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RARE DISEASE CASE REPORT- MICROCEPHALY

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ABSTRACT:

Microcephaly is a rare disorder[01]. We report on 8-year old girl who was being suffering with the Microcephaly was admitted in the hospital with chief complaints and the observed symptoms to admit in the hospital are “Seizures” and “Squint” and not even having a stable vision on any of the particular object. Microcephaly can be caused due to the neurodevelopmental problems which is phenotype in the patients, often genetic causes. Microcephaly can also be defined as lower occipitofrontal than the third percentile or more than two standard deviations below the mean for sex, age and ethnicity. Patients who were being suffering with this disease can have the various neurological manifestations, psychomotor problems, delayed developments, and epilepsy which are frequently shown by the affected patients and also, accompanied by the facial dysmorphism and also affects the major organs present in the body.

Congenital microcephaly is present at birth, whereas postnatal microcephaly occurs later in life[10]. Genetic abnormalities, syndromes, metabolic disorders, infections, prenatal, perinatal, and postnatal injuries[7,9]can cause both congenital & postnatal microcephaly[2].

Neuroimaging with magnetic resonance imaging (MRI) is often the first diagnostic test in evaluating children with microcephaly. Microcephaly is a lifelong condition with no known cure. The prognosis is usually worse for children who experienced an intrauterine infection. Microcephaly has become much more prevalent in the news and scientific community with the recent emergence of Zika virus as a cause of congenital[3].

The major aim of this case report is to present a typical case of this condition, to bring awareness on several diagnostic options and little in treatment too, and to advocate referral a neurologist given its potential severity. There were less treatment opportunities have been found for this condition. Medication, diet, speech or counselling tends to help the patient to improve their activeness or responding to the particular work.

Keywords:

Zika virus,Brain development,Microcephaly,Magnetic resonance imaging(MRI),Congenital microcephaly

Occipitofrontal circumference

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INTRODUCTION:

Microcephaly is the condition in which a baby's head is significantly smaller than the expected, often due to abnormal brain development the baby is either born with a smaller head (congenital) or the condition develops as the baby gets older(acquired). It is a rare condition occurring in 2-12 babies per 10000births and it is present in fewer than one million cases per year in India. The treatment can help, but this condition can't be cured. It requires a medical diagnosis. Lab tests or imaging or often required for the diagnosis of such types of disorders.

The etiology of microcephaly can be broadly divided into 2 categories:

Premature fusion of cranial sutures (I.e, craniosynostosis)are poor brain growth.

- CONGENITAL MICROCEPHALY:

Maternarydeprevation can also .read to microcephaly (e.g., folate deficiency, malnutrition, hypothyroidism).

- POSTNATAL ONSET MICROCEPHALY:

The post natal onset microcephaly can result from inborn errors of metabolism including congenital disorders of glycosylation , mitochondrial disorders, peroxysomal disorders and menkes disease. Disruptive injuries such as traumatic brain injury, hemorrhagic and ischemic stroke, and hypoxic-ischemic encephalopathy can also lead to microcephaly.

Hypoxic-ischemic encephalopathy is considered the main cause of acquired microcephaly.

Although more information is needed to confirm that Zika virus causes this condition, thus far zika virus RNA was isolated from microcephaly foetuses and amniotic fluid.

- Leaning difficulties :

This can be defined as an IQ below 70. On average this can effect 2-3% of the general population. For example, patients with downs syndrome and other syndromic conditions can have microcephaly and are also prone to syndromic intellectual disabilities.

Depending on the individual patients case , learning difficulties can present in several different ways such as:

Speech delays, difficulty with moment, and chilfren may not reach average height rate and may be of short staure or exhibit dwarfism.

