The Treatment of a Child with Birth Asphyxia Induced Brain Atrophy, Adrenal Hemorrhage, and Bilateral Hyperoxaluric Nephrocalcinosis: A Challenging Case and a Unique Experience

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Abstract

Background: Birth asphyxia induced brain atrophy is an irreversible ominous condition that is generally presented as a severe form of cerebral palsy with a high possibility of the development of a serious handicap. There is no medical treatment known to be effective in this condition. The aim of this paper is to describe the treatment of a patient with this ominous condition that was literally brought the child back to life.

Patients and methods: A boy aged one year and nine months with birth asphyxia induced brain atrophy, bilateral hyperoxaluric nephrocalcinosis with early renal dysfunction and ultrasonographic evidence of adrenal hemorrhage. The boy was almost lifeless; he was not opening his eyes nor showing any spontaneous movement. He was not responding to moderately painful stimuli. He was only feeding with difficulties, breathing and his heart was beating. The boy was markedly hypotonic, but with rather brisk knee reflexes.

Results: The boy’s brain atrophy and neurological condition was treated with a new a multi-factorial treatment courses which led in about two years to a great improvement. Treatment of nephrocalcinosis with essential oil terpene preparation and oral pyridoxine resulted in complete disappearance of nephrocalcinosis within three months, and didn’t return with continuation of therapies.

Conclusion: The treatment of severe forms birth asphyxia induced brain atrophy is a highly challenging situation that demands highly motivated parents that are able to cope with multiple therapies over a prolonged period, for an obvious improvement to occur.

Keywords: Brain atrophy, New therapies; multi-fatorial

Introduction

Birth asphyxia induced brain damage with brain atrophy is an ominous condition that is generally presented as a severe form of cerebral palsy with a high possibility of the development of a serious handicap. This condition is irreversible with no medical treatment known to be effective [1, 2]. The aim of this paper is to describe the treatment of a patient with this ominous condition that was literally brought the child back to life.

Patients and Methods

A boy aged about one and nine months who had experienced birth asphyxia induced brain damage with evidence of brain atrophy on MRI study (Figures 1A-1D) was seen. His ominous condition was further complicated by bilateral grade 4 nephrocalcinosis with early renal dysfunction, and also by ultrasonographic evidence of adrenal hemorrhage.

The boy had three healthy siblings; two boys and one girl. The boys aged 14 and 10 years, whereas the girl aged 12 years. No family history of any neurological disorder was reported. The mother had recurrent renal stones since the age of 21, and her two brothers both had history of
The boy was delivered by normal vaginal delivery to consanguineous parents. The mother reported that after birth, the boy didn’t cry or breathe after several minutes, possibly more than ten minutes. According to the mother, the baby was deeply cyanosed, and the doctors resuscitated him, but they didn’t intubate him as they expected to do. The exact details of the resuscitation received by the child remained unknown. However, the resuscitation the patient received can never be described as an intensive resuscitation without performing intubation with endotracheal tube to facilitate effective ventilation.

According to Virginia Apgar scoring system of the severity of birth asphyxia, the child is expected to have a score of two or less in the presence of apnea and deep cyanosis at birth. Remembering that even an Apgar score of three is associated severe asphyxia, without intensive resuscitation (Hillary Scott, 1974, 1976) [1].

The boy was initially hospitalized during the first day of life because of the development of seizures. However, the boy was referred by the treating physicians after about three weeks of hospitalization to another hospital (Central Teaching Hospital of Pediatrics, Baghdad) because of the development of uremia. Laboratory test showed elevated blood urea at 197mg/dL, serum creatinine was 425 mmol/L (62-124 mmol/L), and serum potassium was 7.4 mmol/L (Normal: 3.5-5.3 mmol/L).

The boy was treated with a session of peritoneal dialysis which lowered blood urea to 7.2 mmol, and lowered serum potassium to 3.9 mmol/L. Serum sodium after dialysis was...
126 mmol/L (136-155 mmol/L). During the next few months, urea levels were fluctuating and ranged from 6.4 mmol/L to 11 mmol/L. However, serum creatinine was found to be less than 1 mg in more than one occasion. During these months’ serum sodium concentration ranged from 133 to 140 mmol/L, and serum potassium ranged from 3.7 to 6.3 mmol/L.

Ultrasound examination performed, on the second day of life, and at the age of eighteen days at the Central Teaching Hospital of Pediatrics, Baghdad showed bilateral grade 4 nephrocalcinosis: The right kidney was normal in size, and position with a length of 4.7 cm. The right pelvicalyceal system was also normal. However, there was dense calcified shadow occupying the whole pyramid with poor corticomedullary differentiation. The left kidney was normal in size, and position with a length of 4.5 cm. The left pelvicalyceal system was mildly enlarged and filled with debris. There was also dense calcified shadow occupying the whole pyramid with poor corticomedullary differentiation. The ultrasound examination also showed enlarged adrenal gland (2.2 cm) with cystic changes suggesting adrenal hemorrhage.

