ARTHROGRYPOSIS MULTIPLEX CONGENITA, EPILEPTIC SEIZURES AND CORTICAL DYSPLASIA: A CASE REPORT

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Summary. We have presented a case of a 22-year-old patient having a rare variety of arthrogryposis multiplex congenita - arthrogryposis with epileptic seizures and defect in neural migration. We have described the patient's disease history, the clinical, and laboratory data by giving prominence to the lack of mental retardation and the late onset of the generalized tonic-clonic seizures, despite the present cortical dysplasia. We have also discussed cases reported by other investigators. We consider that our case report is a contribution to the knowledge about the clinical manifestations, the possible results from neuroimaging and electrophysiological methods, and the progression of arthrogryposis multiplex congenita.

Key words: *arthrogryposis, epilepsy, cortical dysplasia*

INTRODUCTION

Arthrogryposis multiplex congenita (AMC) is a heterogenous symptom complex of multiple congenital joint contractures and amyoplasia, associated with both neurogenic and myopathic disorders [1]. It affects 1 in 3000 live births. The etiology remains unclear but generally is associated with reduced fetal movements due to uterine malformations, multiple pregnancy, oligohydramnios, neurological diseases, muscle abnormalities, connective tissue defects, intrauterine vascular malformations, maternal diseases (diabetes mellitus, multiple sclerosis, myasthenia gravis, infection, drugs, trauma). The joint symptoms are associated with internal rotation of the shoulder, extension and pronation of the elbow, fixed flexion of the fingers and thumb in palm, flexion, abduction and external rotation of the hip, flexion of the knee, and clubfoot. AMC is a non-progressive disorder, although complications may include various abnormalities such as scoliosis, lung hypoplasia, growth retardation, midfacial hemangioma, facial and jaw variations,

abdominal hernias, congenital heart defects, tracheoesophageal fistulas, and ophthalmologic abnormalities. The primary diagnosis is made when lack of mobility and abnormal fetal position is noted on ultrasound scan [2]. The muscle biopsy demonstrates the replacement of muscle fibers by connective and fatty tissue [2]. Orthopaedic surgery and physical therapy can be beneficial to mobility improvement.

CASE REPORT

We present a case of a 22-year-old patient having a rare variety of AMC - arthrogryposis with epileptic seizures and defect in neural migration. The patient was a 22-year-old man. He was born from a fifth pathological pregnancy, which was preceded by 4 spontaneous abortions of the mother. During the third lunar month of pregnancy the mother was taking drugs for uterine contractions and bleeding. When the patient was 2 months old, muscular hypotonia and multiple contractures in the hips, knees, and ankles were found and later operated. The diagnosis of AMC was accepted based on clinical manifestations and disease course. Genetic testing was never performed. The patient started walking when he was 1 year and 4 months old. He had foot deformations, walked on tiptoes, and crossed his legs. After a neurological examination spastic muscle tone and pathologically increased deep tendon reflexes for the lower limbs were described. In 2001 electromyography (EMG) was performed and segmental demyelination of the nerves of the four limbs was demonstrated which was in support with polyneuropathy in combination with arthrogryposis.

The first primarily generalized tonic-clonic seizure (GTCS) was when the patient was 20 years old. Afterwards the seizure frequency was 1-2 GTCS per month. He was started on topiramate 100 mg daily, which was replaced 1 month later by valproate 1500 mg daily due to adverse events (general weakness and nausea). Valproate was terminated 1 year later because of other adverse events (hair loss and gastric discomfort). The treatment continued with carbamazepine 400 mg daily, which was reduced to 200 mg daily because of sleepiness. The recent seizure frequency increased up to 3 GTCS per month. The computed tomography (CT) scan visualized white matter hypodensity and increased volume. Brain magnetic resonance imaging (MRI) demonstrated focal cortical dysplasia (a significant and irregular dilation of the convexity subarachnoid space, more pronounced in the right, diffuse white matter alterations – T1-hypointensity and T2-hyperintensity, FLAIR high signal alterations, gyration impairment and grey matter thinning).

The patient was declared invalid. Presently, he is a college student and works as an administrator for a hypermarket.

