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Rare disease

Do the physiotherapy results make us happy in a case with 'happy puppet' (Angelman) syndrome?

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Summary

This study aimed to investigate the benefits of physiotherapy programme in a patient with Angelman syndrome (AS) during a follow-up of 3 years. Assessments included: disability level with gross motor function classification systems, gross motor function with gross motor function measurement (GMFM), balance with Berg Balance Scale, motor performance with gross motor performance measurement (GMPM) and tonus assessment with Modified Ashworth Scale. Physiotherapy programme was performed during 36 months, 3 days per week by physical therapist according to Neurodevelopmental Treatment approach. During the 36 months, GMFM increased from 11.46% to 70.82% and GMPM increased from 1.25% to 70.25%. This case report is the first study about the effectiveness of physiotherapy with medium-term follow-up in a child with AS. Physiotherapy results make us happy in this particular patient with 'happy puppet' syndrome.

BACKGROUND

Angelman syndrome (AS) is a neurogenetic syndrome, first described by Dr Harry Angelman in 1965 in three severely mentally retarded children.[1] The incidence of AS is estimated to be between 1/10 000 and 1/20 000.[2] AS is also known as the 'happy puppet' syndrome due to the uncoordinated walking and laughing. Main characteristics of the disease are: severe developmental retardation speech disorders, movement and balance problems, behaviour and personality disorders. In addition, AS presents with severe mental retardation, microcephaly, macrostomia, maxillary hypoplasia, prognathia and neurological problems such as a puppet-like gait, ataxia and epileptic seizures with specific EEG abnormalities.[3]

Beckung *et al* examined motor impairments, neurological signs and developmental level in 23 children and adolescents with AS and concluded that most children with AS needed an early, active and individualised intervention programme.[4]

The aim of this study is to put forward the effectiveness of early physiotherapy as indicated in the literature and to discuss results of 3-year medium-term follow-up periods in a patient with AS. In this case presentation, we tried to find an answer to 'do the physiotherapy results make us happy in a case with 'happy puppet' syndrome?'

CASE PRESENTATION

Physiotherapy intervention commenced at 6 months as a part of routine follow-up of infants born preterm and delivery at gestational age of 33 weeks and a birth weight of 1900 g, by spontaneous vaginal delivery. There was no consanguinity in the family. He had a medical history of hospitalisation because of pneumonia at the age of 3 months and hip dislocation. Physical examination at the age of 12 months revealed: weight, 8 kg (25 p); height, 72 cm (50 p); head circumference, 43.2 cm (≤3 p) according to his corrected age (10 months). He was unable to bare weight on his legs and was able to sit with support. Deep tendon reflexes were normal without pathological signs. There was a mild increase in the lower extremity tonus. During the follow-ups, he began to stand and take a few steps at the age of 2 years and was able to walk with a wide-based gait after the age of 3 years. He was first evaluated as a child with motor and mental developmental delay and prematurity. Routine investigations including serum and urine aminoacids and thyroid function tests were normal. MRI showed mild dilatation of the third and lateral ventricles and mild delay in white matter myelinisation. EEG tracing during sleep and on awakening at 15 months showed a low electroconvulsive threshold with no active epileptiform abnormality at the time of the test. Microcephaly, mental-motor retardation and gastro-oesophageal reflux were present. A right thoracic scoliosis of 18 degrees was confirmed during orthopaedic evaluation when he was 30 months old. The Ankara Developmental Screening Inventory[5] results of our case when he was 3 years old showed a general normal development level of 12 months, language and cognitive development level of 11 months, fine motor development level of 9 months, gross motor development level of 12 months and social ability level of 12 months. He developed unexplained attacks of laughing and stereotypical movements more pronounced at the age of 3 years. He was then evaluated in the Genetics Department and found to have a deletion confirming the diagnosis of AS.

