11. Hadinnapola C., Bleda M., Haimel M., Screaton N., Swift A. [et al.] Consortium NB-RD, Idiopathic UKNCSo, Heritable PAH, Graf S, Morrell NW: Phenotypic characterization of EIF2AK4 mutation carriers in a large cohort of patients diagnosed clinically with pulmonary arterial hypertension. *Circulation*. 2017;136(21):2022-2033. https://doi.org/10.1161/CIRCULATIONAHA.117.028351
12. Montani D., Lau E. M., Descatha A., Jais X., Savale L. [et al.] Occupational exposure to organic solvents: a risk factor for pulmonary veno-occlusive disease. *Eur. Respir. J.* 2015;46(6):1721-1731. https://doi.org/10.1183/13993003.00814-2015
13. Chamorro F. C. I., Garces C. P., Perez M. R., Sanchez S. R. M., Ferrando S. C. [et al.] The first experience of pulmonary veno-occlusive disease treatment with macitentan and sildenafil. *Rev. Esp. Cardiol. (Engl. Ed.).* 2017;70(5):396-397. https://doi.org/10.1016/j.rec.2016.07.011
14. Montani D., Girerd B., Jais X., Levy M., Amar D. [et al.] Clinical phenotypes and outcomes of heritable and sporadic pulmonary veno-occlusive disease: a population-based study. *Lancet Respir. Med.* 2017 Feb;5(2):125-134. https://doi.org/10.1016/S2213-2600(16)30438-6
15. Eyries M., Montani D., Girerd B., Perret C., Leroy A. [et al.] EIF2AK4 mutations cause pulmonary veno-occlusive disease, a recessive form of pulmonary hypertension. *Nat. Genet*. 2014;46(1):65-69. https://doi.org/10.1038/ng.2844
16. Tenorio J., Navas P., Barrios E., Fernandez L., Nevado J. [et al.] A founder EIF2AK4 mutation causes an aggressive form of pulmonary arterial hypertension in Iberian Gypsies. *Clin. Genet.* 2015, 88(6):579-583. https://doi.org/10.1111/cge.12549
17. Best D. H., Sumner K. L., Austin E. D., Chung W. K., Brown L. M. [et al.] EIF2AK4 mutations in pulmonary capillary hemangiomatosis. *Chest.* 2014;145(2):231-236. https://doi.org/10.1378/chest.13-2366
18. Eichstaedt C. A., Song J., Benjamin N., Harutyunova S., Fischer C. [et al.] EIF2AK4 mutation as «second hit» in hereditary pulmonary arterial hypertension. *Respir. Res*. 2016; 17(1):141. https://doi.org/10.1186/s12931-016-0457-x
19. Liang L., Ma G., Chen K., Liu Y., Wu X. [et al.] EIF2AK4 mutation in pulmonary veno-occlusive disease: A case report and review of the literature. *Medicine (Baltimore).* 2016;95(39):e5030. https://doi.org/10.1097/MD.0000000000005030

About authors:

Dankovtseva Elena Nikolaevna, MD, PhD, Lecturer; tel.: +74991468205; e-mail: e-n-d@bk.ru

Osipova Natalya Borisovna, post-graduate student; e-mail: natalya.kudashewa@yandex.ru

Minushkina Larisa Olegovna, MD, PhD, DrSci(med), Professor; tel.: +79036738976; e-mail: minushkina@mail.ru

Speshilov Gleb Igorevich, Head of the genetic laboratory; e-mail: g.speshilov@chromaspark.com

Nikitin Alexey Georgievich, PhD, Head of the genetic laboratory; e-mail: avialn@gmail.com

Galyavich Albert Sarvarovich, MD, PhD, DrSci(med), Professor; e-mail: agalyavich@mail.ru

Remblevskaya Krestina Valerievna, post-graduate student; e-mail: nadelhalter@mail.ru

Zateyshchikov Dmitry Alexandrovich, MD, PhD, DrSci(med), Professor; tel.: +74991464151; e-mail: dz@bk.ru

