

Conclusions Taken together, these results exclude possible imprinting in 2q as a cause of RSS in this child and suggest an autosomal recessive mutation which was unmasked by the segmental maternal isodisomic abnormality. Next Generation Sequence analysis of chromosome 2q regions of homozygosity identified in this child is underway and will most likely identify another novel RSS locus.

247 SERIAL CYTOKINE EXPRESSIONS IN INFANTS WITH INCONTINENTIA PIGMENTI

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Background NF- κ B dysfunction resulting from NEMO (NF-kappaB essential modulator) mutation can lead to significant alterations in cytokine production. However, little is known about changes in the expression of downstream molecules in patients with incontinentia pigmenti (IP).

Objective This study aims to investigate serial cytokine expressions during the first 2 years of life in young infants with IP, the period in which skin inflammation and morphological changes are most significant.

Methods Gene analysis was performed for the two neonates with IP. Peripheral mononuclear cells were obtained shortly after birth and successively at a 6-month interval up to the age of two years. Levels of TNF- α and IL-6 were analyzed with ELISA before and after stimulating with TLR ligands.

Results The male patient had normal NEMO allele. His cytokine level, although initially lower, had returned to a level comparable with those of controls at 12 months of age. The female infant had a mutated NEMO gene. Her baseline TNF- α level was significantly higher than those of the control subjects at birth and remained high by 6 months of age. All cytokine responses had decreased significantly by 2 years of age, the time in which all vesicular skin lesions had resolved.

Conclusion This is the first report that demonstrates serial changes of cytokine profiles in humans with IP. This study showed that in the presence of NEMO mutation, alteration of cytokine production was remarkable during the first year of life, which may account for the prominent inflammatory changes in skin morphology.

248 NOVEL MUTATION CAUSING GLUCOSE 1 TRANSPORTER DEFICIENCY SYNDROME

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Introduction Glucose transporter-1 (GLUT1) deficiency syndrome (OMIM #606777) is an autosomal dominant condition resulting in reduced glucose transport into the brain. GLUT1 deficiency syndrome was first described in 1991 by De Vivo et al. The diagnostic finding is a low glucose concentration in the cerebrospinal fluid (CSF; mean 1.7 [SD 0.3mmol/L]) in the presence of normoglycaemia. GLUT1 deficiency syndrome can be confirmed by mutation analysis of the SLC2A1 gene. The spectrum is ever expanding with new mutations as also varying presentations. We present one such novel mutation.

Case report A Caucasian male was referred to the neurology department with global developmental delay, head nods, seizures and excessive daytime sleepiness. Over the years he had many investigations including repeated MRIs and EEGs and investigations for conditions with progressive myoclonic epilepsy. At the age of 14 years the parents gave a history of food intake reducing his head

nods and other seizure types. He was then investigated for possible GLUT1 deficiency.

Results The initial investigations revealed a CSF sugar of 2.4 when the blood sugar was 5.9 (ratio of 0.4) which was low but not low enough for GLUT1 deficiency. Genetic testing revealed a mutation in the Exon 5 of the SLC2A gene c.647T>C (p.Ile216Thr) not previously reported.

Conclusion GLUT1 deficiency should be suspected in a child with developmental delay, epilepsy and movement disorder. Novel mutations can result in the condition. Our case is one such example for novel mutation as well as refusal of ketogenic diet from late diagnosis.

249 CEREBRAL PALSY AND CHEMOKINE CCL18 POLYMORPHISM IN VERY PRETERM INFANTS

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Background Cerebral palsy (CP) is a nonprogressive motor impairment syndrome caused by damage in the developing brain and it reveals clustering to preterm infants. Recently, genetic factors have been suggested as risk modifiers for CP. However, the individual genes causing predisposition to CP are still poorly understood. Low cord blood levels of CCL18 have been found to associate with CP in preterm infants. Since CCL18 gene is restricted to primates, it may be considered as a candidate for functionality in human brain.

