Nagłe zatrzymanie krążenia poza szpitalem – późne następstwa neurologiczne, psychologiczne i w badaniach metodą rezonansu magnetycznego: seria przypadków

Out-of-hospital cardiac arrest – the late neurological, psychological functions and cerebral change on MRI study: a case series

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STRESZCZENIE

Cel. Dzieci po pozaszpitalnym nagłym zatrzymaniu krążenia (PsZZK) mogą doświadczać neurologicznych powikłań – od łagodnych zaburzeń poznawczych po ciężkie deficyty psychomotoryczne. Zbadaliśmy odległe następstwa neurologiczne, psychologiczne oraz funkcjonowanie ośrodkowego układu nerwowego (OUN) u dzieci po PsZZK i resuscytacji. **Materiał i metody.** Przedstawiamy serię 6 przypadków pacjentów (płeć męska, wiek: 9–17 lat), którzy przeżyli nagłe zatrzymanie krążenia bez urazu OUN, w okresie obserwacji odległej od 1 do 5 lat (mediana: 2,5 roku). Pacjenci poddani zostali diagnostyce obrazowej głowy w polu elektromagnetycznym z zastosowaniem sekwencji FLAIR (FLAIR MRI). Do oceny neurologicznej oprócz przedmiotowego badania neurologicznego wykorzystano funkcjonalną skalę niezależności (FIM) oraz wskaźnik funkcjonalny „Repty” (RFI). Ocena psychologiczna dokonana została przy użyciu Testu Ravena, Kwestionariusza oceny jakości życia SF-36 oraz Kwestionariusza zdrowotnego dla dzieci i młodzieży KIDSCREEN-52. **Wyniki.** W badaniu FLAIR MRI obserwowano zmiany pod postacią zaników korowych u 2 spośród 5 pacjentów. W ocenie funkcjonalnej 5 pacjentów uzyskało maksymalną wartość wskaźnika RFI. Trzech badanych uzyskało wyniki poniżej 25. percentyla w skali Ravena (znaczne obniżenie zdolności wnioskowania), jeden pacjent uzyskał wynik powyżej 75. percentyla (wyższy niż przeciętny poziom zdolności wnioskowania). Ocena subiektywnej jakości życia wykazała wysoką ocenę sprawności fizycznej i zadowolenia z życia 5 pacjentów. Jeden badany zgłaszał znacznie obniżoną sprawność fizyczną i obniżony nastrój. **Wnioski.** W warunkach PsZZK u dzieci gdy pomoc w zakresie BLS udzielona jest szybko i kontynuowane jest postępowanie resuscytacyjne oraz leczenie w OIOM, można liczyć na pomyślne rokowanie. Ocena jakości życia wskazuje, że dzieci po NZK zachowały sprawność fizyczną w wysokim stopniu, jednak część badanych deklaruje trudności w nauce i przeciętną samoocenę życiową.

Słowa kluczowe: jakość życia, intensywna terapia, rezonans magnetyczny, pediatria, nagłe zatrzymanie krążenia u dzieci

ABSTRACT

Aim. Children who survive out-of-hospital cardiac arrest (OHCA) may suffer neurological consequences, ranging from mild cognitive impairment to severe psychomotor deficits. We investigated the long-term neurological, psychological and central nervous system (CNS) function in children after OHCA and resuscitation. **Methods.** This is a case series of six patients (all male, aged 9–17 years) after OHCA without CNS injury, with a follow-up of 1 to 5 years (median 2.5 years). Patients were subjected to diagnostic imaging using fluid attenuation inversion recovery magnetic resonance imaging (FLAIR MRI). They also had a routine neurological examination, with additional assessment using the Repty Functional Index (RFI). A psychological assessment with the Raven's Progressive Matrices (RPM), The Short Form (36) Health Survey (SF-36) and The KIDSCREEN-52 questionnaires were performed. **Results.** MRI revealed features of cortical atrophy in two of five patients. Five patients obtained a maximal RFI score in most categories in their functional evaluation. Three patients received results below the 25th percentile on the Raven's scale (i.e., lower level of intelligence), and one patient was above 75th percentile (i.e., high level of intelligence). Quality of life evaluation revealed a high level of physical fitness and life satisfaction in five patients. One patient reported reduced physical ability and a depressed mood. **Conclusions.** Favourable outcomes in children are expected when basic life support and resuscitation are provided immediately after OHCA, and the treatment is continued in the ICU. This long-term quality of life analysis indicates these children retain their physical ability but may have learning problems and average self-esteem.

