mm/l) (9), but unlike those who had Fetchner syndrome, they didn't have trombopenia (10). Complications occured in a form of arterial hypertension in 4 out of 5 patients. All of them are anemic (average value of haemaglobin was 11.7 g/dl) and they were all on Epoetin Beta (Recormon®). Two out of five patients were hepatitis "B" seropositive. They had mild intellectual deficit. In addition to this, the patients were very undisciplined, had a great increase in weight interdialysis and had a poor social background.

Conclusions

This data obviously leads to a confirmation of the diagnosis of Alport syndrome, as a severe (juvenile) form (<31 years) shown by a great percentage of patients underwent dialysis in one generation, who started at early age. Analyzing the genealogic tree of this family, a direct X chromosome and autosomal-recessive way of heredity has not been confirmed, therefore the autosomal-dominant mode is much more possible. There is a puzzling point patient (IV:22), who is 8 years old and who has a persistent micro/macro haematuria, and mild deafness. That suggest father to son transmission and autosomal-dominant mode of transmission. Considering the fact that all the affected are from a Gipsy family, we must think of consanguinity, which is not confirmed, but a number of kindreds will be higher, and they can disperse far and wide. This family must have a detailed screening. Considerably great frequency of AS in our dialysis center is confirmed in comparison to other centers in our country, which is probably caused by consanguinity or mutation that is not connected with X chromosome, or due to other factors that are not of genetic nature like lifestyle, diet, infections or something else.

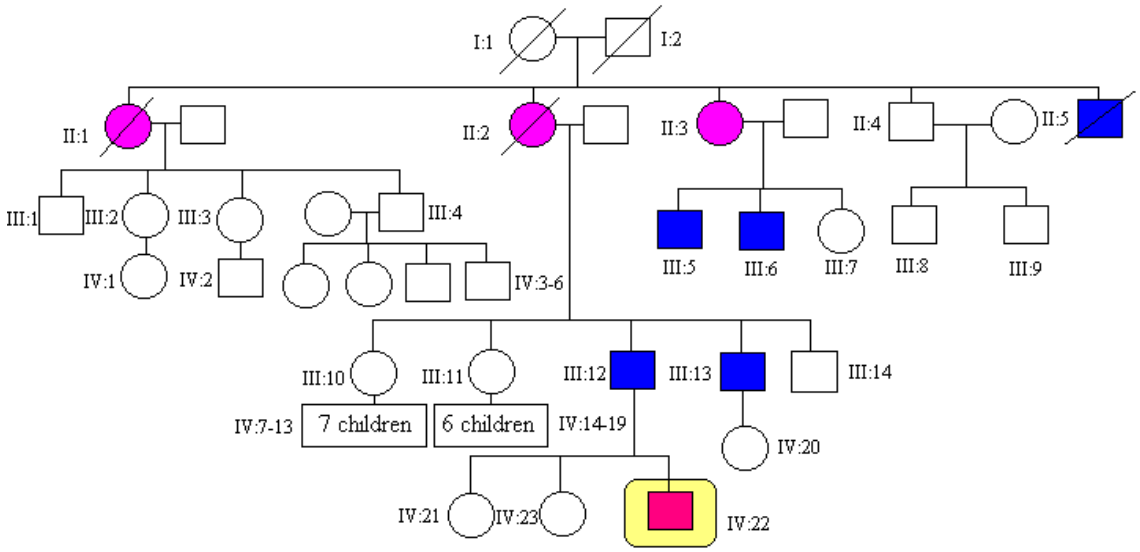

Fig 1. Genealogy family tree with ID-Vrsac. The filled symbols represent affected males ( )and affected females( ) – reached dialysis. The crossed symbol represents deceased family members. The numbers by each symbol refer to generation and person ID (GPID).The framed symbol represent affected 8 year old member with micro/macro haematuria, deafness

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