The epidimologic study of the microcephaly includes:

Microcephaly is not a common condition[5]. state birth defects tracking systems have estimated that microcephaly ranges from 2 babies per 10000 live births to about 12 babies per 10000 live births in the United states. 2 large population-based studies have found similar incidents of microcephaly in new borns:0.56% and 0.54% perspectively[1,2]

Similar studies for post natal onset microcephaly could not be found and are not mentioned in the American Academy Of Neurology's (AAN).Practice Parameter : Evaluation of the child with microcephaly (an evidence-based review [3].

Types:

Two different types of microcephaly are recognized:

Primary and secondary

- PRIMARY MICROCEPHALY:

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It occurs when the brain does not grow to the normal size in utero. Irradiation of the abdomen in pregnant women or maternal infection with cytomegalovirus, rubella(German measles),toxoplasmosis, varicella (chickenpox),or Zika virus during the first 3months of pregnancy may sometimes result in primary microcephaly in the infants.

Evidence suggests that maternal alcohol consumption during pregnancy and poor nutrition may also contribute to primary microcephaly. Genetic factors also plays a main role. For example, autosomal primary microcephaly is caused by mutations of any of at least 7 different Gene's.

- SECONDARY MICROCEPHALY:

It generally occurs when the brain, roughly normal in size at birth but the brain doesn't grow there after. brain infection traumatic brain injury, and oxygen deprivation in the brain are caused of post natalonset[7,9]. This type of microcephaly can also occur in association with certain metabolic disorders or genetic syndromes such as rett syndrome.

History:

Microcephaly was first discovered by D.Holmes Morton and Richard Kelley of the clinic for special children. Dr.Morton, who established the clinic as both a paediatric practice and a genetics diagnostic laboratory, saw the first case of Amish microcephaly in 1988 when a family asked him to come and see their child.

People with small heads were displayed as a public spectacle in ancient Rome people with microcephaly were sometimes sold to freak shows in north America and Europe in 19th and early 20th centuries.

Case Presentation:

An 8 year old girl admitted into the hospital with the chief and observed complaints of Squint eye and seizures frequently and not having a stable vision on any of the particular object. The diagnosis after admission has reported that she has been suffering with microcephaly.

Diagnostic Error:

This Microcephaly can be detected or diagnosed during the foetal life to prevent further complications in her life. Her condition was not diagnosed during her foetal life (during pregnancy of her mother) by the diagnosers[4,8]. Repeated radiational x-rays or any scannings may also effect the genes and cause the mutations which can be the major reason for this disease.[9]

- ✓ **Computed tomography (CT or CIT) scan:**

This technology employs x-rays along with a computer to create more detailed horizontal or axial 3D slices of a body part. This is useful for revealing information about the organs, bones, muscles and fat. CT scans are particularly good for studying bone injuries. Ct scans are not advised during pregnancy.

Ct study of brain plain:

Serial axial sections of the brain were studied from the base of the skull to the vertex without added contrast