Keywords: pediatric cardiac arrest, children, pediatrics, neurology, psychology, central nervous system

1. INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) in children is a therapeutic and social problem that can seriously affect a child's development. The early studies showed that only 5% to 10% of children survive OHCA, and the ones that do, often suffer severe neurological consequences [1]. Therefore, the most important late endpoints in children after OHCA is a return to social life and the ability to cope with the tasks of everyday life without help.

Recent multiple studies have shown a greater survival after OHCA in cases when cardiac arrest occurred in the presence of witnesses and in older children, who have an even better prognosis than adults [2]. The low survival of paediatric patients after cardiac arrest is mostly in infants, who have the worst prognosis [2].

The general use of automated external defibrillators has significantly increased the survival after sudden cardiac arrest, in both adults and children [3]. Neurological symptoms in patients after sudden cardiac arrest are largely dependent on the duration of the coma [4]. Therefore, the time taken for the patient to regain consciousness is the first and the most important prognostic factor regarding the degree of damage to the central nervous system (CNS) after cardiac arrest in both, adult and paediatric, populations.

Although some causes of cardiac arrest are common to adults and children, including craniocerebral injuries and flooding, pathologies of the respiratory system are the main cause of paediatric cardiac arrest.

In their epidemiologic review of OHCA in children Donoghue et al. described poor overall survival outcomes, with lower survival cases fitting rigorous cardiac arrest definition [5]. Nevertheless, as confirmed by long-term observations, the neurological status in children during cardiac arrest recovery is more favourable than adults [6].

The spectrum of neurological symptoms observed in patients after cardiac arrest ranges from mild cognitive impairment to severe psychomotor deficits.

Hypoxic-ischemic encephalopathy is the most common complication and varying degrees of cognitive impairment are observed in these patients. Retrospective studies in adults have shown that global hypoxia damages pyramidal cells in the hippocampus (CA1 region), amygdala and subiculum. Therefore, it can be concluded that even short-term global cerebral hypoxia will result in short-term memory disorders. Indeed, previous studies have reported varying degrees of memory impairment in the majority of cardiac arrest patients [7]. However, the authors of this study argue that small brain damage after cardiac arrest and minor neurological abnormalities do not exclude the full recovery after rehabilitation [7].

While parameters relating to the hypoxic-ischemic encephalopathy after cardiac arrest have been well-studied in adults, the paediatric equivalents are not widely available and more information about appropriate proceedings for treatment are required. Therefore, the aim of this case series study was to investigate the long-term neurological, psychological and CNS function in children after OHCA.

2. METHODS

2.1. Study participants

Participants of this observational study were six children aged 9–17 years who experienced OHCA, were hospitalised in the Intensive Care Unit (ICU) of the Polish Mother's Memorial Hospital Research Institute and survived to hospital discharge. The baseline characteristics of the patients have been shown in table I (tab. I). Exclusion criteria included OHCA due to external causes with injury to the CNS

Table I. Baseline characteristics of the study group

Patient	Sex	Age at OHCA	Time of cardiac arrest [minutes]	Time of resuscitation [minutes]	Age at the study
1	M	16	1	Over a dozen	21
2	M	17	15	15	21
3	M	14	1	Over a dozen	16
4	M	17	Several	1	20
5	M	9	Several	Over a dozen	11
6	M	11	1	Several dozen	12

M – male; OHCA – out-of-hospital-cardiac-arrest.

and neurological abnormalities diagnosed before OHCA, e.g. cerebral palsy.

2.2. Neurological and psychological assessment

In the follow-up study, patients underwent neurological examination with i.e. Lovett classification [8], additionally, for neurological assessment we used the Functional Independence Measure (FIM) [9] and the Repty Functional Index (RFI) [10], as well as diagnostic imaging of the head.

The FIM scale is one of the most accurate ones, assessing 18 basic activities of daily life in a seven-point scale: from one point meaning total assistance provided by a helper, to seven points meaning complete independence. The scale was developed to evaluate patients after cranio-cerebral traumas, but due to its universality, it has been more widely used to assess rehabilitation.