INVESTIGATIONS

Physiotherapy and rehabilitation assessments

(1) **Disability level** The level of disability was determined using the gross motor function classification system (GMFCS). The classifications range from I (independent mobility but some minor difficulties of speed, balance or coordination) to V (no independent mobility,

physical impairment restricts voluntary control of movement and antigravity postures). The GMFCS is widely recognised and used as a means of categorising motor function in children with cerebral palsy (CP) and in some other paediatric disability such as AS.[6]

(2) **Gross motor function measurement (GMFM)** The gross motor function of the case was assessed with GMFM. The original validation sample included children 5 months to 16 years of age. The GMFM (either version) would be appropriate for children whose motor skills were at or below those of a 5-year-old child without any motor disability. This test scores how individual motor actions and postures compare with specific descriptors and record change over time. The GMFM-88 item scores can be summed to calculate raw and percent scores for each of the five GMFM dimensions, selected goal areas and a total GMFM-88 score.[7]

(3) **Gross motor performance measurement (GMPM)** Gross motor performance was assessed with GMPM which was developed to evaluate quality of movement and change over time in children with CP age range from 5 months to 12 years.[8]

(4) **Balance** Balance is the main component of ambulation. The Berg Balance Scale (BBS) can be an indicator of balance and motor ability at the mean independent walking age. Balance was measured by BBS.[9]

(5) **Tone evaluation** The presence/absence and severity of spasticity were evaluated on the basis of the Modified Ashworth Scale (MAS).[10]

TREATMENT

Physiotherapy programme at the early rehabilitation period

The physiotherapy programme began when our case was 6 months old and was continued 3 days per week for 36 months by a paediatric physical therapist according to the Neurodevelopmental Treatment approach.

OUTCOME AND FOLLOW-UP

The percentage of total GMFM and GMPM scores of our case at 6, 12, 18, 24, 30, 36 and 42 months and the 36–42-month BBS scores are shown in table 1. The percentage of GMFM total scores are 11.46%, 23.33%, 24.47%, 35.55%, 40.57%, 52.47% and 70.82%, respectively. The percentage of GMPM total scores are 1.25%, 3.75%, 5.00%, 20.83%, 35.00%, 57.03%, and 70.25%, respectively. The correlation between GMFM and GMPM is shown in figure 1.

Our patient's trunk was hypotonic at 6, 12 and 18 months while the plantar flexor muscles of his feet showed hypertonus with a severity of 2 according to the MAS. He could sit independently when 3 years old with normal trunk tonus and a value of 1 (MAS) was recorded for the plantar flexors.

DISCUSSION

Children with AS frequently have normal prenatal and natal history. The developmental delay becomes evident during the very first months of life in severe cases and 6–12 months in moderate cases.[11] In this case, the patient was born preterm (33 weeks) contrary to the literature with low birthweight (1900 g), was a high-risk infant and was followed-up in an early intervention programme.

The use of special nipples may improve feeding in newborn AS babies with feeding difficulties. Gastro-oesophageal reflux is often present and requires upright positioning or specific motility medications. Laxative agents or a diet rich in fibre or can be helpful in patients with constipation.[12] Appropriate feeding positions were taught to the family as part of the physical therapy in our case.

Butinx *et al* found severe mental retardation and speech disorder in all their patients together with symptoms such as laughing attack, happy facial appearance, hyperactivity, ataxia, prognathism and macrostomy at various rates.[13] Our case exhibited all the characteristics of 'happy puppet' appearance with severe speech disorder, ataxic gait and happy facial appearance.

Studies on AS have found that about 90% of patients develop seizures in their first year of life.[14 15] The hospital record EEG results of our patient indicated that he did not have epileptic seizures.

Hartin *et al* stated that delayed myelinisation, white matter volume reduction and focal white matter signal abnormalities are much more common in AS than expected.[16] We similarly found a 'mild delay in myelinisation' in our case.

Beckung *et al* emphasised that the risk of increasing impairment needs to be anticipated by therapists to prevent long-term effects of muscle imbalances and motor asymmetries.[4] Our case was therefore followed-up with early rehabilitation.

Decreasing mobility with age, increasing joint contractures in the lower limbs and scoliosis have been described by Clayton-Smith.[17] Thoracic scoliosis is reported in about 40% of the adults and mostly in females.[18] Our case was similarly found to have 18 degrees of right thoracic scoliosis when 30 months old.

