Case study

A case of hypocic – ishemic spinal cord lesions in cerebral palsy

ABSTRACT

Aims

To focus attention of physicians on spinal cord examination at cerebral palsy, as spinal cord lesions contribute to clinical picture of spastic diplegia, and thereby to improve the treatment outcome of cerebral palsy.

Presentation of case

We report the case of 4-year-old male with lower paraplegia and speech delay. Clinical examination has revealed the muscle tonus to be increased bilaterally in gastrocnemius muscles and thigh adductors. The muscle tonus was decreased bilaterally in iliopsoas to such extent that he could not hold passively rised legs. Electrophysiological examination revealed signs of decreased excitability of motoneurons at the level L 2 – S 2. MRI has confirmed lesions of spinal cord at that level in addition to injury at thoracic level and brain lesions. MRI spinal angiography has detected tortuous anterior spinal artery. The patient benefited from the electrophoresis with theophylllinum, applied on lower thoracic and first lumbar vertebrae with improvement of his legs motor function.

Discussion and Conclusion

The first explorer of cerebral palsy, Dr. Little, based his view of cerebral palsy on thorough postmortem examination, performed by himself and by his colleges. In accordance with data, obtained from the section, he reported the cerebral palsy to result from perinatal injury of either brain or spinal cord. However, his follower, Dr. Freud, limited his pathlogoanatomic research exlusively to brain cuts, diverting attention of neurologists from the spinal cord. Nevertheless, our presentation proves involvement of spinal cord in pathogenesis of Cerebral Palsy and benefits from therapy applied on spine and, thus, confirms Little's point of view.

Keywords: *cerebral palsy, anterior spinal artery, spastic diplegia, Adamkiewicz artery*

INTRODUCTION

Cerebral palsy (CP) is the most common cause of childhood-onset, lifelong physical disability in most countries, affecting about 1 in 500 neonates with an estimated prevalence of 17 million people worldwide [1]. Cerebral palsy is not a disease entity in the traditional sense but a clinical description. Though there is a lot of good evidence and literature about cerebral palsy, still considerable controversy exists regarding the locus morbi of this comdition. Clinical findings are consistent neither with ex vivo magnetic resonance imaging (MRI) – computed tomography (CT) examination of the brain, nor with postmortem study. We believe that the reason of the obscurity is our deviation from the position of the first explorer of Cerebral Palsy, Dr. Little. Dr. Little documented in his proceedings in 1853 and in 1861 [2], that he and many of his colleges had examined spinal cord postmortem thoroughly and almost in every case of spastic rigidity he had found lesions. He wrote "I am justified in referring the spastic rigidity which follows asphyxia at birth to lesion of spinal cord, and not to lesion of brain or medulla oblongata". However, his great follower Freud, in 1893 and 1897 in

his proceeding, devoted to cerebral palsy [3], rested exclusively on brain examinations, and consequently did not find correlation between clinical phenomena and postmortem findings. For explanation of this discrepancy, Freud suggested several tricky hypotheses, like paramedian injury, repair of initial brain lesion, psychological maternal disturbances, appearance of primitive reflexes and so on. Our contemporary view of cerebral palsy is based mostly on above mentioned hypotheses of Freud, because of his great influence on neurologic community, while concept of Little has been almost forgotten. In 1979, as exception to this tendency, appeared report of Palenova N. G. [4], confirmed in 1986 – 1989 by R. Clancy, J. Sladky, and L. Rorke [5, 6]. These authors detected spinal cord lesions in most of cases postmortem examinations of the human newborn, expired from asphyxia. Examination of our patient with cerebral palsy revealed structural and vascular spinal cord lesions besides brain injury, and thus, is consistent with reports on human neonates of Dr. Little, Dr. Palenova and Dr. Clancy et al. Animals studies also testify spinal cord involvement [7-11]. Nowadays many noninvasive methods of spinal cord investigation are available, and we advocate their use in cerebral palsy.