UDC 616.711.718:616.831.45-08
DOI – https://doi.org/10.14300/mnnc.2018.13101
ISSN – 2073-8137

CLINICAL CASE OF TREATMENT OF THE LEGG – CALVE – PERTHES DISEASE BY EXTENDED PARASYMPATHETIC BLOCKADE

Akhtyamov I. F. [1, 2], Lobashov V. V.[1, 3], Zaidullin D. G. [3], Anisimov O. G. [1]

[1] Kazan State Medical University, Russian Federation
[2] Republican Clinical Hospital, Kazan, Russian Federation
[3] Clinical Hospital № 7, Kazan, Russian Federation

КЛИНИЧЕСКИЙ СЛУЧАЙ ЛЕЧЕНИЯ БОЛЕЗНИ ЛЕГГА – КАЛЬВЕ – ПЕРТЕСА МЕТОДОМ ПРОДЛЕННОЙ ПАРАСИМПАТИЧЕСКОЙ БЛОКАДЫ

И. Ф. Ахтямов [1, 2], В. В. Лобашов [1, 3], Д. Г. Зайдуллин [3], О. Г. Анисимов [1]

[1] Казанский государственный медицинский университет, Российская Федерация
[2] Республиканская клиническая больница, Казань, Российская Федерация
[3] Городская клиническая больница № 7, Казань, Российская Федерация

This article presents a clinical case of an effective conservative treatment of the Legg – Calve – Perthes disease in girl eight years old. The follow-up period was 7 years. The selected method of treatment was an extended parasympathetic blockade in the spine lumbar part using a Ropivacaine 0.2 % solution administered daily for 12 hours. The treatment duration was 8 days.

Keywords: Legg – Calve – Perthes disease, non-operative treatment, prolonged epidural analgesia

Представлен клинический случай эффективного консервативного лечения промежуточной стадии болезни Легга – Кальве – Пертеса с выраженной деформацией эпифиза головки бедренной кости у пациентки 8 лет. Отдаленный результат отслежен на сроке 7 лет после начала лечения. В качестве метода лечения использована продленная парасимпатическая блокада (12 часов в сутки) в поясничном отделе позвоночника раствором Ропивокаина 0,2 %. Продолжительность курса лечения составила 8 суток.

Ключевые слова: болезнь Легга – Кальве – Пертеса, консервативное лечение, продленная эпидуральная анальгезия

For citation: Akhtyamov I. F., Lobashov V. V., Zaidullin D. G., Anisimov O. G. CLINICAL CASE OF TREATMENT OF THE LEGG – CALVE – PERTHES DISEASE BY EXTENDED PARASYMPATHETIC BLOCKADE. *Medical News of North Caucasus.* 2018;13(3):542-545. DOI – https://doi.org/10.14300/mnnc.2018.13101

Для цитирования: Ахтямов И. Ф., Лобашов В. В., Зайдуллин Д. Г., Анисимов О. Г. КЛИНИЧЕСКИЙ СЛУЧАЙ ЛЕЧЕНИЯ БОЛЕЗНИ ЛЕГГА – КАЛЬВЕ – ПЕРТЕСА МЕТОДОМ ПРОДЛЕННОЙ ПАРАСИМПАТИЧЕСКОЙ БЛОКАДЫ. *Медицинский вестник Северного Кавказа.* 2018;13(3):542-545. DOI – https://doi.org/10.14300/mnnc.2018.13101

LCPD – Legg – Calve – Perthes Disease

MRI – Magnetic Resonance Imaging

The Legg – Calve – Perthes disease (LCPD) is a juvenile form of idiopathic avascular necrosis of femoral head with an occurrence rate of 5.1 to 16.9 per 100,000 people. Despite numerous researches and trials and above a hundred year history, the numerous beliefs about the disease remain questionable [1]. In general, pathogenesis of the disease is attributed to the atrophy of the joint as a whole and the femoral head in particular.

