

IMMUNE MEDIATED RENAL DISORDERS WORKING GROUP

Report January 2016 to ESPN Council

Previous activities coordinated by Dr. A. Amore

It is on the working group page

As summar

- 1. Cinical Indications And Technical Details For Renal Biopsy In Children (And In Adults) With Glomerular Diseases On Native Or On Transplanted Kidneys** (Coordinator A. Amore) This study presented at ESPN Porto 2014 and ESPN Brussels 2015
- 2. A European Registry Of Children With Henoch Schonelein Nephritis To Detect Clinical, Genetic And Immunological Risk Factors** (Coordinator L. Peruzzi) this study is still active. It was granted with 10.000 Euros by ESPN and part of the work will be presented at ERA EDTA 2016 on behalf of ESPN Immune Mediated Renal Disorders Working group.

ESPN 2015 Brussels Immune Mediated Renal disorders Symposia Lectures

- **ESPN-ERA-EDTA Survey On Indications And Modalities Of Renal Biopsy In Children (A. Amore)**
- **Complement involvement in primary glomerular diseases(JC Davin):**
- **New drugs entering in the portfolio for the treatments of immune mediated glomerular diseases (R Coppo)**
- **Lupus Nephritis(R Topaloglu)**

NEW and CONTINUING PROPOSALS FOR 2016

1. Lupus Nephritis Patients' Treatment Schedule And Long Term Outcomes (Coordinator R.Topaloglu)

Recent advances in the management of lupus nephritis, together with earlier renal biopsy and selective use of aggressive immunosuppressive therapy, have contributed to a favorable outcome in children and adolescents with systemic lupus erythematosus (SLE). Nevertheless, we believe that a more effective and less toxic treatment is needed to attain an optimal control of the activity of lupus nephritis. We also believe that a multidrug therapy may be an attractive option for young patients with SLE and lupus nephritis.

Aim of this work multicenter pediatric survey will be to analyze the treatment schedule and outcome measures of pediatric lupus nephritis patients -
Secondary aim will be to identify the factors associated with response to induction therapy and number of relapses

Finally a comparison of the efficacy and safety of different drug regimens will be performed

INCLUSION CRITERIA

- Diagnosis of SLE according to SLICC or ACR criteria
- Diagnosis of lupus nephritis (LN) before 18 years of age
- Diagnosis of LN between 2004-2014
- Minimum 12 months follow-up after LN diagnosis
- The patient should have renal biopsy at LN diagnosis

Every European and Turkish Pediatric Nephrology referring to ESPN will can reach an excell form finalized to clinical and laboratory data of all patients with Lupus Nephritis. Particular regard will be devoted to the therapy and eventual relapse of disease will be recorded as well as eventual changes in therapeutical approach.

Filled form will collected by Dr. Rezan Topaloglu

Department of Pediatric Nephrology, Hacettepe University Faculty of Medicine, Ankara Turkey for the statistical analysis,

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2. A European Registry Of Children With Henoch Schoenlein Nephritis To Detect Clinical, Genetic And Immunological Risk Factors (Coordinator Licia Peruzzi)

Proposal for 2016

In 2014 a new study, coordinated by Licia Peruzzi, investigating the outcome of recent cases of HSP and the risk factors for progression in a pan-European cohort was met by ESPN research call and granted with 10.000 Euros

This project is articulated in 2 parts:

a) Hsp Nephritis Registry: a retrospective data-base to collect clinical data at time of biopsy and during yearly follow up in European children who underwent a renal biopsy for HSP nephritis in the last 20 years.

20 centers so far declared their interest (Lithuane, Romania, Serbia, Montenegro, Poland, Turkey, France, Germany, Great Britain, Switzerland, Italy, Portugal, Finland, Belarus, Belgium, The Netherlands, Sweden) and 10 have sent back the filled excel database concerning the summary data at disease onset for 192 subjects who underwent a renal biopsy for HSP nephritis and the main outcome results for 146 cases.