Ventricular system, cisternal spaces and cerebral sulci in general are normal

No shift of mild line structures

Attenuation values of the brain parenchyma are normal

No evidence of Haemorrhage or Tumour

No intra or extra axial SOL

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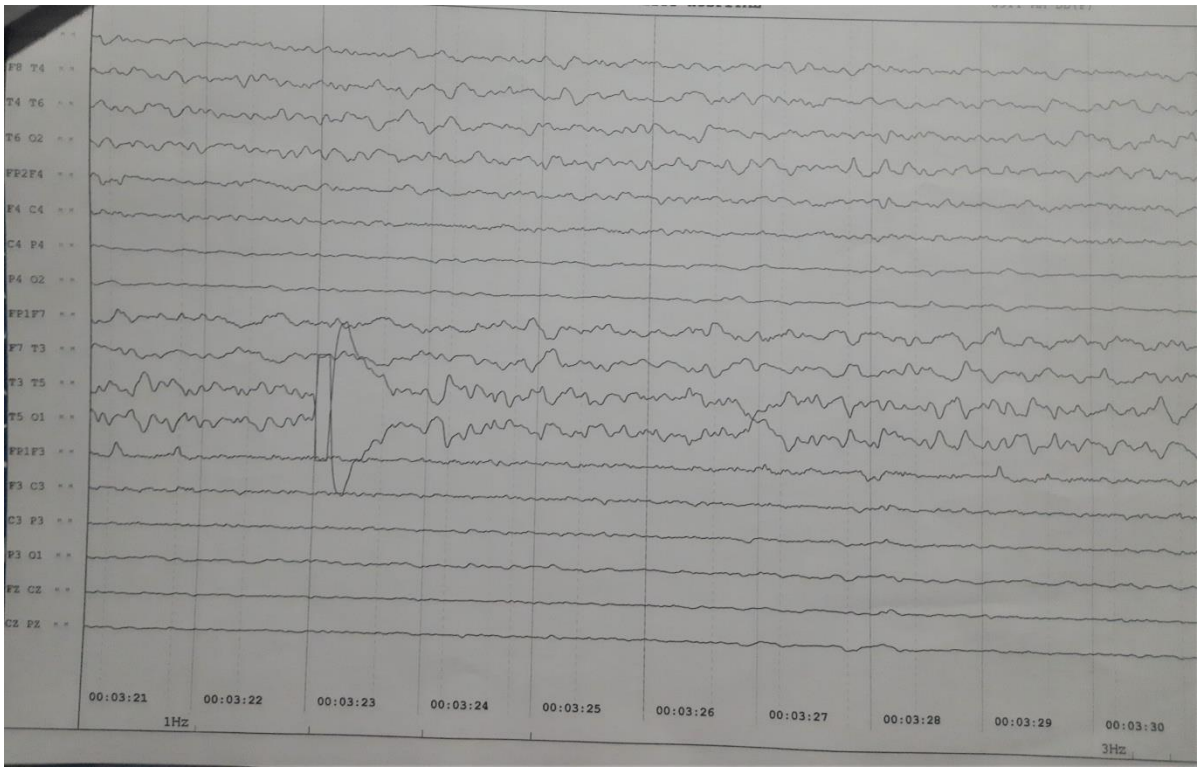
*Sutures of skull are narrowed with early closure of anterior fontanella.

*BPD is corresponding to 35 Weeks

EEG shows:



IMPRESSION: Craniosynostosis resulting in microcephaly

Drugs using by the patient:

s.no	Drug	Dose	ROA	Frequency
1	Tab.Phenytoin sodium	100mg	P/O	BID
2	Syrup.Sodium valproate	Each 5ml contains 200mg	P/O	BID

- **Follow-up and outcomes**

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According to all the laboratory profiles, mentioned above the patient has been diagnosed with Microcephaly Disease and physicians prescribed the following medications in order to control or to prevent the further complications of the disease.

Discussion:

Microcephaly is an autosomal recessive disorder. It is often shortened to MCPH(Microcephaly Primary Hereditary). It is a condition in which the new born infants are with a very small head and with a small brain.

The term "Microcephaly" is a Greek word which means a "small head". These infants who were affected have an unusually small head circumference compared to other infants of the same age and sex.

This disease causes intellectual disability, which may be typically mild to moderate and it may not become more severe with age. Most affected infants on growing, they have delayed speech and language skills.

The conditions that affect the brain growth may to cause infections, genetic disorders and severe mal nutrition.

The genetic conditions that cause microcephaly includes; Cornelia de Lange Syndrome, Cri du chat Syndrome, Down Syndrome, Seckel Syndrome, Trisomy 18, Trisomy 21 etc..

Microcephaly can also lead to problems such as uncontrolled Phenylketonuria(PKU) in mother, (congenital rubella, congenital toxoplasmosis, congenital cytomegalovirus(CMV) etc….

Microcephaly is also caused when the pregnant woman is infected with Zika virus. it is reported that in the US, microcephaly occurs in 2 to 12 babies per 10,000 births.