CASE PRESENTATION

Case report of the patient V., male, 4 years old, whose parents complained on disturbance of speech and gait. It was the fifth pregnancy for mother at the age of 40 and the 4th labor. Three previous pregnancies had resulted in birth of the healthy children; one pregnancy had frozen on the 9th week. All children are from the same father. This, 5th pregnancy, initially went unremarkable with normal Ultrasound and Cardiotocography. However, unexpectedly it resulted in premature labor on 29th week, with tocolysis. Eventual delivery occurred by means of urgent cesarean section due to tetanic uterine contraction with prolapsed arm and umbilical cord entanglement. The newborn had Apgar score 6/7, weight of 1460 gr, height 40 cm. For the periventricular hemorrhage, detected by ultrasound, and respiratory failure, he was treated in critical care nursery of the maternal hospital for 4 days and received CPAP respiratory support. On the 5th day he was delivered to the resuscitation unit of the pediatric hospital. After 10 days care, he was discharged into the neonatology division. At the age of 33 days, he was discharged home with the weight 2100 gr. Neurosonography revealed periventricular/interventricular hemorrhage, periventricular leukomalacia in cystic phase. Duplex sonography revealed decreased blood flow velocity in anterior cerebral arteries, venous flow being normal.

Motor function development: holds his head from 2 months, rolls from back into tummy from 7 months, sits unsupported from 1.5 years, crawls from 11 months, crawls on his four from 1.5 years, rises and stands holding the prop from 1.5 years, walks holding the furniture from 1.7 years, rises himself and walks holding the baby stroller from 2.5 years, walks and runs with walkers Crocodille R82, from the 3 years, cannot stand alone. At the age of two years duplex sonography revealed decrease of the blood flow in the right vertebral artery when turning the head to the left. At the age of three years old duplex sonography revealed non-pathologic tortuosity of both common and internal carotid arteries and vertebral arteries in V 1 segment. Clinical examination at the age of 4 years old: comprehends the speech and carries out all verbal commands. Expressive speech is represented by several dysarthric words. Pupils are equal, direct and consensual pupilloconstriction are normal. Extraocular movements are restricted in directions of gaze up and right. Rare nistagmoid vacillations of the globes when gazing laterally. The face is symmetrical. The tongue is not deviated, but undulates when sticked out. The oral automatism reflexes are revived. Upper tendon reflexes are decreased evenly. The patellar reflexes are revived, the Achilles reflexes increased up to clonus. Babinski sign is positive bilaterally. Motor findings – muscle bulk was slightly decreased in paravertebral muscles at Th 6 – 9. Tetraparesis much more pronounced in legs. Spastic paresis was observed in gastrocnemius muscles, adductors of thighs and in less extent in biceps brachii. Flaccid paresis was observed in iliopsoas muscles. Sensory findings – pain sense was normal, vibration sense was diminished in lower extremities (22 second in legs while 11second in arms) No meningeal signs.

Electromyography (EMG) at two years old included:

1. Study of motor nerve conduction velocity (NC) and M – wave (CMAP) parameters during the stimulation of tibial and peroneal nerves from both sides.

2. Study of H – reflex from both sides

3. Needle EMG of the left tibialis anterior and of the left vastus lateralis

4. Interferential analysis

Stimulation of motor fibers of the left peroneal nerve has revealed decreased amplitude of M – wave (CMAP) of 1,01 mV, and deformed the form of M wave, while the motor nerve conduction velocity being normal. Stimulation of right peroneal and tibialis nerves revealed normal amplitude of both distal and proximal M wave (CMAP) and normal motor nerve conduction velocity. (proximal amplitude of M wave of right peroneal nerve – 4,04 mV) H – reflex is registered from the left, being normal in amplitude, while is not registered from the right.

Needle EMG of the left anterior tibialis muscle and of the left vastus lateralis has not detected any spontaneous activity. Motor unit potentials are of normal duration and phase, while their amplitude being sometimes slightly decreased. Interferential curves are saturated and of normal amplitude.

Conclusion:

Signs of decreased excitability of motoneurons at the level L 2 – S 2. There were no signs of neither polyneuropathy nor spinal muscular atrophy nor myopathy.

Brain and spine MRI with angiography and tractography at 4 years old.