Pharmacological sympathectomy in the form of a prolonged epidural analgesia at early stages of dystrophic processes is one of the possible options for restoring the nutritional balance in the femoral head [2]. Considering that avascular necrosis is accompanied with severe venous stasis and a high intraosseous pressure, blocking the sympathic innervation of veins of lower extremities may lead to their dilation and an increase of the venous shunt. As a consequence, it improves blood circulation, thus introducing a pathogenetic component to this type of therapy [3].

While the preventive [4] and therapeutic effect at early stages of treatment of the avascular necrosis of femoral head in children and adults [3] has already been proven, an extended parasympathetic blockade at later stages of the disease (let us call them intermediate stages preceding the healing stage) has not been studied. The purpose of this observation was to study the possibility of avoiding surgery among LCPD-affected children.

Material and Methods. Female patient M., 8 years old, was admitted to the orthopaedic department with complaints of pain in the left hip joint. The pain syndrome intensity increased with load and time (first symptoms were noticed 11 month before). The patient started limping. Both the child and the parents deny any preceding injury in the joint area or any cold-related diseases. Non-narcotic analgesic drugs administration allowed reducing the pain syndrome and limping for 4–8 hours, but then they re-emerged with the same intensity. The pain severity as per the VAS was 4.9 on the examination day.

A physical examination spotlighted an anatomical shortening of the left femoral component by 1.5 cm along with a defence attitude and an insignificant internal rotation and bending in the hip joint. At that, flexion contracture was 175 degrees and external rotation contracture was about 5 degrees. When walking, the patient limped on her left foot in an effort to compensate for the functional (1.5 cm) and anatomical shortening, with her foot being in an equinus position. There was noted a deficit in external rotation up to 30 degrees (with the pain syndrome increase) and bending deficit of 20 degrees as compared to the function of the symmetrical joint. The deviation amplitude in both joints was on a par, but the left joint was apparently causing discomfort to the patient.

The two X-ray projection image showed destruction and reduction in the femoral epiphysis height (Fig. 1A, 1B). Its external outline was incongruent with the acetabulum, and only 77 % of the head was covered by the acetabulum. The pathology was also verified with the MRI. According to the Catterall classification [4], this stage of the process could be referred both to group II and group III of the disease. While the outcome in group II is favourable, the success rate in group III, according to T. Terjesen [5], is only 4 %. Nevertheless, considering that the lateral portion of epiphysis in our patient was to a degree preserved (without fragmentation), it inspired hope for its possible recovery during treatment. A. Ferguson [6]

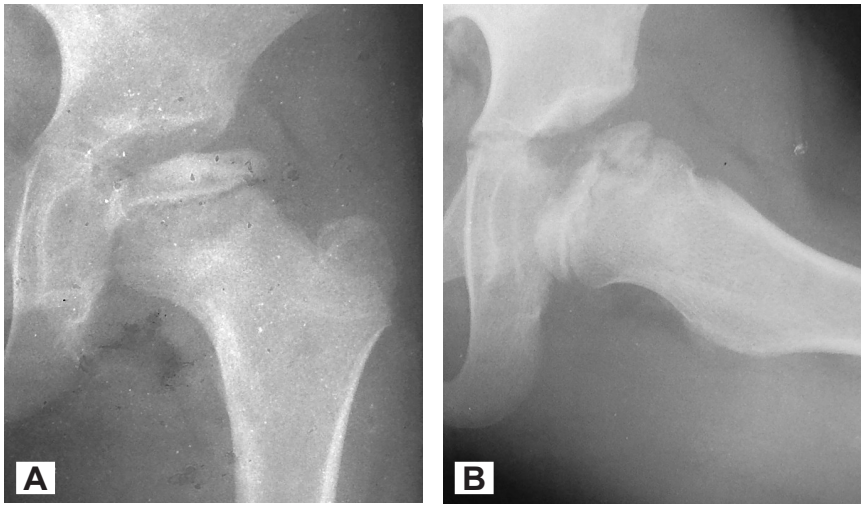

Fig. 1. X-ray of left hip joint A – front plaine, impression and total involvement femoral head, and B – frog-leg position. Anterior part of femoral head is preserve, while posterior is impressed and has epyphisional cyst