Van Buggenhout *et al* feel that physical therapy with adaptive chairs or positioners is needed for unstable or non-ambulatory children and for extremely ataxic children.[19] As

Table 1 GMFCS, GMFM, GMPM, BBS results

Age	6 Months	12 Months	18 Months	24 Months	30 Months	36 Months	42 Months
GMFCS level	**V**	**IV**	**IV**	**III**	**III**	**III**	**II**
The percentage of GMFM total score	11.46	23.33	24.47	35.55	40.57	52.47	70.82
The percentage of GMPM (%) total score	1.25	3.75	5.00	20.83	35.00	57.03	70.25
BBS score						0	18

BBS, The Berg Balance Scale; GMFCS, gross motor function classification system; GMFM, gross motor function measurement; GMPM, gross motor performance measurement.

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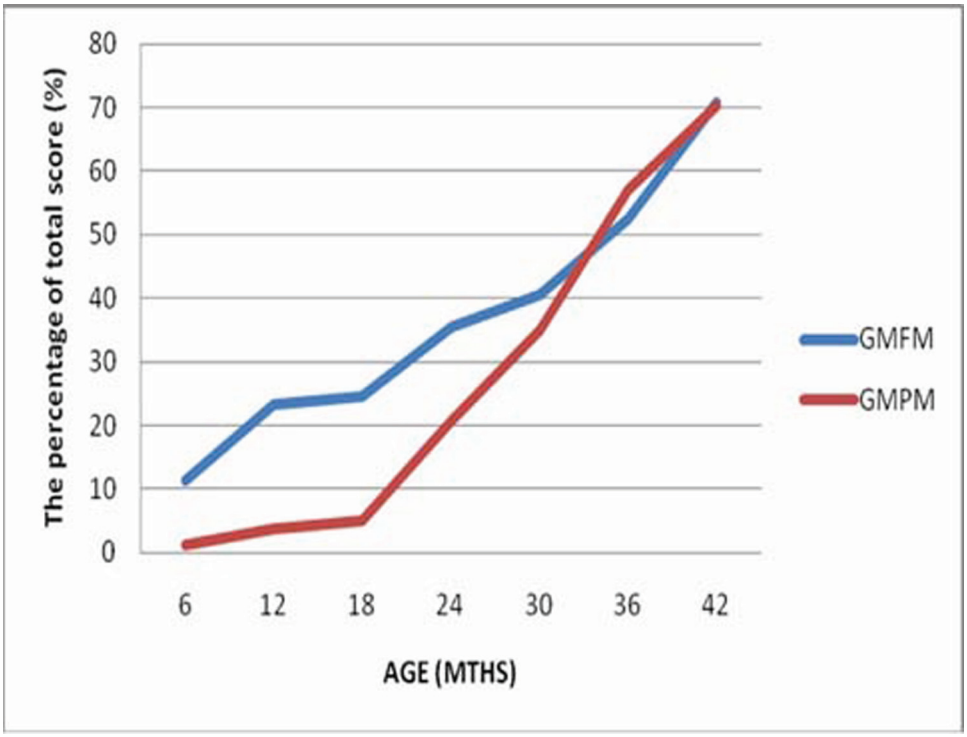

Figure 1 Gross motor function measurement and gross motor performance measurement results.

decreased mobility leads to difficulty in walking, prevention should be focused on providing rehabilitative, early intervention and psychosocial services in cases with severe neurological instability.[12] Occupational therapy is needed to stimulate fine motor and oral-motor control skills. Speech therapy including non-verbal methods of communication, picture cards or communication boards should be introduced, as active communication is poorly developed in this group of children.[19] Our case also received occupational therapy and speech therapy (reported elsewhere).

