The Neu-Laxova Syndrome: analysis of a cluster of cases in the Maltese Islands

A Cuschieri[1], E Said[1], J De Gaetano[2], S Ali[2], S Suleiman[1], [1]Department of Anatomy, University of Malta; [2]Department of Pathology, St. Luke's Hospital. Malta

The Neu-Laxova syndrome is generally described as a rare lethal autosomal recessive disorder. We report on a cluster of six cases of the Neu-Laxova syndrome that occurred in the Maltese Islands within a period of less than one year between August 2002 and June 2003. The characteristic features in the babies with this syndrome were intra-uterine growth retardation, severe microcephaly, protruding eyes, microphthalmia, cataracts, absent eyelids, cleft lip and palate, small limbs, limb deformities, multiple joint contractures, oligodactyly, syndactyly, ichthyosis and gross subcutaneous edema. The brain was invariably very small with agyria or pachygyria, relatively large ventricles, agenesis of the corpus callosum and a hypoplastic cerebellum. There were marked and very characteristic radiographic abnormalities affecting the skull and limbs. We report new histological findings affecting the skin and subcutaneous tissues. The inter-familial variability of this condition was analyzed. Although there was a statistically significant temporal clustering of cases of this rare condition, there was no identifiable uniformity in relation to geographic distribution, maternal and paternal ages and occupations, unusual exposures to chemicals or radiation during pregnancy. There was of a possibly affected sib in only one of the families, while the family histories were negative in all the other families. Such a cluster of cases has not been previously reported and is discussed in relation to the available evidence on which this syndrome is presumed to be autosomal recessive.

p-022

46, XX Gonadal dysgenesis, short stature and mental retardation in three sisters

E Said[1,2], A Cuschieri[1,2], [1] Department of Anatomy, University of Malta; [2] Genetics Clinic, St Luke's Hospital, Malta

Gonadal dysgenesis in 46 XX individuals is genetically heterogenous. Both sporadic and inherited forms have been described. Some cases have been reported to occur in association with congenital deafness, dysplastic kidneys, short stature or episodes of metabolic acidosis. We report here three sisters, in a sibship of nine sisters and 1 brother, who have primary ovarian failure, mental retardation and short stature. All three sisters were found to have streak gonads on ultrasound. They all had primary amenorrhea and normal secondary sexual characteristics. Their endocrine profile showed high levels of FSH and LH and one of the sisters had prolactinaemia. Their intellectual capabilities are impaired and they are moderately mentally retarded. Their height is far below the third centile and below the average height in their family. All three sisters have a characteristic facies, with a short philtrum, long columella and prominent antihelix. They also have a short neck with a moderate degree of kyphoscoliosis. One of the sisters had a congenital papillomatous lesion behind the right ear. Routine chromosomal analysis showed a 46XX karyotype.

p-023

Rett syndrome – Clinical and molecular genetic correlations

E Said[1,2], A Cuschieri[1,2], D Soler[3]

[1] Department of Anatomy, University of Malta;
[2] Genetics Clinic, St Luke's Hospital; Department of Paediatrics, St Luke's Hospital. Malta

Rett syndrome is an X-linked dominant condition resulting from mutations in the MECP2 gene. Approximately 99.5% of cases are sporadic. Classical Rett syndrome affects girls. It is a progressive neurological disorder characterized by normal birth and apparently normal psychomotor development during the first 6-18 months of life and the loss of purposeful hand use. The diagnostic criteria for Rett syndrome also include an acquired microcephaly, severe impairment of expressive and repetitive language skills, severe psychomotor retardation and the development of gait apraxia and truncal ataxia between the ages of 12 months and 48 months. However since the use of molecular biological techniques for the diagnosis of Rett syndrome, several atypical cases have been identified. Mutations in the MECP2 gene have been identified in individuals with patients previously diagnosed with autism, mild learning disability or mental retardation with spasticity or tremor. Males meeting the clinical criteria for Rett syndrome have identified with a postzygotic MECP2 mutation resulting in mosaicism.

We present here our initial experience with molecular diagnosis in Rett syndrome. In two girls who presented with the clinical picture of Rett syndrome, a different truncating mutation was identified in each. A rare single nucleotide substitution was detected in a third girl with an atypical presentation. These cases will be presented and discussed.

p-024

Familial periventricular heterotopia: Mutation in the FLN1 gene

E Said [1,2], A Cuschieri[1,2], A Galea Debono[3], [1]Department of Anatomy, University of Malta; [2] Genetics Clinic, and [3] Department of Neurology, St Luke's Hospital. Malta

Familial bilateral periventricular heterotopia (BPNP) is a neuronal migration disorder characterized by the presence of uncalcified nodules of neurons ectopically situated along the surface of the lateral ventricles. It is an X-linked dominant condition and has been associated with protein truncations or splicing mutations, which tend to cluster at the N-terminal of the FLN1 protein causing severe predicted loss of the protein function. Prenatal lethality is associated with hemizygous boys.

We would like to present two sisters who presented with epilepsy. Their MRI investigation showed bilateral periventricular nodular heterotopia. A third sister presented with recurrent miscarriages but on investigation, her MRI also showed signs of periventricular heterotopia. Their mental capabilities were normal. DNA analysis of their DNA for mutations in the FLN1 gene showed a dinucleotide substitution leading to protein truncation, which was maternally inherited.

p-025

The national human DNA biobank in the post-genomic era

I Borg, D Galea, W Cassar, A E Felice,

Laboratory of Molecular Genetics, Department of Physiology and Biochemistry, University of Malta

The DNA biobank at the laboratory of molecular genetics, based at the University of Malta, was established five years ago. It holds a substantial collection of DNA which was generated from blood samples, submitted to the laboratory for molecular diagnosis of genetic disorders and through the neonatal and antenatal screening programmes for thalassaemia and other haemoglobinopathies. Recently, Malta became a partner in a new Eurordis project entitled EuroBioBank. This project brings together eight[+] different countries of the European Community, thus gathering twelve[+] banks and facilitating the access to a total of nearly one hundred and fifty thousand samples of DNA, tissues and cell cultures. The main aim of the project is to set the first operating network of rare diseases biological banks, thus reaching a critical mass of collections indispensable for research on rare diseases affecting around ten[+] to twenty[+] million people in Europe. Through this project the management of the Maltese biobank is being upgraded to European standards. Ultimately, European recognition and certification, would also endow our biobank with the status of a teaching centre on biobanking.