assumed that if the lateral portion of the femoral head is preserved, then it becomes a sort of a «spacer» protecting the epiphysis central part from the body weight load. An experimental work by G. Rab et al. [7] has confirmed the assumption that the lateral column integrity of the femoral head forms a biomechanical basis for a favourable outcome of the Perthes disease. It gave occasion to apply a conservative treatment approach and to avoid surgery. Along with the clinical and functional assessment and visualisation of the joint's structures, we used instrumental procedures that allowed to track changes in blood circulation and conditions of tissues near the hip joint in real time. Micro-circulation near the hip joint was analysed using the LAKK-02 apparatus based on the laser doppler flowmetry principle. Obviously, we assessed only the para-articular structures condition (due to the limited functionality of the apparatus), but we did manage to obtain an indirect information on the changes in micro-circulation, including the osseous tissue. The quantitative values upon the patient's admission were as follows: perfusion (M)=1.9 mm/s, average perfusion fluctuation (б)=0.2 Hz, micro-circulation factor (Kv)=8.2. The results obtained were checked against the average age-matched normal values and the condition on the contralateral side, but for brevity we used only values relating the affected joint's area over time. Haemoglobin concentration in tissues was analysed with the use of the INVOS 5100 Somanetics device, Troy, Michigan, USA (rSo2). The initial assessment showed a concentration of 47 %. We recoursed to the global myography to analyze the muscular system condition by using the Neurosoft MVP-4 apparatus for the purpose. The amplitude value was 0.394 (A, mV), and frequency of voluntary quadriceps contractions was 102 (F, Hz). The child's parents consented to a minimally invasive treatment complemented with an extended drug-induced parasympathetic blockade. The treatment in compliance with the applicable legislation and respective ethical standards was performed.

Treatment Plan. In a clinical setting, a catheter was introduced into the epidural cavity on the L2–L3 level of the spine under Ketamine general anaesthesia in a proportion corresponding to the age and weight of the child. The skin was double-tunnelled with the catheter exiting on the level of the left midaxillary line with further attachment of the catheter using a sterile waterproof plaster. The catheter was connected to the Vogt medical 250 ml infusion pump. Ropivacaine 0.2 % drug was introduced at an initial flow rate of 6 ml/h for 12 hours per day. As early as 20 minutes after emergence from general anaesthesia the patient noted a warming sensation in the entire left extremity and numbness of skin when palpated. On that ground the infusion rate was reduced to 4 mm/h and maintained for the entire treatment period (8 days). Motion activity was preserved in full. Active rehabilitation, including exercises aimed at the recovery of the muscle mass in the left hip area, was started on the second day. The patient was permitted to walk with a load on the affected lower extremity limited to 50 %. No side effects or adverse events were observed.

Results and Discussion. The day before discharge from the in-patient clinic the catheter was removed and the patient was subjected to the staged examination as per the above mentioned plan. Pain syndrome, according to the VAS rating, was 0. The joint's vicious position was entirely corrected, and the rotation range deficit in the left hip joint was reduced to 10 degrees. The proximity shortening remained within the limits of the epiphysis anatomical defect (15 mm). Micro-circulation in tissues adjoining the affected hip joint was as follows: M=3.2 mm/s, б=0.6 Hz, Kv=6.0. Haemoglobin concentration in tissues of the area under scrutiny reached 75 %. Changes in the electromyography data were insignificant, namely: A=0.395 mV, and the frequency of voluntary quadriceps contractions was 100 Hz. The patient was permitted to exert full load on the left hip joint only in three months upon the discharge from the in-patient clinic. A follow-up care allowed to ascertain the treatment effectiveness which was evidenced by the lack of any pain-related complaints, recovery of the left hip joint's motion range, gradual recovery of the correct motion pattern. The final examination was performed seven years after the treatment. Clinician-observed: equal length of lower proximities, full range of motion as compared to the healthy side. No pain syndrome. No gait abnormalities. Equal hip width. A better sphericity and full recovery of the femoral head's structure as evidenced by X-ray and MRI images (Fig. 2A, 2B; Fig. 3A, 3B). According to the data on micro-circulation in the tissues adjoining the left hip joint, the perfusion (M) was 4.8mm/s, average perfusion fluctuation (б)=0.8 Hz, micro-circulation factor (Kv)=4.5. Haemoglobin concentration in tissues remained equal to about 70 %. Myography data increased significantly, namely: the amplitude rose to 0.594 (A, mV), and frequency of voluntary quadriceps contractions rose to 247 (F, Hz).

