A EUROPEAN REGISTRY OF CHILDREN WITH HENOCH SCHOENLEIN NEPHRITIS TO DETECT CLINICAL, GENETIC AND IMMUNOLOGICAL RISK FACTORS

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Henoch-Schönlein purpura (HSP) is the most common vasculitis in children, with variable extrarenal signs and variable renal involvement, ranging from 20% of children in tertiary to less than 5% in unselected series, according to the literature of the past decade.

Paediatric Nephrologists have perceived that the outcome of HSP in children has changed over the last decade, possibly because of a greater attention to the development of renal complications, however, progressive cases still exist.

In 2014 the need for a new study 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 collecting 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.

b) PROSPECTIVE STUDY FOR VALIDATION OF IMMUNOLOGIC RISK FACTORS*:* 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 deGAl IgA1, oxidative stress markers (AOPP), GWAS in collaboration with Columbia University

Complement activation study is being defined in collaboration with the Pediatric Nephrology group of Nijmegen who received an ESPN research grant for complement study in 2014 coordinated by Elena Volkhina.

The study was approved by the local Ethical Committee in February 2015 and since then an invitation letter to join the study was sent to pediatric nephrologists of most EU countries.

20 centers declared their interest (Lithuane, Romania, Serbia, Montenegro, Poland, Turkey, France, Germany, Great Britain, Switzerland, Italy, Portugal, Finland, Belarus, Belgium, The Netherlands, Sweden) and so far 8 centers 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 follow up data with at least one evaluation per year are being filled.

The preliminary analysis over 146 cases evidences an equal distribution between gender (82 M, 84F), a main caucasian ethnicity (90%). Mean age at onset of the disease was 8.05±3 years. 122/146 displayed palpable purpura as dominant sign, accompanied by abdominal pain (10%) or arthralgias (5%).

Renal involvement appare at a median of 20 days after purpura, with a wide range and some late involvement (range 1d-6 years).

The renal biopsy was performed at a median time of 37 days after the first signs of nephritis (range 1 d-10 years). At time of biopsy 81/146 were already treated with steroids, 9/146 with steroids and immunesuppressors, 14 ACE-I and 38 had not received any therapy.

The renal biopsy was classified according to ISKDC and MEST:

ISKDC I	ISKDC II	ISKDC IIIa	ISKDC IIIb	ISKDC IVa	ISKDC IVb	ISKDC Vb
16	51	54	14	1	3	1

M0	M1	E0	E1	S0	S1	T0	T1	T2
67	61	87	41	106	22	114	12	1

90/146 reached the remission of hematuria at a median of 19 months (range 0.4-98) and of proteinuria in 98/146 at a median of 9 months (0.2-92m). One patient reached ESRF 15 months after the disease onset, none died.

Logistics of laboratory samples for new incident patients for the immunological and the GWAS study has been settled in collaboration with Columbia University. Sio far 12 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 Commitee approval hasbeen requested by most center sto collect samples and data from new incident patients.

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

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ECONOMIC UPDATE

The start-up funding of 10.000 Euros granted by the ESPN allowed to support the cost for reagents for the immunological study:

Until now 6870 euro + 21% VAT were employed for purchasing reagents for Taqman for Immuneproteasome, TLR (specific primers and consumables).

Residual funding will be used for shipment of biological samples.

The project was cofinanced by “Fondazione Giovanni Goria” Asti Italy, with a fellowship for a biologist.

Additional European centers are invited to join.

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