The “Repty” index was developed by simplifying the above FIM scale, as it only uses a four-grade scale (self-care, sphincter control, mobility and locomotion), without assessing the psychosocial status. The RFI is used mainly in the assessment of children with cerebral palsy. However, if one takes into account the most common aetiology of cerebral palsy, i.e. perinatal hypoxic-ischemic encephalopathy, one can expect similar symptoms in patients after cardiac arrest [11].

Patients were subjected to diagnostic imaging of the head in magnetic field using fluid-attenuated inversion recovery magnetic resonance imaging (FLAIR MRI). Psychological assessment was made with Raven’s Progressive Matrices [12], SF-36 [13] and The KIDSCREEN-52 questionnaires [14].

3. RESULTS

3.1. Case 1

A 16-year-old boy was brought by emergency medical services to the ICU after cardiac arrest during physical effort. He lost consciousness, stopped breathing, and presented with convulsions and vomiting. Witnesses performed basic life support (BLS) before the emergency medical services recognised cardiac arrest by the ventricular fibrillation mechanism. A single effective defibrillation was made and the patient was intubated.

The medical history implied a feeling of tightness in the chest during physical strain, regular judo classes and chronic use of thermogenic food (caffeine, piperine, epigallocatechin gallate, tyrosine and synephrine). On admission to the ICU the boy was unconscious, with eyeballs directed to the right, narrow reactive pupils and he presented with convulsions. The CT of the head and cervical spine showed no swelling or bleeding, and the fluid reserve was preserved. After intubation neuroprotective treatment, analgesia, and controlled moderate hypothermia were introduced.

On the fourth day the patient was extubated, displayed efficient circulation and respiration, was conscious and responsive.

Five years after the cardiac arrest neither the patient nor people from his surroundings reported any problems or abnormalities in his behaviour or functioning. Neuro-

logical examination did not indicate any clinical signs of focal damage to the CNS. The RFI in all categories reached maximum value. The MRI image of the brain showed mild cortical atrophy within the temporal lobes, but this was not reflected in the functional assessment of the patient.

3.2. Case 2

A 17-year-old boy was brought by emergency medical services after cardiac arrest as a result of drowning in a natural water reservoir. The patient remained under water for over 15 minutes, after which he was resuscitated for 15 minutes, received 3 mg of adrenaline (epinephrine) and was intubated. On admission to the ICU, the patient had massive pulmonary oedema, with foamy, bloody fluid from the respiratory tract, cyanosis, and a barely discernable pulse. Signs of pulmonary hypertension were found in the echocardiography.

In the first three days, because of unstable hemodynamic status, the infusion of dobutamine, dopamine and noradrenaline (norepinephrine) was administered. A head and cervical spine CT showed no changes. Anti-oedema treatment, hypothermia and analgesia were applied.

The patient was extubated on day eight, he was conscious and verbally responsive. However, he displayed occasional visual hallucinations, restlessness, and retrograde amnesia. After 11 days of hospitalisation in the ICU, the patient was discharged to the Department of Neurology.

Four years after the cardiac arrest, the patient did not report any problems. Gait disturbances occurred in the initial period after the event but subsided after rehabilitation. The RFI score in all categories was assessed at 7 points. Neurological examination found reflexive, left-sided hemiparesis, with bilateral hallux areflexia by the plantar reflex test. A head MRI showed no cortical or subcortical atrophy.

3.3. Case 3

A 14-year-old boy brought by emergency medical services after sudden cardiac arrest as a result of electrocution with network electricity of 230 V. The witness of the event (his father) performed BLS. Upon arrival emergency medical services recognised ventricular fibrillation and performed a single effective defibrillation (120 J). On admission to the ICU the patient had efficient circulation and respiration, he was able to blink and could respond with a flexion reaction to external stimuli.

Neuroprotective and anti-oedema treatment was applied. The CT image of the brain and cerebellum showed no focal lesions, a symmetrical, non-dilated ventricular system without dislocation, and that the subarachnoid spinal fluid reserve was preserved. On the third day, the patient was extubated, he was conscious and verbally responsive. His pupils were equal and narrow. The patient had no convulsions, but he was occasionally excited, disorientated, and had short-term memory impairment. The patient was hospitalised for 6 days in the ICU.

