What is angelman syndrome biology essay

Parents: What is Angelman Syndrome? Me: Angelman syndrome is a nervous disorder of the brain also called as Puppet syndrome. The syndrome was first reported by a British pediatrician Dr. Harry Angelman in 1965. It leads to mental disorder accompanied with speech problems. This is a very rare condition that sometimes even doctors are not completely aware of it. The syndrome is often misdiagnosed with cerebral palsy, autism or other mental disorders of children. The occurrence is approximately 1 in 25, 000.

Parents: What is the Prognosis of the syndrome?

Me: The individuals with this condition have quite a healthy and normal life span. Some of the common features that can be noted are sleeping disorders, attention deficiency, speech problems and hyperactivity. Even these can slowly diminish with age. Their sexual development is normal. Puberty and menstrual cycle are also normal and occur at the right approximate age. There are high risks of having severe developmental delays which can be minimized or avoided to an extent by early diagnosis and therapy. They can lead an independent adult life except people who also have epilepsy along with this syndrome.

Parents: We found her being slightly abnormal, she wasn’t able to grasp what we are telling and is really struggling to pronounce words. What are the other possible symptoms?

Me: The main symptoms of the disease are mental retardation, speech problems and hyperactive behavior. It is usually present right from birth but the symptoms of it are mostly not noticed until the age of 3. But certain developmental delays can be noted between 6 to 12 months of the child.

Usually their MRI and CT scan reports show structurally normal brain features. They may have no speech or very low speaking capacity. They have higher tendency in actions rather than verbal communication.

They show some unique behavior like hand flapping, attention deficiency, frequent laughter, sleeping disturbances, delayed toilet training, feeding problems and easily excitable personality.

Seizures are noted only after the age of three so the possibility of identifying the syndrome before this age is not always possible. Their Electroencephalography (EEG) reports turn out to be abnormal; EEG is a test used to check the neural activity of the brain. They have much attraction to water and are highly sensitive to heat.

It is not completely known why laughter is so frequent in this syndrome. Continuous smiling, abnormal facial gestures followed by burst of laughter in public are noted in almost 70 – 75% of the cases.

They may not have good balancing capacity to walk. Trembling legs are noted along with ataxia. Ataxia is a condition where there is no co-ordination of muscular movements. They have trembling feet resulting is disability to walk. Normal sitting and walking may take 3-4 yrs of age. In highly severe cases walking is not possible until they are older, or it may be robotic.

100% of the cases are mentally retarded with attention deficit and which is non-progressive. They may be severe in most of the cases. Mostly they would need a sheltered life in their adulthood.

Parents: Oh! Do they show any abnormal physical features? Because our daughter seems to look quite normal.

Me: Yes! They do. Some of the common ones are a flat head at the back, wide opened mouth with spaced teeth, light hair and eye color, deep set eyes, excessive chewing behaviors, lightly pigmented skin texture, uplifted arm position, enlarged toes, soft and tender palms, tongue thrusting, and frequent drooling. A small head may be found in certain cases. All the symptoms which I have said both physical and clinical need not necessarily be found in all kids with this syndrome. They may occur in different combinations and in different levels.

Parents: How did the condition arise?

Me: Angelman syndrome occurs due to the deletion of a part of the chromosome 15 known as 15q11-13 that comes from the mother which results in abnormal or no expression of the maternal chromosome in the child. And hence all the functions of the chromosome 15 are being affected. Around 60-65% patients are affected by this cause.

In 2-5% of the cases there may be two copies of chromosome 15 from the father and no chromosome from the mother. This condition is termed as uniparental disomy. Sometimes the chromosome obtained from the mother functions exactly the same as the chromosome obtained from the father.

Rarely AS may result due to breaks in the chromosome like translocation where two chromosomes break and exchange their broken pieces. The other type is inversion where a chromosome breaks and gets attached in the

opposite direction. In both these cases the exact combination of amino acids is changed which would affect the production of ubiquitin ligase protein.

And finally in 20% cases there may be a fault in the UBE3A gene which is present on chromosome 15. UBE3A is ubiquitin ligase, which is considered as one of the major factors for the normal development and functioning of the brain. The relevancy of this gene to the disease is not yet completely known. 15-20% of the cases are unidentified mutation. They are still under study and a clear cause is not defined.

Parents: What is the importance of these chromosomes?