During the examination we found postoperative scars in the region of ankles and elbows, a growth retardation of the arms. The patient had no cognitive decline and psychiatric symptoms. The neurological exam demonstrated: 1. Amyotrophic syndrome consisting of decreased muscle power of the four limbs, mostly in the

proximal regions, hypotonia of the four limbs, contractures of the elbow, wrist, and ankle joints, decreased deep tendon reflexes of the upper limbs and lacking for the lower ones, hypotrophy of the four limbs, mostly of the hands; 2. Polyneuropathic syndrome consisting of distal hyperesthesia along the middle third of the forearms and the ankles.

We performed laboratory tests (full blood count, biochemistry, coagulation status, carbamazepine blood level). The only abnormal laboratory findings were a slightly increased alanine aminotransferase (ALT) level, which was 56 U/l (reference value up to 40 U/l) and an increased creatine kinase (CK) level, which was 680 U/l (reference value up to 200 U/l).

Electroencephalography (EEG) was with a normal background, without focal or paroxysmal activity. The patient had 2 previous EEGs which were also normal. However, the clinical manifestations of seizures were definitely of GTCS and we accepted the diagnosis of generalized epilepsy.

EMG results corresponded to myogenic impairment of the upper limbs proximal muscles and lower limbs distal muscles. Electroneurography (ENG) results proved a great decrease in the conduction of the motor neurons of both fibular nerves.

An anticonvulsant treatment with carbamazepine 200 mg daily and levetiracetam in a gradual up-titration dose to 2000 mg daily was recommended, having in mind the seizure type and the previous adverse events from topiramate and valproate. Carbamazepine was later terminated. In the next 1 year seizure frequency was reduced by 50%, no change in the neurological status was found.

DISCUSSION

The definition of AMC is purely descriptive - congenital, non-progressive contractures in more than two joints and in multiple body areas. Based on the clinical findings, disease course, EMG and ENG description, laboratory findings, we confirmed the diagnosis AMC with peripheral neuropathy and secondary myopathy in our patient. As a differential diagnosis our case differs from the hereditary neuropathies, firstly, in being present at birth and showing no tendency to progress thereafter. This is in marked contrast with the slow and continuing deterioriation seen for example in Friedreich's ataxia, limb and girdle muscular dystrophy or dystrophia myotonica. In fact, the described case is a rare variety of AMC, because of the presented epileptic seizures and defect in neural migration. The most probable cause is the pathological pregnancy of the mother and drug intake. In 1994 Hageman et al. reported a case of a 21-year-old woman without cognitive impairment having arthrogryposis with neurogenic congenital contractures of the lower limbs, hyperreflexia, partial epilepsy, and bilateral opercular (perisylvien) cortical dysplasia revealed by MRI [3]. In 1995 Brodtkorb et al. discovered a constellation of arthrogryposis, which included epileptic disorders (partial seizures or GTCS)

and neural migration abnormalities (polymicrogyria, pachygyria, schizencephaly) in adult patients, the hypothetical cause of which was a frequent defect of the neural migration across the entire neural axis [4]. Regarding the main clinical signs, our case report is similar to few cases described by other investigators. The lack of mental retardation and the late seizures onset, despite the cortical dysplasia, are interesting findings in our patient's history disease. A possible explanation of the unsatisfactory seizure control is the frequent change of antiepileptic drugs due to adverse events and the treatment with suboptimal doses.

In conclusion, the presented case requires special attention because of the rare combination of arthrogryposis, epileptic seizures with late onset, and cortical dysplasia without cognitive impairment. Having in mind the lack of progression of arthrogryposis, and the performed surgical correction of the joint contractures, future treatment of this patient would focus on improving seizure control and quality of life.

REFERENCES

1. Banker, B. Q. Neuropathologic aspects of arthrogryposis multiplex congenita. – Clin. Orthop. Relat. Res., **194**, 1985, 30-43.
2. Kalampokas, E. et al. Diagnosing Arthrogryposis Multiplex Congenita: A Review. – Obstet. Gynecol., 2012, 2012, 264918.
3. Hageman, G., T. U. Hoogenraad et R. L. Prevo. The association of cortical dysplasia and anterior horn arthrogryposis: a case report. – Brain. Dev., **16**, 1994, № 6, 463-466.
4. Brodtkorb, E. et al. Epileptic seizures, arthrogryposis and migrational brain disorders: a syndrome? – Acta Neurol. Scand., **91**, 1995, № 6, 518-519.

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