Two years after the sudden cardiac arrest the patient complained of slight impairment in short-term memory, but that did not affect his daily functioning. On neurological examination, there was no evidence of focal lesions or deficits in the CNS. The RFI score in all four categories

was 7 points, indicating full independence. With respect to verbal communication, the patient received 5 points. The value was reduced due to a slurred, slightly dysarthric speech, although this symptom was observed before the incident of cardiac arrest.

A head MRI revealed neither periventricular leukomalacia nor grey matter atrophy. This was probably due to immediate resuscitation, which resolved the cerebral ischemia successfully.

3.4 Case 4

A 17-year-old boy brought by emergency medical services from home to the ICU after respiratory arrest and subsequent cardiac arrest occurred in the course of asthmatic state. On the arrival of emergency medical services, the patient was unconscious and livid. Cardiac massage was performed, the patient was intubated and the emergency medical services applied theophylline, ephedrine, hydrocortisone, clemastine and midazolam.

The patient had been treated for asthma for four years but did not follow the medical recommendations. There were several asthmatic attacks in his medical history. In the ICU, he was initially unconscious with an extreme shortness of breath. The murmur over the lung fields was barely audible, and characteristics of lung obstruction ($\text{SpO}_2 < 80\%$) and tachycardia were observed.

The infusion of salbutamol and nebulisations with adrenaline were applied. The patient's condition improved and he regained consciousness, with efficient circulation and respiration. On the second day, he was verbally responsive. The patient stayed in the ICU for two days.

Three years after sudden cardiac arrest, slight cognitive deficits were observed. The patient did not complete education in the secondary school. Neurological examination showed reflexive right-sided hemiparesis, with a difference in the Babinski sign response (i.e. areflexia on the right side, flexia on the left side). The RFI score in the categories of self-care, mobility, locomotion, and sphincter control reached the maximum seven points. The communication score was reduced to 5 points due to a decrease in auditory or visual understanding, while speech was rated at 7 points. A head MRI demonstrated atrophy of the cerebral cortex mainly in temporal lobes, which can reflect hypoxic-ischemic encephalopathy.

3.5. Case 5

A 9-year-old boy brought by medical air rescue from a construction site, where respiratory arrest and subsequent cardiac arrest occurred after a multi-organ injury (without CNS injury) as a result of being crushed by the ferro-cement panels. The mother found the child unconscious, livid, flaccid, and she began BLS. Upon emergency medical services arrival, the boy was intubated and indirect cardiac massage was performed.

In the ICU, breathing replacement was applied and the patient showed efficient circulation. Numerous crepitations and rales were audible over the lung fields. The patient had medium sized, equal and reactive pupils. A trauma scan found a bilateral lung bruise, total parenchyma airlessness in the upper lobe of the right lung, and a fracture of the

branch of the right ischium. Reduced ventricular contractility of 53-57% was observed in echocardiography and elevated levels of troponins were found in laboratory studies, which normalized in subsequent days.

After 9 days the patient was extubated, stayed conscious and verbally responsive. He was hospitalised in the ICU for 11 days.

Two years after sudden cardiac arrest, neurological examination showed slight reflexive paresis of the right upper limb. After the incident the boy required long-term rehabilitation, especially of the right upper limb. However, he was successful in learning to write. No other neurological disorders were observed. A head MRI showed no atrophy of the cerebral cortex or other characteristics of hypoxic-ischemic encephalopathy.

3.6. Case 6

An 11-year-old boy brought by emergency medical services from home, where cardiac arrest occurred without any perceptible cause. Medical history indicated no health problems, no contact with drugs and other medicines. His parents, who witnessed this event, started BLS. Upon arrival, emergency medical services recognized ventricular fibrillation and applied defibrillation (120 J), which led to transitional Pulseless Electrical Activity (PEA), and then ventricular fibrillation occurred again. This cycle was repeated twice. A total of three defibrillation shocks were applied and 2 mg of adrenaline was given. The patient was intubated and spontaneous circulation returned.

Patient's pupils were undilated, equal, and they became narrow on sedation. Head hypothermia was used for the first day. Amiodarone and the infusion of dopamine and milrinone were administered and because of long QT propranolol was included in the treatment. In laboratory studies elevated levels of troponin, NT-proBNP and creatine kinase-MB were found. Echocardiography showed no significant deviations from normal.

The patient recovered from the coma on the third day, he showed flexion reaction to strong stimuli, and presented cough of unknown cause. On day five, he was extubated, breathing on his own and he was conscious of his surroundings.