(MR tomograph Siemens Skyra 3 T, Protocol T2 TRA, T2 FLAIR TRA FS, T1 SAG 3D, T2 COR, MDDW 20, Programm “Whole Spine)”

MRI features consistent with profound chronic posthypoxic and postischemic encephalopathy with the loss of white matter bulk and with periventricular leukopathy (areas of gliosis with cystic transformation). Symmetrical areas of hyperintensity in posterior parts of basal ganglia of residual posthypoxic origin. Both cortico – spinal tracts with the signs of Wallerian degeneration. Minor pineal cysts. Corpus callosum subatrophy. Hydrocephalus ex vacuo of lateral ventricles, cavum vergae. Spinal subatrophy at the Th 6 – Th 9 level with asymmetrical hyperintensity areas, more pronounced along the lateral columns. Diffuse weak heterogeneous increase of MRI – signal from the spinal cord below Th 6 vertebrae, along all the length of the cord, down to conus, apparently due to degeneration. Uncomplete fusion of laminae arcus vertebrae S 2 – S 3. Tortuosity of anterior spinal artery. Indicators of tractography were measured at 25 axial cuts from the level of Th4 down to Th12. (The length of the field study was 14 cm) – The robust tendency to decrease of fractional anisotropy (FA) from Th 4 downword toward Th12 was observed, with peaks being pronounced at level Th8 (cut №11 - 442), Th10 (cut №20 - 283), and Th12 (cut №25 - 171). Meanwhile another important tractography indicator – apparent diffusion coefficient (ADC) was increasing toward the distal direction with strong negative correlation in relation to FA. (Figure 1)