Aims To investigate the association between the CCL18 gene single nucleotide polymorphisms (SNPs) and the cord blood levels of CCL18. Further to study the association between the CCL18 SNPs and the susceptibility to CP.

Methods A prospective cohort consisted of 161 children born very preterm (gestation < 32 weeks) in Oulu University Hospital during 1997–2006. Concentration of the cord blood CCL18 was analysed (n=99). Five CCL18 SNPs (rs1102934, rs2015086, rs2015070, rs2735835, rs712044) were genotyped. Cerebral palsy was confirmed at 5 years of age.

Results Two CCL18 SNPs associated with CCL18 (P=0.011; P=0.039). Additionally, CCL18 (SNP rs2735835) associated with CP. Thus, CP occurred in 11 (18%) of 61 children with GG genotype compared with 6 (6%) of 100 children with AA/GA genotype (OR 4.1; 95% CI 1.3–12.5, P=0.013).

Conclusions Variation of the CCL18 gene associates with CCL18 concentration and with predisposition to CP in very preterm infants. This is consistent with the hypothesis that CCL18 has a role in the complex sequence leading to brain damage.

250 SEASONALITY OF CONGENITAL ANOMALIES IN EUROPE

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Investigation of seasonal patterns of congenital anomalies (CAs) can help identify environmental risk factors. Smaller datasets and spatiotemporal variation in previous studies have led to conflicting evidence. The aim of our study was to investigate previously described associations and to generate new hypotheses on the role of seasonal factors in the etiology of CAs using a large high quality European dataset.

The European Surveillance for Congenital Anomalies (EUROCAT) is a European network of standardized population-based registries for the surveillance of CAs. A 2000–2009 dataset involving 19 EUROCAT registries and over 63,000 CAs was utilized to investigate seasonal patterns. Analysis of EUROCAT defined CAs was

performed in two steps; first on CAs previously associated with seasonal factors and second on all remaining CAs. CAs and monthly births were calculated back to month of last menstrual period after which trigonometric regression analysis was performed to explore seasonal trends in CA prevalence.

Our dataset confirmed seasonality for Ebstein's anomaly ($p < 0.05$), tricuspid atresia and stenosis ($p < 0.05$), congenital hydro-nephrosis ($p < 0.001$) and hip dislocation ($p < 0.001$) and a new signal was generated for seasonality of situs inversus ($p < 0.001$). We detected non-significant seasonal peaks for neural tube defects ($p = 0.0683$) and spina bifida ($p = 0.0507$) coinciding with influenza season. We were not able to detect seasonality for any other CAs. We were unable to confirm the associations between neural tube defects, some other anomalies and influenza.

The associations detected and the negative results provided can help future studies unravelling the etiology of CAs.

251 MOLECULAR ETIOLOGY OF CHILDHOOD HEARING IMPAIRMENT ASSOCIATED WITH NON-SYNDROMIC ENLARGED VESTIBULAR AQUEDUCT IN SOUTHEASTERN CHINA

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Background Mutations in *SLC26A4*, and in rarer cases double heterozygous mutations of *FOXI1/SLC26A4* or *KCNJ10/SLC26A4*, lead to childhood hearing impairment associated with non-syndromic enlarged vestibular aqueduct (EVA), the most common inner ear malformation. Molecular etiology studies of non-syndromic EVA will provide important data to facilitate DNA diagnosis and genetic counseling of this disease.

Methods Mutation screening of *SLC26A4* was performed in 126 probands with non-syndromic EVA in Southeastern China. Those detected with mono-allelic or no *SLC26A4* mutation were subjected to mutation screening of *FOXI1* and *KCNJ10*.

Results Bi-allelic, mono-allelic, and no *SLC26A4* mutation were detected in 70.6%, 8.0% and 21.4% of the probands with non-syndromic EVA. Sixteen of the 40 *SLC26A4* mutations detected were novel. While the c.919-2A>G mutation accounted for 41.3% of the mutant alleles of *SLC26A4*, none of the other 39 mutations accounting for more than 5.6%. No pathogenic *FOXI1* or *KCNJ10* mutation was identified in this study.