24 hours evaluation of urinary excretion of calcium was performed on the first month of life: The urine volume was 160 ml per 24 hour and urinary calcium was 40.9 mmol/24 hours (Normal: 25-75). Urinalysis performed during the second month of life showed normal findings. During the first year of life, urine examination was performed several times and showed intermittent pyuria and slight albuminuria, and microscopic hematuria. Granular cast excretion of 6-8/HPF was detected twice during the same year. The boy was receiving antibiotics for these urinary abnormalities.

Another ultrasound examination was performed by another radiologist during the fourth month of life showed grade 2 bilateral nephrocalcinosis. Both kidneys were normal in size, and echogenicity with well corticomedullary differentiation. However, patchy calcification was occupying the whole pyramids in both kidneys. Other abdominal organs including pancreas, liver and spleen were normal with no mesenteric lymphadenopathy or ascites.

The family consulted many doctors, and they told the family that the best option for is to leave the child without treatment to die early. However, the family brought him to our clinic asking for any hope and refused other doctors’ opinion, and refused to give up.

Results

When first seen at the age of one year and nine months, the boy was almost lifeless; he was not opening his eyes nor showing any spontaneous movement. He was not responding to moderately painful stimuli. He was only feeding with difficulties, breathing and his heart was beating. The boy was markedly hypotonic, but with rather brisk knee reflexes. He was having frequent generalized tonic clonic convulsions despite treatment with sodium valproate (140 mg twice daily). The seizures were initially controlled by switching sodium valproate to carbamazepine (50 mg daily) and Phenobarbital (15 mg daily). Carbamazepine was increased to 100 mg twice daily with in few weeks to abort completely short mild tonic clonic twitches. A new ultrasound examination was performed and showed diffuse bilateral nephrocalcinosis, and 24 hour urine examinations for oxalate showed hyperoxaluria. Essential terpenes oral capsule (Urinex, Pharco Co, Egypt) was used depending on the available evidence supporting the possible benefits associated with such treatment [2-5]. The oily capsules were divided and given with table sugar three times daily before feedings. For hyperoxaluria, the boy also received pyridoxine 100 mg per day orally.

Treatment resulted in Complete Disappearance of Nephrocalcinosis within Three Months, and Calcification didn’t Return with Continuation of Therapies

The boy’s brain atrophy neurological condition was treated with a new a multi-factorial treatment courses given along with nutritional support provided mainly in the form of royal jelly oral capsules (Table 1), and treatment led in a about two years to a great improvement in all parameters; literally brought him back to life.

The early response to treatment after the second course included improved sucking and feeding, eyes opening, and showing some response to painful stimuli. However, with this improvement spasticity and hypertonia replaced hypotonia. Baclofen, a muscle relaxant was necessary to control hypertonia and was gradually increased from 10 mg daily to 30 mg daily in three divided doses. The observable response to nandrolone decanoate after the seventh course included improved head control, increased movements of the limbs. Before the age of four years by few weeks, after the eighth course of treatment, the boy demonstrated the following abilities:

He was making some active spontaneous movements.

He could be seated on the chair with the help of parents, and he could move his head to look at things of interest (Figure 2).

Table 1: Multi-factorial treatment courses for brain atrophy.

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| Course | Duration | Medications |
|--------|----------|-------------|
| First course (20 days) | | Intramuscular piracetam, 200mg given on alternate days, 10 doses. Intramuscular citicoline 125mg given on alternate days, 10 doses. Oral pyritinol 40mg daily |
| Second course (50 days) | | Intramuscular piracetam, 200mg given every five days, 10 doses Intramuscular citicoline 125mg given every five days, 10 doses. Oral pyritinol 40mg daily |
| Third course (70 days) | | Intramuscular piracetam, 200mg given every week, 10 doses Intramuscular citicoline 125mg given every week, 10 doses. Intramuscular vitamin B12, 500 microgram every week. Oral pyritinol 40mg daily. Oral baclofen gradually increased from 10mg daily to 30mg daily in divided doses. Intramuscular cerebrolysin 1ml, given every week. |
| Fourth course (70 days) | | Intramuscular piracetam, 200mg given every week, 10 doses Intramuscular citicoline 250mg given every week, 10 doses. Intramuscular vitamin B12, 500 microgram every week. Oral pyritinol 60mg daily. Oral baclofen 30mg daily in 3 divided doses. Intramuscular cerebrolysin 1ml, given every week. |
| Fifth course (70 days) | | Intramuscular piracetam, 400mg given every week, 10 doses Intramuscular citicoline 250mg given every week, 10 doses. Intramuscular vitamin B12, 500 microgram every week. Oral pyritinol 60mg daily. Oral baclofen 30mg daily in 3 divided doses. Intramuscular cerebrolysin 1ml, given every week. |
| Sixth course (70 days) | | Intramuscular piracetam, 400mg given every week, 10 doses Intramuscular citicoline 250mg given every week, 10 doses. Intramuscular vitamin B12, 500 microgram every week. Intramuscular cerebrolysin 1ml, given every week. Oral pyritinol 60mg daily. Oral baclofen 30mg daily in 3 divided doses. |
| Seventh course (6 months) | | Intramuscular piracetam, 600mg given every week. Oral citicoline 200mg daily in single dose in the morning. Oral baclofen 10mg daily to 30mg daily in 3 divided doses. Intramuscular cerebrolysin 3ml, given every week. Six intramuscular injections of nandrolone decanoate (12.5mg), given at a one month interval. |
| Eighth course (6 months) | | Intramuscular piracetam, 800mg given every week. Oral citicoline 300mg daily in single dose in the morning. Oral baclofen 10mg daily to 30mg daily in 3 divided doses. Intramuscular cerebrolysin 3ml, given every week. |