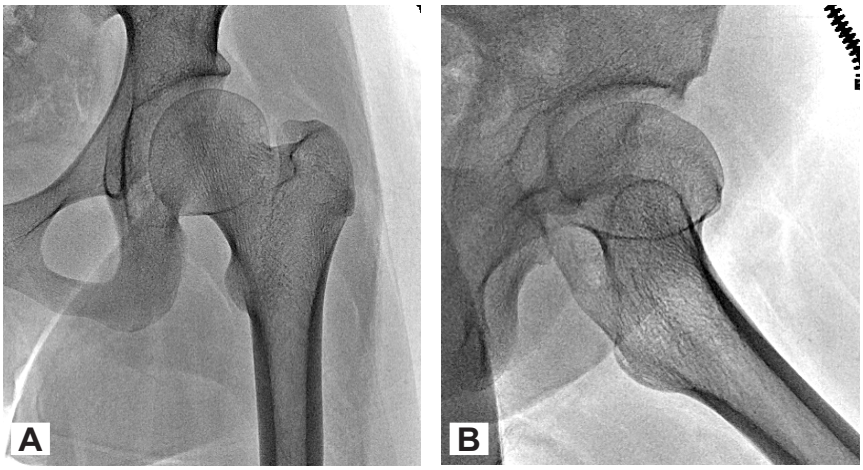

Fig. 2. X-ray left hip in 7 years after treatment: A – at plane radiograph shortness of femoral neck and enlargement of femoral head with ideal sphericity; B – frog leg position sphericity alterations within 2 mm

The treatment of the female patient suffering from the LCPD in the intermediate stage (group II-III, according to Catterall) of the pathological process in the left hip joint made it possible to obtain good clinical and functional results. The increased motion range and pain management immediately after the therapy ensured an active rehabilitation conditioned by a temporary load limitation [1].

A consistent increase of the M and б values against the reduction of the Kv value immediately and in the long term after the treatment could indirectly indicate a micro-circulation improvement in the area under scrutiny. The oxygenation value sensitive to the haemoglobin