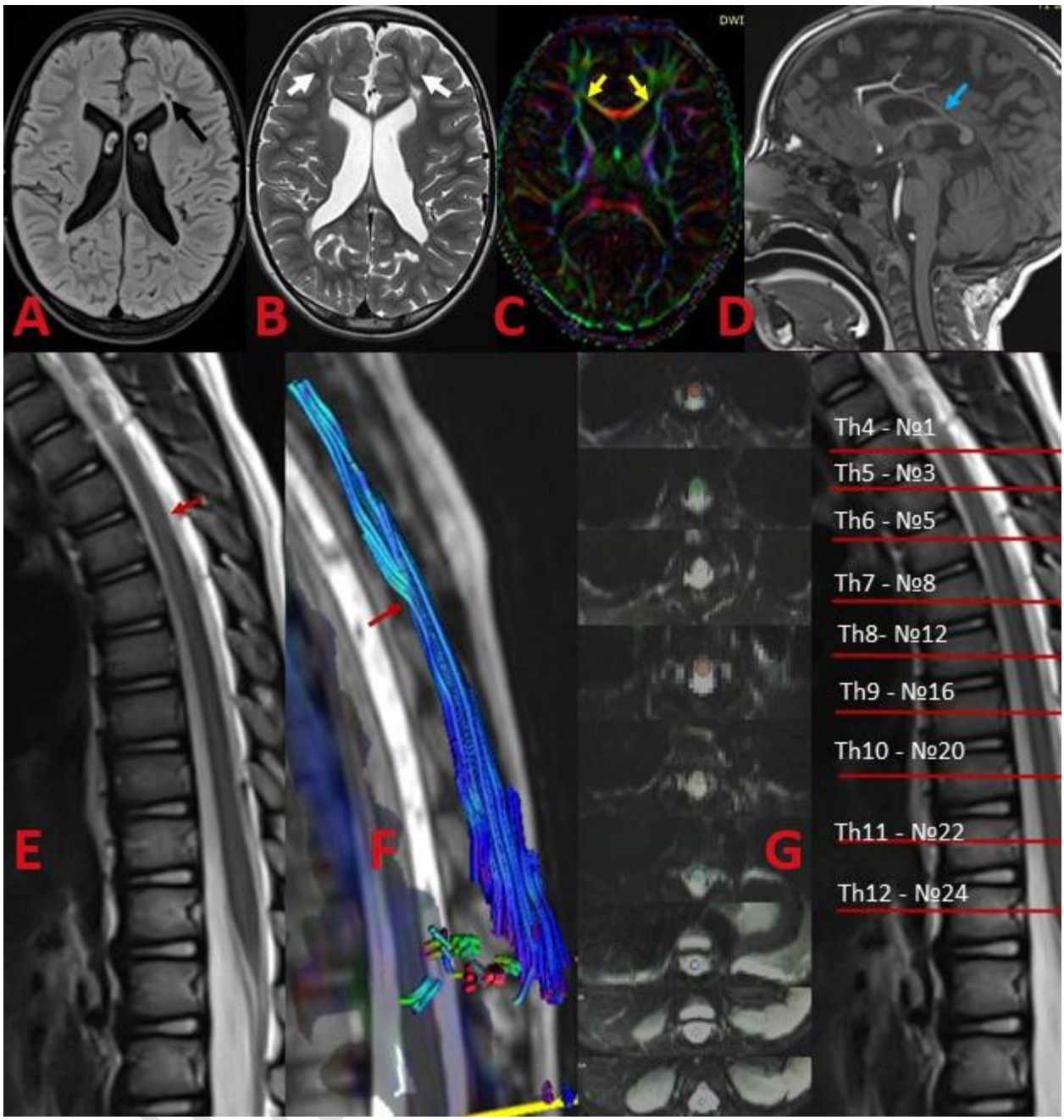

Figure 1. MRI with tractography of brain and spinal cord of patient V. A. T 1-weighted brain axial cut. Black arrow – periventricular areas of gliosis with cystic transformation. B. T 2-weighted brain axial cut. White arrows – periventricular areas of gliosis with cystic transformation, white matter depletion. C. Brain tractography. Yellow arrows - fibers of semioval centers pathways are depleted, cortico – spinal tracts with the signs of Wallerian degeneration. D. T1-weighted brain sagittal cut. Blue arrow - corpus callosum atrophy. E. T2-weighted sagittal spine cut. Red arrow - depletion of spinal conducting pathways. F. Spine tractography. Red arrow - depletion of spinal conducting pathways. G. Those 25 axial spine cuts are indicated, at which the authors have measured fractional anisotropy (FA) and apparent diffusion coefficient (ADC) from the Th4 level down to Th 12 level. (the length of the study field 14 см)

The patient has benefited from electrophoresis with Theophylllinum, applied on lower thoracic and first lumbar vertebrae, followed by acupuncture (Figure 2), with improvement of his legs motor function, such as rising from sitting position and easy walking, holding the prop.

Figure 2. Acupancture treatment of patient V. with 5 minutes exposure on point Shui Gou.

DISCUSSION

Nobuyoshi Kawaharada in 2004 established usefulness of MRA in detection of Adamkiewicz artery (ARM) as well as 3 types of morphology of the anterior spinal artery (ASA) above the ARM junction [12]. Type A is noncontinuation of the ASA above the ARM junction. Type B is continuation of the ASA above and below the ARM junction. Type C is noncontinuation of the anterior spinal artery below ARM junction.

Our case is consistent with Type A according Kawaharada. (Figure 3). This type is more common though more vulnerable to ischemia