Me: Every chromosome is made of DNA which consists of specific amino acids. Different combinations of amino acids help in producing different proteins which are responsible for specific functions in the body. So when there is an alteration in the chromosome it affects the production of the particular protein. So automatically the protein function is lost and the relevant disorder arises. The protein that is involved in brain growth and function is called as ubiquitin ligase protein which is produced from the chromosome 15 of the mother.

The condition is always from the chromosome 15 of the mother. The same chromosome from the father is also equally important but alterations in the fathers gene would lead to a different condition called the Prader Willi Syndrome.

Parents: What are the ways of diagnosis?

Me: Diagnosing AS is difficult during infancy. The criteria for diagnosis was developed only in 1995 and further revised in 2000 by the Angelman syndrome society (USA). In certain cases parents or doctors may find developmental delays between 6-12 months of the child. Even all brain scan reports turn to be quite normal. Only after the age of two or three notable changes can be found like concentration problems, speech impairment, balance disorder, frequent smiling or flapping of hands. After the age of three EEG reports can be found abnormal which is be followed by DNA analysis. Sometimes even genetic reports turn out to be normal which can lead to a lot of confusion and misdiagnosis. Family history of the syndrome and development history of the child is completely studied and genetic expression of the ubiquitin protein is confirmed.

The confirmatory test for the Angelman Syndrome involves testing of blood in four steps:

The size, shape and number of chromosomes in a cell sample are noted for changes. This is known as karyotyping.

Genetic analysis to find missing chromosomes. This is done by a specialized process called FISH (fluorescent in-situ hybridization).

A test called DNA methylation test is done where the result will confirm whether the DNA of both the parents is expressed. If both the DNA copies are expressed it means that they are active. In cases of AS only paternal or the fathers DNA is expressed.

Finally UBE3A protein is sequenced. This is done because sometimes DNA methylation test turns to be normal. This is due to the condition that maternal DNA is normally expressed but mutated.

Parents: Is Gene therapy possible. What are the other possible treatment methods?

Me: There is no possible treatment for the disease at the genetic level. Since 99% of the cases are spontaneous mutation the possibility of prevention is also at the least level. Angelman syndrome is a collection of various medical conditions; hence separate therapies can be carried out for every symptom to provide a better lifestyle for the patient. The therapies are selected according to the noted symptoms and their level of effect on the individual.

From the age of 3 speech and communication therapy is recommended for improving their speaking and communicating skills. Occupational therapy is carried out for everyday living skills. Physiotherapy can help in better walking and other motor activities. Sometimes hypermotoric behaviors can’t be controlled by behavioral therapy so perfectly safe environment must be provided.

If the condition is accompanied by epilepsy, separate medications are followed as prescribed by the physician for treatment of seizures. Medications are also available for sleeping problems, hyperactivity etc. Non prescribed sedatives are not to be given because they may lead to negative side effects. Because that they have feeding problems their nutritional status should be frequently monitored. Surgeries are available for conditions like strabismus and other orthopedic problems. Surgical rod stabilization is done

for severe curvatures. During old age the individuals become less mobile and are not much active. They must be given scheduled work under supervision to avoid obesity and scoliosis. Scoliosis is a condition of severe curvature side to side in the spinal cord.

Parents: What is the mode of inheritance? Will our future children be affected?

The risk of inheritance is based upon the type of mutation that occurs in the parents.

With no family history for the disease and if the occurrence is completely spontaneous during cell division then the chances of getting the disorder in consequent children is <1.

If the mutation was a translocation that is unbalanced or if it is a deletion then the siblings is at a risk of 50%.

If the mutation is uniparental disomy then the risk is <1, but the uniparental disomy patient should be checked for a Robertsonian translocation. Because the presence of this translocation can again increase the risk by 50% in the siblings. Robertsonian translocations are special type of mutations where the short q arm of the chromosomes is completely lost leading to complete loss of the genetic information.

If it is a mutation in the UBE3A gene, and if the same mutation is found even the mothers DNA the the risk of the sibling is likely to be 50%. If the mother is normal then there is only <1% risk.

If it was a imprinting effect with deletion of the imprinting centre then the risk is 50% of all siblings and if it is without the deletion of imprinting centre then the risk factor reduces to <1%.

For all other non identifiable mutations the risk can be upto 50% with no familial risks. But risk factors can be concluded only after having a through DNA test of the child and the parents along with the family history of the disease.

Before having the second child it is recommended you meet a genetic counselor and carry on a prenatal testing.

Parents: What is prenatal testing?

Me: