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case report

Assessment of the case report of an Angelman Syndrome child in Janzour City, Libya

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ABSTRACT

Background: Angelman syndrome (AS) is a genetic neurological disorder that was first described in 1965 by Dr. Harry Angelman Angelman syndrome is a rare neurogenetic disorder that is characterized by microcephaly, severe intellectual deficit, speech impairment, epilepsy, EEG abnormalities, ataxic movements, tongue protrusion, paroxysms of laughter, abnormal sleep patterns, and hyperactivity, To assess the clinical subject in individual with AS, we retrospectively analyzed medical records of 5-yers old male seen at the pediatric physical therapy Clinic at Altahady Center for Intensive Physical Therapy for Children. Janzour City. **Case Presentation:** We present the case of a 5-year-old male patient from Janzour City, Libya, diagnosed with Angelman syndrome, with deletions of the proximal long arm of chromosome 15q11.2–q13 in individuals with Angelman syndrome. The first-line clinical diagnostic test for patients suspected of having Angelman syndrome is DNA methylation testing, including neurological manifestations including include microcephaly, seizure disorder, ataxia, muscular hypotonia with hyperreflexia, and motor delay. Psychomotor delay is evident by 6 months of age, and can be associated with feeding difficulties and muscular hypotonia. This review finding was, a multidisciplinary approach is imperative for managing patients with AS. Parental counseling and genetic advice are crucial for families and caregivers. **Conclusion:** Physicians should consider rare syndromes such as AS in children or adults with neurodevelopmental delay. Noting clinical presentation is very important; extensor and flexor spasms are not typically described as seizure types in AS because clinical suspicions play a crucial role in choosing the required laboratory tests. On the other hand, a multidisciplinary approach is necessary for genetic syndromes like AS because they influence all aspects of patients' lives.

Key words: Angelman syndrome, proximal long arm, hypotonia, hyperreflexia, ataxia, child, Libya.

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INTRODUCTION:

Angelman syndrome (AS) is a genetic neurological disorder that was first described in 1965 by Dr. Harry Angelman Angelman syndrome is a rare neurogenetic disorder that is characterized by microcephaly, severe intellectual deficit, speech impairment, epilepsy, EEG abnormalities, ataxic movements, tongue protrusion, paroxysms of laughter, abnormal sleep patterns, and hyperactivity [1]. In studies published in 1987, Oregon Health Sciences University, Portland, Oregon, high-resolution chromosome banding revealed de novo interstitial deletions of the proximal long arm of chromosome 15q11.2–q13 in individuals with Angelman syndrome; the findings were later confirmed by molecular methods. Subsequent work showed that the deletions always occur on the chromosome 15 inherited from the mother, and the identification of paternal uniparental disomy of chromosome (15upd) (15)pat) in individuals with Angelman syndrome provided further evidence that the disorder results from the absence of maternal contribution of at least one gene in the 15q11.2–q13 region 8. We now know that Angelman syndrome is caused by loss of function of the ubiquitin–protein ligase E3A (UBE3A) gene, which, in neurons, is expressed from the maternal chromosome 15 only [2]. Angelman syndrome (AS) is a neurogenetic disorder present in one in 12,000 to one in 20,000 Live births. It is characterized by severe developmental delay, microcephaly, ataxia, speech impairment, seizures, frequent laughter, and hand flapping. Dysmorphic facial features include a wide mouth, maxillary hypoplasia, and prognathia [2]. The salient clinical features of Angelman syndrome include microcephaly, seizure disorder, ataxia, muscular hypotonia with hyperreflexia, and motor delay. Psychomotor delay is evident by 6 months of age, and can be associated with feeding difficulties and muscular hypotonia, although these features are not specific to Angelman syndrome. Microcephaly is not present at the time of birth, but often develops in the first 3 years of life; normocephaly is not infrequent, but macrocephaly is rare [4].To assess the figure of clinic patients with AS, we retrospectively analyzed medical records of individuals seen at the pediatric physical therapy clinic at the Center for Intensive Physical Therapy for Children.

Case presentation

We present the case of a 5-year-old male patient residing in Janzour city, Libya, diagnosed with Angelman Syndrome (AS). The diagnosis was made by molecular genetic testing, which showed deletions of the proximal long arm of chromosome 15q11.2–q13 in individuals with Angelman syndrome. He was born to non-consanguineous parents who did not suffer from developmental delay or disorder and has a normal 8-year-old daughter, and no family history of genetic disorders.He has had a history of epilepsy since birth. He has had a history of seizures since the age of 1 year to Naw age of 5 years.Case present, Physical examination showed happy facial features, including microcephaly, seizure disorder, ataxia, muscle weakness with hyperreflexia, delayed movement, and inability to respond and stand. After diagnosis, he received treatment with an antiepileptic drug Depakine, Keppra, cortisone, which helped control his seizures effectively, and calcium, magnesium, vit D .A retrospective analysis of data from a 5-year-old male patient with clinical a genetic confirmation of AS was performed, and electroencephalographic not. However, electroencephalography findings were abnormal in the AS patient, and EEG showed a generalized spike and wave pattern (6). Over 855 of AS patients develop seizures in the first 3 years of life. Its onset varies from 1 month to 20 years (7). Epilepsy is severe in AS cases and is hard to control, as in our case. It seems that valproic acid is the therapeutic choice in AS epilepsy (8). Movement disorders of the hands and mouth, laughing spells, severe expressive speech disorders, a happy nature, hyposomnia, and anxiety are the major neurological characteristics of AS in adulthood.In addition, physical therapy was initiated with muscle strengthening exercises, balance exercises, stability exercises, and movement education, and continued with physical therapy until she improved in sitting, leaning on her own, wall walking, standing with assistance, walking with a walker, and speech therapy to address her developmental needs. The parents received genetic counseling and guidance as part of the comprehensive management plan.