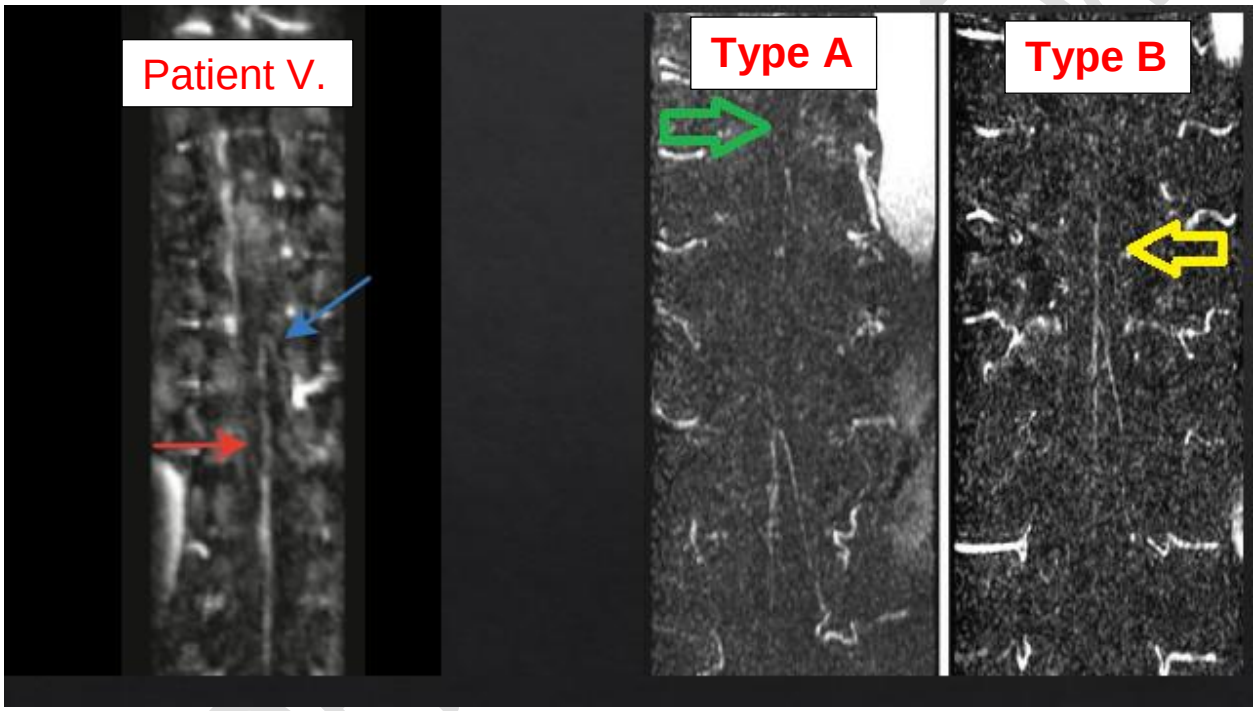

Figure 3. Comparison of spinal angiography of our patient V. (on the left) with established by Kawaharada two possible types of junction of Adamkiewicz artery with anterior spinal artery (on the right). Blue arrow – Adamkiewicz artery, Red arrow – tortuous anterior spinal artery of our patient V., green arrow – continuation of anterior spinal artery only downward in type A junction, continuation of anterior spinal artery upward and downard in type B junction.

Spinal cord in Cerebral Palsy has not been explored by MRI tractography in children. As to adults with consequences of CP - we have found only one research of spine tractography [13]. The most important indicators of quantitative tractography are FA and ADC. Reports of meaning of these two indicators in spinal cord tractography are controversive either in healthy persons or in spinal pathology. Some authors communicated of detection of gradient in FA decrement toward the caudal direction in healthy [14, 15]. In our study of patient with CP quantitative spinal MRI tractography also revealed gradient of decrement of FA toward the caudal segments, but in addition we found reverse gradient of increment of ADC toward dawnward direction with the strong negative correlation between these two coefficients (Spearman's rank correlation coefficient value -0,86) (Figure 4). We presume, that such relation between FA and ADC reflects normal state of thoracic and lumbar spinal cord. Nevertheless, the sharp drop of FA on Th12 level, to our mind, is caused by those lesion of lumbar and sacral segments, that was earlier detected by EMG. Confusing is the fact, that observed narrowing of spinal cord at Th6 level either at

conventional MRI or at tractography is not reflected by drop/rise of values of FA and ADC. Presumably, that could arise as a result of reparation process after perinatal injury at this level.

