International Registry of Steroid-Resistant Nephrotic Syndrome: updated epidemiological and clinical data

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Nephrotic Syndrome

**Definition**  NS is a nonspecific disorder in which the kidneys are damaged, causing them to leak large amounts of protein from the blood into the urine.

**Frequency NS Incidence**  0.2/10000 in children

0.3-0.4/10000 in adults

**Prevalence**  1.6/10000 in children*

**Clinical manifestation**
- heavy proteinuria
- hypoalbuminemia
- hyperlipidemia
- edema

Nephrotic Syndrome

Etiologic classification

- Primary NS: unknown causes
- Secondary NS:
  - Familial and genetic forms
  - Infections
  - Immunological disorders
  - Drugs
  - Diabetes, ...

Treatment: steroids

- Responders
- Not responders

Steroid-Sensitive, steroid-dependent or multirelapsing Nephrotic Syndrome

Steroid-Resistant Nephrotic Syndrome

ESRD (dialysis, renal transplantation)
Our organisation

Clinical data

Biological samples

Nephrologists

Clinical geneticist

Laboratory of genetics

- Differential diagnosis
- Identification of familial forms
- Treatment
- Trials of new experimental therapies

- Differential diagnosis
- Identification of familial forms
- Database management
- Identification of screening strategy
- Patients’ genetic counselling

- Identification of screening strategy
- Mutational screening of known genes
- Identification of new genes
- Functional studies of mutated proteins
Cohort description (I)

• SRNS Patients recruited: 165
  – Italian cases: 137
  – Foreign Cases: 28
  – Familial Cases: 86, belonging to 34 unrelated families

• Participating centers of Nephrology Units:
  – From Italy: 15
  – From Europe/Extra-Europe: 4
Cohort description (II)

Classification of sporadic and familial cases

<table>
<thead>
<tr>
<th>Form</th>
<th>No Extra-renal Manifestations</th>
<th>With Extra-renal Manifestations</th>
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</thead>
<tbody>
<tr>
<td>Sporadic Form</td>
<td>23%</td>
<td>77%</td>
</tr>
<tr>
<td>Familial Form</td>
<td>30%</td>
<td>70%</td>
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Classification of the main extra-renal manifestation in familial and sporadic cases

- Eye involvement
- Ear involvement
- Cancer
- Skin manifestations
- Hematologic abnormalities
- Other

Legend:
- Sporadic Form
- Familial Form

No Extra-renal Manifestations
With Extra-renal Manifestations

Distribution of the age of SRNS-onset
Cohort description (III)
Genetic analysis of known genes

• Identification of genetic mutation in 16% of our patients: INF2 (9), WT1 (7), MYO1E (4), PLCE1 (4), NPHS2 (1) and CD2AP (1)

• Clinical suggestions allowed to identify a few of cases of Alport, Denys-Drash and renal-coloboma syndromes

• Every patient received result and genetic counselling
Identification of new genes causing SRNS

MYO1E Mutations and Childhood Familial Focal Segmental Glomerulosclerosis


The New England Journal of Medicine, 2011
International Network

- Participation in the PodoNet Consortium
  International Consortium including 1607 patients, from 89 nephrology centers, 36 Countries

- Progresses in SRNS causing-gene

Disruption of \( PTPRO \) Causes Childhood-Onset Nephrotic Syndrome

Fatih Ozaltin,1,2, Tulin Ibsirlioglu,2 Ekim Z. Taskiran,3 Dilek Ertoy Baydar,4 Figen Kaymaz,5 Mithat Buyukcelik,6 Beltinge Demircioglu Kilic,6 Ayse Balat,6 Paraskevas Iatropoulos,7 Esin Asan,5

The American Journal of Human Genetics, 2011

Genetic screening in adolescents with steroid-resistant nephrotic syndrome

Beata S. Lipska1,2, Paraskevas Iatropoulos3, Ramona Maranta3, Gianluca Caridi4, Fatih Ozaltin5,6, Ali Anarat7, Ayse Balat8, Jutta Gellermann9, Agnes Trautmann1, Ozlem Erdogan10, Bassam Saeed11,

Kindney International, 2013
Conclusion

• We understood that a multidisciplinary approach for rare diseases can allow
  • The achievement of a more accurate diagnosis and a better characterization in clinical and genetic features
  • The possibility to offer genetic counselling for SRNS patients and their relatives

• The analysis of SRNS allows progresses in knowledge:
  • Identification of MYO1E and PTPRO as a new SRNS-causing genes and their underlying pathogenic mechanisms
  • Study of a very rare condition as adolescents-onset SRNS

• National Registries may promote the establishment of International Network as a high-potential resource
Thank you for the attention