

PodoNet: A Clinical, Genetic and Experimental Research Initiative for Hereditary Diseases of the Podocyte

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Introduction

The etiology, phenotypic variability, treatment response and clinical outcome of steroid-resistant nephrotic syndrome (SRNS) are incompletely understood. While some patients respond to intensified immunosuppressive (IS) treatment, a large fraction is attributable to abnormalities in podocyte-specific genes. Although the identification of a genetic cause is of eminent clinical importance with respect to IS efficacy and risk of post-transplant recurrence, genetic workup commonly remains incomplete. Interpretation is often challenging due to variable response to IS, loose genotype-phenotype correlations and anecdotal IS-responsive genetic cases. A large subset of cases persists who are refractory to IS and have no mutations in known SRNS genes.

PodoNet-Projects

The PodoNet consortium integrates an international clinical SRNS registry with a concerted search for new genes causing SRNS. The online registry, accessible through the consortium's web site (www.podonet.org), aims for a complete clinical and genetic characterization and follow-up of cases, to define the demographics, phenotypic appearance and prognosis of genetic and other forms of SRNS. As of September 2009, 31 centers from 18 countries have subscribed to the online clinical registry. New SRNS genes will be sought for by joint analysis of existing and new informative families.

A sub-project will focus on the role of mitochondriopathies as a cause of SRNS. Experimental sub-projects will explore novel pharmacological treatment approaches by stimulating deficient intracellular podocin trafficking.

The information generated by the PodoNet initiative will likely enhance the understanding of the demographics, causes and prognosis of SRNS in children and adults, facilitate the establishment of rational diagnostic and therapeutic guidelines, define genotype-phenotype correlations, and enable the search for new genetic entities of SRNS.

Online Registry – www.podonet.org

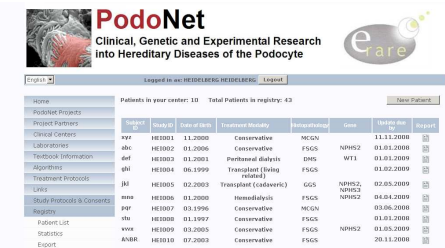


Fig. 1 Patient List

Patient lists inform each clinical center about the number, age, treatment modality, histopathologic and genetic diagnoses, update of the registered patients.

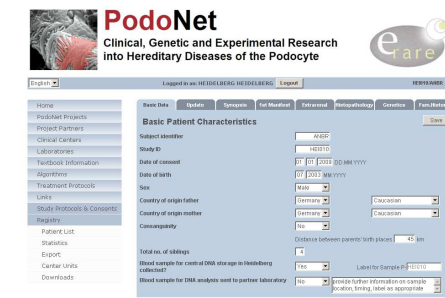


Fig. 2 Data Base Entry

Retrospective and prospective clinical data will be entered:

- Basic patient characteristics
- First manifestation of disease
- Associated co-morbidities
- Histopathology
- Genetic studies
- Family history
- Pharmacological treatment
- Course of disease

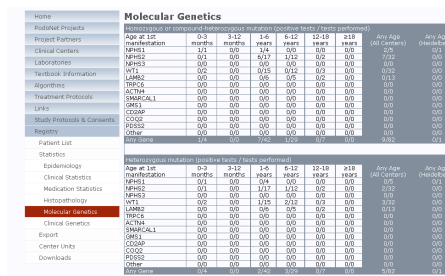


Fig. 3 Statistics

Several statistics will be generated, e.g.

- Epidemiologic data
- Clinical aspects
- Pharmacological treatment
- Histopathologic diagnoses
- Molecular genetics
- Family history

Algorithms

The PodoNet website provides evidence- and consensus-based clinical practice guide-lines (Fig. 4). In the long-term, the aim is the harmonization of SRNS management in Europe. The PodoNet consortium suggests also to initiate a standardized genetic diagnostic work-up of SRNS patients if not done so already (Fig. 5).

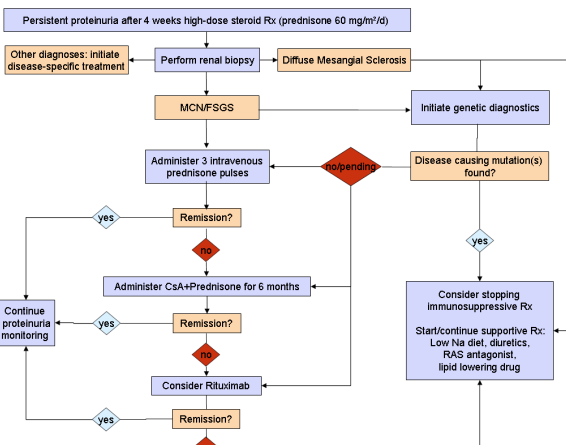


Fig. 4 Proposed clinical management of nephrotic syndrome in children

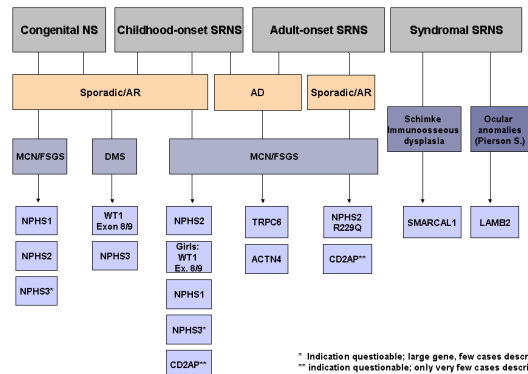


Fig. 5 Suggested strategy of genetic mutation screening in SRNS

* Indication questionable; large gene, few cases described
 ** Indication questionable; only very few cases described