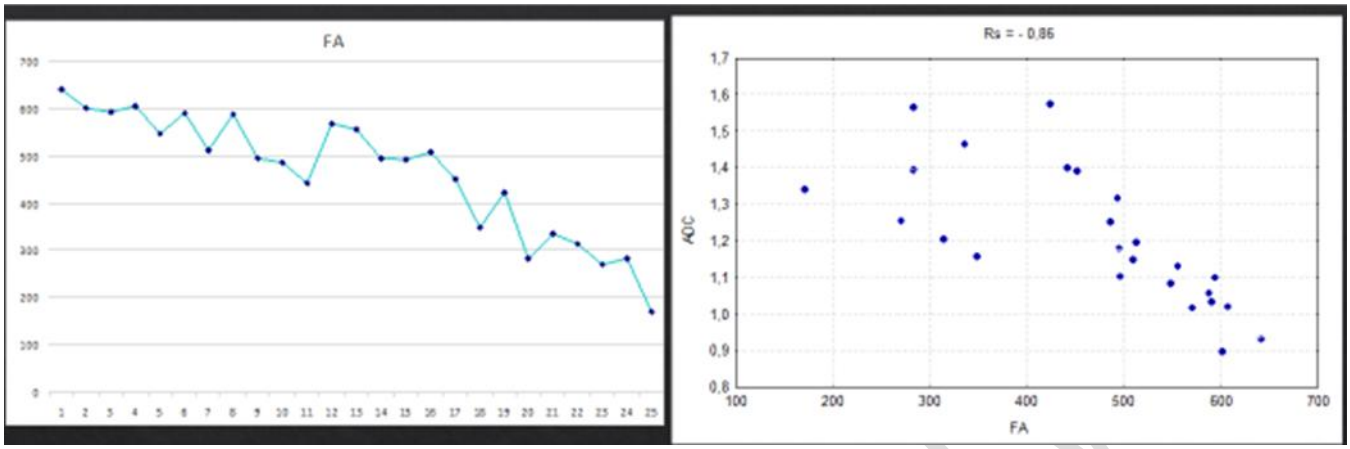

Figure 4. Negative correlation between FA and ADC. On the left – the meaning of FA at different vertebral levels, from the 4th toward the 12th. On the right – scatter plot for both FA and ADC.

The first explorer of cerebral palsy, Dr. Little, reported his experience and of his colleges, when the spinal cord was always studied at autopsy, and lesions had been found in spinal cord almost in every section of spastic diplegia. The summary of his view of cerebral palsy could be expressed by the following: The injury in Cerebral palsy could result from birth trauma or hypoxia/ischemia or hemorrhage of both brain and spinal cord. Topical diagnosis is possible and imperatively required.

40 years later Dr. Freud, exploring cerebral palsy, came to opposite conclusion, as he neglected postmortem spinal cord examination [16]. His review was the following: There is a poor correlation between clinical syndromes and neuropathologic lesions. Topical diagnosis of cerebral palsy is impossible. Neurological and psychiatric disorders cannot be firmly localized to a specific area of the cerebral cortex. The foundation was thus set for his broad and speculative explanations of cerebral palsy symptoms, as the sum of suffering of the parasagittal fetal brain area and its compensation process, and also based on the theory of psychoanalysis; a theory based on a theoretical construct of the mind that had little correlation with the brain's anatomic pathology. Until now, we regard cerebral palsy from the Freud's point of view. The only exception were reports of Dr. Palenova in 1979 and of the group of scientists in 1986 – 1989, namely R. Clancy, J. Sladky, and L. Rorke. These authors detected spinal cord lesions in most of cases postmortem examinations of the human newborn, expired from asphyxia.

Most cases of cerebral palsy arise because of hypoxic – ischemic encephalopathy (HIE). HIE in its turn arises as response to change of systemic blood pressure, and accompanied by hemorrhagic insult, or ischemic insult, or periventricular leukomalacia, or parasagital lesions or combination of these forms. Preterm infants are known to be much more vulnerable to changes of blood pressure because of lack of muscle layer in brain vessels. The lack of autoregulation in preterm infant is also true for the Adamkiewicz artery, the main blood supply to the lower spinal cord. When ischemia or hemorrhage takes place in brain, we just must expect the same event in spinal cord and include spinal cord in MRI study.

We are aware of several common traditional and modern explanations of relation of brain lesions to spastic paraplegia phenomena. Initial explanation was proposed by Freud, who had stated, that frequent parasagittal injury of the newborn affects mainly legs areas of homunculus. In our days those thesis is generally accepted, that periventricular injury by leukomalacia and/or by widened anterior ventricular horns compromise mainly pyramidal leg

tracts, as they are situated closer to ventricular lateral walls. We suggest that spinal circulation is vulnerable to perinatal stress, and that lower paraparesis could develop from hypoxic – ischemic myelopathy.

CONCLUSION

We believe that spastic diplegia phenomena could not be explained by brain injury alone, and that spinal cord ischemic – hypoxic lesions contribute much to lower paraparesis in cerebral palsy. Many advanced methods of noninvasive spinal cord investigation are available nowadays, and our case one more time advocates the return to Dr. Little's view of cerebral palsy, with the use of abovementioned diagnostic tools.

Disclaimer regarding Consent and Ethical Approval:

As per university standard guideline, participant consent and ethical approval have been collected and preserved by the authors

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