Dan *et al* have listed spastic diplaegia as a feature of AS.[20] They performed a kinematic and kinetic study of a standardised squatting movement in a group of children with spastic diplaegic CP and children with AS compared with normally developing controls. Children with spastic CP and AS were described as sharing some clinical features, such as trunk hypotonus and lower-limb hypertonus that was more marked distally and increased with active mobilisation. The children with AS displayed no anticipatory changes in muscle activity. There was lower extremity stiffening, agonist–antagonist muscle coactivation patterns and non-conservative postural reactions of the trunk, head and arms in both patient groups. However, this view may be contested as children with CP have more distinct neurological and functional abnormalities. Beckung *et al* aimed to examine the character of motor dysfunction in children and adolescents with AS.[4] This study focused on motor function and motor development. Gross and fine motor developmental level was assessed with the Cailler–Asuza Scale,[21] a validated motor assessment tool that measures the age of acquisition of motor milestones.[22] Gross motor function level was classified according to the GMFCS.[6] We similarly used the following functional outcome measurement in our evaluation: GMFCS, GMFM, GMPM, BBS.

In Beckung *et al* study, 23 children and adolescents (13 males, 10 females; median age 5 years 6 months; range 21 months to 23 years) with AS were included. Beckung *et al* found that in all 23 children and adolescents the gross and fine motor developmental levels were generally low.[4] Muscle tone was normal in 12 subjects, low in 11 subjects and high with general hypertonus in 10 participants. Trunk hypotonus was present in 17 subjects while muscle weakness was present in 21 subjects.[4] At 3 years of age our patient had a gross motor level of 12 months and fine motor level of 9 months. In addition, the first evaluation of our case showed hypertonus of the lower extremities and hypotonus of the trunk while 3 years later the trunk tonus was normal and plantar flexors were 1 according to MAS.

Beckung *et al* found a mean motor developmental age of 24 months that was less than half of the actual age in their study on subjects with a median age of 6 years. The immaturity of the subjects may explain why one-third of the participants in this study were classified at GMFCS level IV.[4] The GMFCS classifies motor function in children with CP, a heterogeneous group of children. The distribution of the GMFCS levels for children with CP has been described in two population-based studies.[23 24] Children with ataxic diplaegia were predominately classified at GMFCS levels I and II in both studies. Children with spastic diplaegia were distributed to all levels. Beckung *et al* stated that the motor dysfunction in subjects with AS was more homogeneous and the GMFCS appeared not to be a suitable classification for this group, mainly because of the inability of those who could not walk to make use of assistive devices. The validity of the GMFCS for children with AS was difficult to evaluate in this small sample. Although motor impairment is obvious in participants with AS, gross motor function is one of their best skills.[4] Despite the disadvantages of

using the GMFCS in AS patients, we used this scale for the classification of the disability level in our case. The gross motor development level increased from level V to level II during medium-term follow-up.

Balance skills are an integral part of gross motor abilities and poor balance causes difficulties with functional tasks involved in activities of daily living.[9] The BBS has potential for use with children as a measure of functional balance. Its ease of use makes it an appealing clinical measure. More research is needed to evaluate its reliability with a paediatric population and its use with a younger age group. It would be valuable as an evaluative index in children with CP and future research should also include evaluation of its responsiveness with a paediatric population.[9] We assessed our patient with BBS between 36 and 42 months. We could not perform a reliability study because we only had one case and we therefore compared our results internally. A BBS score of 40 and above is shown to constitute a high risk of falling. Our patient already had a high risk of falling but there was improvement over 6 months. The family was provided instructions on the home programme and how to make the essential arrangements at home.

Gowland *et al* investigated 28 children (25 with CP, 2 non-disabled, 1 with head injury) between the ages of 1 and 10 years to estimate the inter-rater, intra-rater and test-retest reliability of the GMPM and found high reliability.[8] We measured gross motor performance by GMPM. Our case's gross motor performance clearly improved after 3 years of follow-up. This demonstrates that physical therapy may improve the quality of gross motor performance as well as increase gross motor function.

Learning points

- To the best of our knowledge, this case report is the first article on the effectiveness of physiotherapy with medium-term follow-up in a child with AS. Physiotherapy results therefore did make us happy in a case with 'happy puppet' syndrome. Additional studies and well-established randomised controlled trials are clearly needed prior to determining the benefits and efficacy of early intervention for cases with AS in long-term follow-up within the clinical setting.

Competing interests None.

Patient consent Obtained.

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