It is a rare condition and there is no specific tests to determine if a baby more likely to have cerebral palsy.

WHO has been working closely with countries affected by Zika virus and related complications on the investigation and response to the outbreak since mid-2015.

Microcephaly is the condition in which genotypically and phenotypically heterogeneous causes. The cooperation between molecular geneticists was interdisciplinary and clinicians play a major role in to facilitate the elucidation of the underlying causes of microcephaly.

According to the genetic spectrum, microcephaly may differ from ethnic groups, even in the case if clinical characteristics are similar. Therefore consideration of the radical background may be helpful to interpret WES results.

WES and CNV for the patients who were being suffering with microcephaly is useful and time-/cost-effective for genetic diagnosis and treatment considerations. According to the study on the microcephaly disease, autosomal recessive microcephaly was rare and autosomal dominant was the predominant mode of inheritance.

Microcephaly can be also be present as non-syndromic or with various hereditary syndromic features. According to the OMIM database they have been reported that over 900 OMIM phenotypes and genes related to the microcephaly.

The CNV analysis can increase the diagnostic rate from 30 to 47.5%. The rate of diagnosis on pathogenic CNV's in neurodevelopmental disorders, including primary microcephaly, has been reported to be 13.2-20.8%.

The WES and CNV are the most effective approach to diagnose the underlying causes of the disease microcephaly. The diagnosis of the microcephaly via.., WES and CNV analysis can help to determine the genetic mechanism of the disease and predict the prognosis.

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Additionally these may provide further information to the patients who were being suffering with this disease about the future reproductive decisions and also about the genetic counceling, including the oppurtunities for targeted therapies.

Now-a-days most of the diagnosed patients are detected with the variants showed an autosomal dominant inheritance pattern. In those variants, two of them were associated with the autosomal recessive and x-linked dominant inheritance, respectively.

According to the previous studies, they have been dealt with the congenital microcephaly in kindred-ship families and focussed on neurodevelopmental defects in the foetal period.

If the sutures fuse permanently ,the skull may take on abnormally shape and the head circumference will grow at a much slower rate than age matched controls.

Decreased brain growth would than lead to decreased outward force exerted on the skull, and decreased expansion of the head circumference. This process my result in a normally shaped or symmetric head, as opposed to the abnormal shape that results from cranio synostosis .Less commonly, genetic neurodegenerative diseases (e.g., Rett syndrome) will cause progressive microcephaly in infants and toddler.

Treatment:

Microcephaly is a life long condition. There is no known cure or standard treatment for microcephaly. Because microcephaly can range from mild to severe, treatment options can range as well. Babies with mild microcephaly often don't experience any other problems beside small head size. These babies will need the routine check-ups to monitor their growth and development.

For more severe microcephaly, babies will need care and treatment focused on managing their other health problems as mentioned above :

Development services early in life will often help babies with microcephaly to improve and maximize their physical and intellectual abilities. These services, known as early intervention, these can include speech, occupational and physical therapies. Sometimes medications are also needed to treat seizures or other symptoms.

The patient now being treated with the prescribed drugs by the physician which can help for slight moment or to decrease the chances of getting further health complications.

Conclusion:

In this case we've focussed on the causes of microcephaly, types and drugs which are used in the treatment of that disease. We have to know the importance of the diagnosis of the pregnancy woman during the pregnancy period. We also got o know the detailed history and physical examination which suggest a diagnosis or further testing.

Microcephaly is defined as a head circumference more than two standard deviations below the mean for gender and age. It may be present at birth or develop postnatally. While a number of genetic, metabolic, environmental, and infectious may play a major role in disturbing the brain growth and cause microcephaly, no etiology is identified in up to 40% of cases. Further diagnostic evaluation may include neuroimaging, and metabolic or genetic testing.

Ethical committee approval:

Obtained approval from theLatha hospital ethical committee. We also obtained informed consent from the patient which we have attached with this case report for the journal's reference.

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