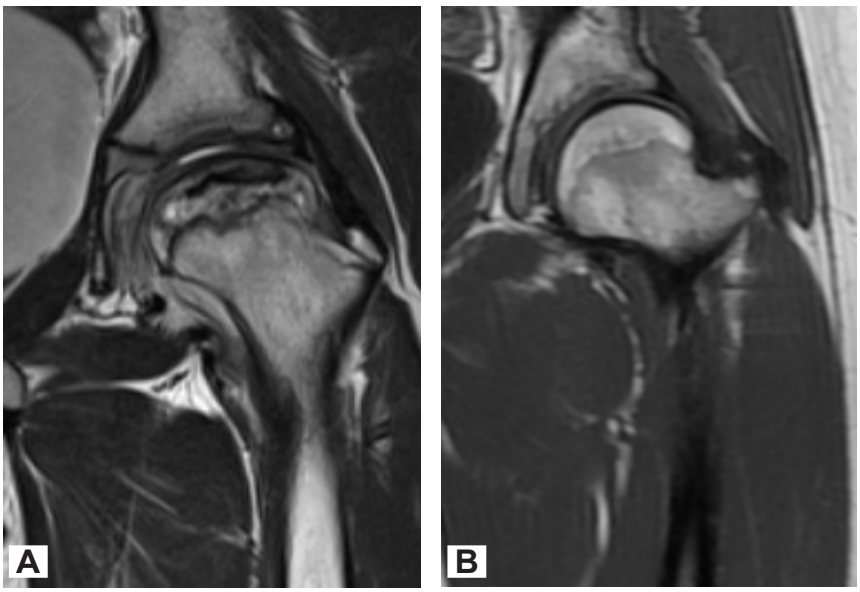

Fig. 3. MRI left hip before treatment, subtotal involvement of necrotic process, although lateral pillar is preserved 9A); 7 year after treatment. Structure of femoral joint is recovered with satisfied congruency (B)

concentration in tissues adjacent to the hip joint almost doubled from 47 % to 75 % immediately after the treatment (rSo2).

The electromyography data progressively grew over time and with the patient's growing activity. The joint's elements visualisation using X-ray and MRI imaging showed good result of the treatment as per the international system for assessing the severity of the LCPD.

According to the international studies covering a multitude of centres, there is a high percentage of the conservative treatment unsatisfactory outcome among the patients with the intermediate and final stages of LCPD [8, 9], while Russian publications report a positive effect of peripheral blockades [2, 3, 4] which emphasizes the necessity to continue further studies in this field.

Conclusions. This clinical case allowed to demonstrate the possibilities of the prolonged epidural analgesia (parasympathetic blockade) in treating a female patient for the LCPD (intermediate stage). After 7 years the function of the affected hip joint is fully recovered. In addition, the sphericity of the femoral head was restored without pain syndrome.

A favourable outcome in the particular case leaves room for estimating positive prospects of a wider use of the prolonged epidural analgesia (parasympathetic blockade) method for treating this disease among children not only in early stages, but also in intermediate stages.

Disclosures:
The authors declare no conflict of interest.

References

1. Akhtyamov I. F. New approach of treatment early stages of avascular necrosis of hip. *Vestnik travmatologii i ortopedii im. N. N. Priorova*. 2011;1:33-37.
2. Akhtyamov I. F., Anisimov O. G., Lobashov V. V. Method of threatment early stages of Perthes desease. *Zhurnal travmatologii i ortopedii Rossii*. 2014;3:122-128.
3. Kamosko M. M., Zabolotskii D. V. [et al.] Method of treatment development dislocation of hip. Patent RU 2 417 080 C2 03.02.2009
4. Catterall A. The natural history of Perthes' disease. *J. Bone Joint. Surg. Br.* 1971;53(1):37-53.
5. Herring J. A. *Legg-Calve-Perthes disease. Part II: Prospective multicenter study of the effect of treatment on outcome. J. Bone Joint. Surg. Am.* 2004;86(10):2121-2134.
6. *Kim H. K.* Pathophysiology and new strategies for the treatment of Legg-Calvé-Perthes disease. *J. Bone Joint. Surg. Am.* 2012;94(7):659-669. https://doi.org/10.2106/JBJS.J.01834
7. Rab G. T., Wyatt M., Sutherland D. H., Simon S. R. A technique for determining femoral head containment during gait. *J. Pediatr. Orthop*. 1985;5(1):8-12.
8. Terjesen T., Wiig O., Svenningsen S. The natural history of Perthes' disease. *Acta Orthop*. 2010;81(6):708-714. https://doi.org/10.3109/17453674.2010.533935
9. Ferguson A. B. Jr. Pathology and treatment of Legg-Perthes disease. *Jr. Pediatr An.* 1976;5(4):113-129.

About authors:

Akhtyamov Ildar, PhD, Professor, Head of department of trauma and orthopaedic surgery and emergency surgery; Principal scientist; e-mail: Yalta60@ya.ru

Lobashov Vladislav, postgraduate student; tel.: +79274284449; e-mail: lobashoff@yandex.ru

Zaidullin Damir, MD, Chief of department orthopaedic trauma department; tel.: +78432213678

Anisimov Oleg, PhD, Principal scientist; tel.: +78432213980