Evidence of a symmetrical signal increase in T2-weighted images and FLAIR sequences was observed on both sides in the MRI in the caudate nucleus, putamen, cuneus and precuneus cortex, as well as in the cortex of the upper frontal furrow of both cerebral hemispheres. This may be related to the late post-ischemic changes. However, there were neither focal lesions in the brain nor features of contrast enhancement after intravenous administration of contrast medium. The patient was hospitalised in the ICU 11 days.

The patient was neurologically diagnosed with hypoxic-ischemic encephalopathy, regressive quadriplegia and chorea. Moreover, he underwent implantation of an implantable cardioverter-defibrillator (ICD) after cardiac arrest, which had occurred twice in the ventricular fibrillation mechanism.

A year after sudden cardiac arrest, the patient was treated pharmacologically due to arrhythmia and had an

ICD. Therefore, no CNS imaging in a magnetic field was performed. Neurological examination showed right-sided pyramid hemiparesis, with positive Babinski sign on the right side. His speech was slurred, quiet, and slowed-down, with the characteristics of dysarthria. A right upper limb tremor, increasing when attempting to write, was observed. Many neurological abnormalities in terms of locomotion and communication were present and the patient received the lowest score (5 points) in the category of self-care: upper body dressing, lower body dressing, attention paid to appearance and personal hygiene. Similarly, he had low scores (5 points) in the category of mobility: bed to chair transfer and locomotion, which were the result of hemiparesis.

3.7. Psychological evaluation

Overall the patients achieved results from the 1st to the 90th percentile (mean = 38) on the Raven's Progressive Matrices (RPM), which is an international test of intelligence and measures the ability to make sense or meaning of visual data. Half of the patients (n = 3) received the results below 25th percentile, indicating a significant reduction in their ability to deduce from visual data (tab. II). One patient received a score of above 75th percentile, indicating a higher than average level of intelligence (tab. II).

The six patients were also examined with SF-36 and The KIDSCREEN-52 questionnaire, which were used for self-assessment of their overall quality of life. Five patients highly rated their physical fitness. One patient described himself as sick, exhausted and unable to make any effort. Five patients described themselves as satisfied with their lives. Only one person felt unsatisfied with his life and had a depressed mood.

All patients assessed themselves as emotionally balanced, without major depressive states and described their self-esteem as average. Their relationship with the environment, their experiences with social support, financial resources and acceptance from other people, were all described as satisfactory. Four patients described themselves as independent and were able to make their own

decisions (relevant to their age). Two patients rated themselves as not having sufficient autonomy and felt subordinate to those around them. All of the patients at school age (n = 3) declared learning difficulties.

4. DISCUSSION AND CONCLUSIONS

According to a large, national registry of pediatric OHCA (Cardiac Arrest Registry to Enhance Survival - CARES) unlike in adults with OHCA, survival rates in children have not improved in recent years [15]. According to Nagata et al. the most significant factor associated with the clinical outcomes of paediatric cardiac origin OHCA is public AED use, whereas for non-cardiac OHCA, the most significant factor is bystander-performed rescue breathing [3].

Neurological impairment after cardiac arrest is dependent on the degree of brain damage suffered during the arrest [7]. The implementation of new therapies such as goal-directed therapies and therapeutic hypothermia has the potential to further improve survival rates following pediatric cardiac arrest [16].

This case series shows that OHCA in children has a good outcome when BLS is provided immediately and is followed by resuscitation performed by a team of emergency medical services and subsequent treatment in the ICU. Self-assessment of quality of life indicated that children who have suffered from a cardiac arrest preserved their physical ability over time and this ability does not differ from their healthy peers. However, a notable proportion of OHCA paediatric patients declared difficulties in learning, and reported an average overall quality of life in their self-assessment. Finally, changes in the CNS observed by MRI imaging, like atrophy or other features of hypoxic-ischemic encephalopathy such as periventricular leukomalacia, were observed more frequently in children with diagnosed neurological abnormalities.

CONFLICTS OF INTEREST

None declared.

Table II. Results of the Raven's Progressive Matrices (RPM)

Patient	Sex	Age at the study	RPM score	RPM percentile	Answering the questions
1	M	21	38	44	Independently
2	M	21	46	66	Independently
3	M	16	54	90	Independently
4	M	20	20	1	Independently
5	M	11	34	17	Independently
6	M	12	28	11	With help

M – male.

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