Conclusions The c.919-2A>G mutation of *SLC26A4* is highly prevalent and should be the primary target of genetic testing for patients with non-syndromic EVA in Southeastern China. The spectrum of the other *SLC26A4* mutations, however, is highly heterogeneous and differs from those reported in Taiwan or other regions of mainland China. Mutations in *FOXI1* or *KCNJ10* were not the major cause of non-syndromic EVA in Southeastern China.

252 WHOLE GENOME MICRORNA EXPRESSION PROFILING IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: A PROSPECTIVE EVALUATION

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The aim of the study is to evaluate the associations between microRNAs (miRNAs) and childhood acute lymphoblastic leukemia (ALL). Forty-three children with ALL and 14 age-matched controls were included in the study. Microarray expression profiling

consisting of 1136 miRNAs was performed in peripheral blood and bone marrow samples of patients. Diagnosis, differential diagnosis, outcome and prognosis associated with aberrant microRNA expressions were prospectively evaluated. Significant miRNAs on admission were confirmed and re-evaluated after 6 months following treatment period by real time RT-PCR. The effect of miRNAs on overall survival (OS) and event free survival were presented. The most significantly upregulated miRNAs were miR-548i (12.5 fold), miR-708 (10 fold), miR-181b (6.25 fold) and most downregulated miRNAs were miR-145 (-2.52 fold) and miR-640 (-2.3 fold) compared to control group in microarray profiling. miRNAs according to immunophenotype revealed 22 upregulated and 13 downregulated in T-ALL. In the B-lineage ALL group, 7 miRNAs were upregulated and 2 miRNAs were downregulated. Expression of miR-146a, miR-155, miR-181a and miR-195 significantly changed after 6 months of treatment period. miR-145 was associated with OS. t(12; 21) and t(9; 22) were significantly associated with certain miRNAs. In conclusion miRNA expression profile could be used as biomarker in the diagnosis, differential diagnosis, monitoring the disease and prognosis of ALL.

253 MANAGEMENT OF HEMANGIOMAS: A SINGLE CENTER EXPERIENCE

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Aim To share our experience of 185 (F/M: 2.4) patients with hemangiomas followed between 2003–2011 at Cerrahpasa Medical Faculty, Istanbul.

Results Onehundred-twentyeight (69%) had a single lesion whereas 31% had multiple lesions. Most of the patients (n:94) were followed by a “watch and wait” policy and 40 of them did not require any medical or surgical intervention as the lesion convoluted on follow-up. Only 6 (3%) patients required surgery. Nine patients with lesion around eye required intralesional steroids to prevent visual disturbance. Bleomycin was used as a sclerosing treatment in 2 patients with a giant hemangioma. In 21 patients with multiple diffuse lesions causing cosmetic problems, interferon was given. Medical treatment was given in other patients on follow-up due to growth, ulceration, bleeding or persistence of the lesions at older ages; 14 were treated by systemic steroids, 73 by propranolol and 39 by combination therapy due to insufficient response. Propranolol was the first choice of treatment in patients diagnosed after 2008. All patients treated by propranolol were evaluated by echocardiography and electrocardiography, no cardiac side effects were noted. One patient under treatment presented with increased sweating and was found to have hypoglycemia associated with propranolol during periods of restricted oral intake. The drug was restarted increasing the frequency of breastfeeding with no further hypoglycemia attacks.

Conclusion The excellent clinical outcome and apparent lack of side effects of propranolol makes it a good choice as a first-line treatment for hemangiomas. Hypoglycemia may be noted in infants under propranolol in restricted periods of feeding.

254 NEONATAL BLOOD TRANSFUSION-CAN WE MAKE IT SAFER?

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Background and Aims A specific blood transfusion booklet was implemented in the Southern Health and Social Care Trust in 2010 for babies less than four months of age. This aimed to provide a