DISCUSSION:

We introduced a child diagnosed with AS (deletions of the proximal long arm of chromosome 15q11.2–q13) who exhibited the primary clinical manifestations of the disorder, including had severe learning disability, epileptic seizures, ataxia, absent speech, and happy facial features with a prominent chin, deep set eyes, wide mouth with protruding tongue, and microcephaly with a flat

occiput(Figure 1 , The first-tier clinical diagnostic test for patients suspected of having Angelman syndrome is DNA methylation testing[5].This condition, originally known as the "happy puppet" syndrome, is now known by the less pejorative term of Angelman syndrome. For over 20 years, it was considered a rare disorder, and although the occurrence of families with affected sibs suggested a genetic aetiology, no known cause could initially be identified. In 1987, Magenis et al2 identified a deletion of chromosome 15q11-13 in two patients with Angelman syndrome, and subsequent work has shown that Angelman syndrome can be caused by a variety of genetic mechanisms which involve this imprinted region of the genome. The initial generalized extensor spasms involving both upper limbs and the head, occurring as short-lasting clusters (one spasm would persist for about 1 to 2 seconds, with recurrence in 10 to 20 clustering events, each occurrence lasting for about 3 to 5 minutes), transformed by the age of 1 year and 2 months into spasms of a flexor type resembling infantile spasms. All of these mechanisms affect maternal expression of the UBE3A gene, which lies at the 15q11-13 locus [4].Brain MRI in individuals with Angelman syndrome typically shows delayed myelination in combination with microcephaly, but no anomalies in brain structure or gross pathology21–23. Diffusion tensor imaging has indicated defects in language pathways. Tremulous limb movements begin in infancy and can cause unstable crawling, which progresses to truncal ataxia. Tremor in Angelman syndrome may represent cortical myoclonus with or without synchronizing EEG changes, or may represent only postural tremor [5].

Figure 1. Image of a child with a genetic diagnosis of Angelman syndrome

On physical examination, he had mandibular prognathism, strabismus, and an unusual laughing facial expression Figure 1. His head circumference was 51 cm.Most children with Angelman syndrome do not walk until they are 3–4 years of age. The gait can be distinctive, having a marionette-like, jerky quality associated with an out-toed, wide-based stance with pronated ankles. The arms may be uplifted and flexed at the elbows. About 10% of individuals with this condition do not achieve ambulation and are wheelchair-bound [6].A specific behavioural phenotype often leads the clinician to suspect Angelman syndrome, Affected individuals display excessive laughter and happy grimacing, easily initiated by social interaction and often associated with a protruding tongue, Individuals with Angelman syndrome show sufficient development in their social interaction domains to establish intentional relationships; they seek personal interaction and can understand simple commands, but they generally have little or no expressive speech26–28. Children with this

condition are active explorers, and are often described as being in constant motion and 'into everything'. This hyper motoric state, coupled with the tremulous movements and laughter, further reinforces the syndrome's distinctive behavioural phenotype. Children with Angelman syndrome are well known to have nighttime awakenings and have an apparently diminished total sleep time. Other clinical and behavioural features have been identified, and consensus criteria for clinical diagnosis have been published [7] Patients have severe intellectual disability and delayed motor development. They sit unsupported at about 12 months, begin to crawl (commando-walk) or walk on their buttocks at 18-24 months, and walk at an average age of 4 years (range 18 months to 7 years). 5 This child has a skeletal disability and delayed motor development and began to roll onto his elbows, stand with a cane, and walk on the wall after an intensive physical therapy programme [6]. In this review, sleep time and other clinical behavioural features have been identified,

CONCLUSION:

This case report discusses the clinical characteristics and genetic findings of a 5-year-old boy diagnosed with Angelman syndrome (AS). Early diagnosis of Angelman syndrome and appropriate therapy enable a better quality of life for children diagnosed with AS. The symptoms and signs are consistent with the documented clinical presentations of A. The first-line clinical diagnostic test for patients suspected of having Angelman syndrome is DNA methylation testing, deletions of the proximal long arm of chromosome 15q11.2–q13 in individuals with AS. Caregivers and healthcare providers should be aware of the high prevalence of these issues, as proper treatment may improve not only AS but also sleep and behavioral issues.

Consent for Publication

A consent form was provided by the patient's father, informing that acceptance of the publication of this case report, any information or documents that an individual gave were anonymized. An institutional approval letter was provided by Altahady Center for Intensive Physical Therapy for Children

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