The analysis of the first 146 cases has produced interesting results submitted as abstract to the next ERA-EDTA Congress on behalf of the ESPN Immune mediated renal disorders WG.

The main points evidenced by this pilot analysis are:

- the confirmation of pediatric nephrologist's feeling of a substantial better prognosis in recent years than in past cohorts: 67.1% reached remission of proteinuria at 9m median (0.2-92m) and 61.6% of hematuria at

19months median (range 0.4-98). 0.7% reached ESRD 15m after disease onset, none died.

- children are treated sooner, often before biopsy: at biopsy 55% had already received steroids, 6% steroids and immunosuppressors, 9.5% renin-angiotensin system blockers and 26% no therapy
- biopsy is performed at a median of 37 days after purpura onset
- histology was not predictive for remission of hematuria or proteinuria either according to ISKD or MEST classification

The questions raised from these data, that could be answered by the implementation of the case series as well as by the completion of the follow-up sheet of database are:

- **type of induction therapy adopted**
- **duration of therapy**
- **immunosuppressors adopted: duration and doses**
- **Follow-up data at timely points**

All the participating centers as well as the centers part of the ESPN WG Immune mediated renal disorders will be solicited to send follow-up data and to participate with new cases to achieve the completion of a solid database foundation of the HSP Registry

b) Prospective Study For Validation Of Immunologic Risk Factors: with the aim to recruit a new cohort of 50 incident children receiving a renal biopsy for HSP nephritis to perform a large panel of immunological studies at the moment of maximal activity, at time of renal biopsy and possibly before treatment, together with the genetic study. These studies include immunoproteasome switch, TLR expression, altered glycosylation of IgA1 and antibodies against deGAI IgA1, oxidative stress markers (AOPP), GWAS in collaboration with Columbia University

- Complement activation study was also included in collaboration with the Pediatric Nephrology group of Nijmegen who received an ESPN research grant for complement study in 2014 coordinated by Elena Volokhina.

Logistics of laboratory samples for new incident patients for the immunological and the GWAS study has been settled in collaboration with Columbia University. So far only a small number of samples were gathered for immunological and genetic study: this delay in collection of biological samples is due to regulatory restrictions in the different countries for biological sampling and Ethical Committee approval has

been requested by most centers to collect samples and data from new incident patients.

Centers who will not be able to participate with HSP with renal biopsy will participate with cases without renal involvement to the GWAS study filling a different appropriate database for genetic testing controls.

All Centers will be solicited to contribute to the study with biological samples
Additional European centers are invited to join.

For any question please contact liciaperuzzi@hotmail.com or licia.peruzzi@unito.it

3. Crescentic glomerulonephritis in children (Proposed By Esra Baskin)

Crescentic glomerulonephritis (CsGN) is an uncommon disorder in children and it is characterized by crescents in 50% or more of glomeruli. The clinical hallmark of CsGN is rapidly progressive glomerulonephritis. This manifests as sudden and progressive deterioration in renal functions. Three types of Cs GN have been identified (immune complex, anti GBM and pauci immune). It is well known that the etiology and the initial pathogenetic factors are different in the three types, but the final mechanisms leading to crescent formation and the renal signs and symptoms are similar. Early recognition and timely intervention are required to prevent progression to chronic renal failure. Thus CsGN should be diagnosed early and treated as a renal emergency.

It has been reported that CsGN comprises 2-10% of the total number of kidney biopsies. The clinical and epidemiological factors of CsGN and their histopathology and outcome in the childhood are unclear and data in children are scarce.

I would like propose a study about crescentic glomerulonephritis. In case of acceptance of the study, which will be retrospective, a registry of crescentic glomerulonephritis cases should be created. Data from all patients who underwent renal biopsy with histologic diagnosis of crescentic glomerulonephritis and follow up of 5-10 years will be collected. Aim of the study will be to obtain data on the etiology, clinical features, prognostic factors and long-term outcome of CsGN in pediatric patients.

If the study will be accepted by the WG Board and ESPN council, firstly we can send a web survey to all centers and then we will send invitations to participate in the study.

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