Figure 2: The patient, few weeks before the age of four, at the clinic

He was responding to sounds by moving his eyes to the sound.

He was differentiating family members from other persons

He was distinguishing children from adults and expressing happiness when they come to play with him.

He was showing signs of happiness and smiles when caressed by parents, and was producing squeals to express marked happiness (Figure 3).

Figure 3: The boy was showing signs of happiness and smiles when caressed by parents, he was also producing squeals to express happiness [Photos are extracted from a video recorded by parents at home].

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He was showing signs of fear when hearing loud noises even from the street outside the house.

He was showing sometimes clear preference to watch TV when animated cartoons were displayed while never showed any attention to other TV programs.

Discussion

Birth asphyxia resulting from inadequate oxygenation during birth can cause hypoxic injury and damage to any organ (heart, lungs, liver, gut, and kidneys), but brain damage has generally the most serious consequences which may include hypoxic ischemic encephalopathy, cerebral palsy, brain atrophy, developmental delay or intellectual disability. Severe birth asphyxia is an ill-omened condition that can lead to death or a severe form of cerebral palsy and irreversible brain atrophy with subsequent serious disability. No therapies known to be associated with significant improvement in this ominous condition [1]. In this boy with a severe form of birth asphyxia induced brain atrophy, ultrasound examination also showed evidence of adrenal hemorrhage which is a well-recognized complication of birth asphyxia (Küçüködük, 1994) [6].

Essential oil terpenic preparations such as (Urinex, Pharco Co, Egypt) which contains pinene (31%), camphene (15%), and borneol (10%), and anethol (4%), fenchone (4%) and cineol (3%) have been used in childhood urolithiasis with important benefits. Urinex (Pharco Co.) is the essential oil preparations mostly available in the Middle East [3-5]. In this boy, the evidence-based rational use of essential oil terpene preparation for the treatment of nephrocalcinosis was shown to be beneficial. In fact, there is more recent evidence suggesting the possible benefit of essential oil terpenic preparation in the treatment of childhood urolithiasis [7]. There is some research evidence suggesting that piracetam can has a beneficial effects on impaired brain function, by improving neuronal and cognitive functions through increasing blood flow and oxygen consumption in the brain, and also improving the function of the neurotransmitters and brain neurotransmission. Piracetam has no significant side effect nor has acute toxicity at the doses used in human studies. The LD50 is 5.6 g/kg in rats and 20 g/kg in mice, indicating extremely low acute toxicity [8-12]. Piracetam has recently been used in the treatment of cerebral palsy [9-11].

Citicoline is a water-soluble naturally occurring substance that is generally grouped with the B vitamins. It is also considered a form of the essential nutrient choline [13,14]. Citicoline has been recently used with benefit in the treatment of some childhood neuro-psychiatric disorders including, pervasive developmental disorders including Rett syndrome [1,2], and kernicterus [15-20]. It has been shown that cerebral blood supply is increased by pyritinol resulting in an improvement of nerve cell metabolism, and it was used with benefit in milder forms of cerebral palsy [21,22].

Cerebrolysin is a mixture of free amino acids (85%) and 15% biologically active low molecular weight amino acid sequences which include low molecular weight neuro-peptides (Brain-derived neurotrophic factor, glial cell line-derived neurotrophic factor, nerve growth factor, ciliary neurotrophic factor [23].

Cerebrolysin has been used safely with benefit in a variety of neuro-psychiatric disorders including idiopathic mental retardation [24-27], cerebral palsy [9-11], myelomeningocele [28], pediatric juvenile spinal muscular atrophy [29,30], pediatric Charcot Marie Tooth disease [31,32], kernicterus [19,29-33], agenesis of corpus callosum with colpocephaly [8,34].

Nandrolone decanoate has recently been used with benefit in the treatment of patients with cerebral palsy, refractory vitamin D-resistant rickets, and achondroplasia. In contrast to 17- testosterone derivatives, nandrolone esters do not cause sodium sulfobromophthalein retention; therefore hepatic complications are infrequent with their use in ordinary doses for short periods. The use of nandroloines has been reported to be associated with beneficial positive effects such as muscle strengthening [9,10,11,21,22,35,36].

Conclusion

The treatment of severe form birth asphyxia induced brain atrophy is a highly challenging situations and demands highly motivated parent that are able to cope with multiple therapies over a prolonged periods for an obvious improvement to occur.

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