**TREATMENT OF COMPLEX REGIONAL PAIN SYNDROME AFTER FILLING A SINGLE BONE-CYST CAVITY WITH BETA-TRICALCIUM PHOSPHATE GRANULES**

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**Background.** Complex regional pain syndrome is a condition associated with a multitude of clinical factors. Its characteristic feature is persistent pain caused by injuries and is not anatomically limited to the location of a particular peripheral nerve.

**Clinical case.** This article describes a case involving the treatment of complex regional pain syndrome in a thirteen-year-old patient, which resulted in a simple bone cyst surgical treatment of the lower-third of the fibula. Diagnostics were based on clinical, laboratory, histological, radiological, and instrumental methods of research. The treatment methods included medication (nonsteroidal anti-inflammatory drugs, antidepressants, antipsychotics, anticonvulsants, non-opioid analgesics of central action, and bisphosphonates), cold plasma ablation, neurolysis of the sural nerve, prolonged regional anesthesia, tunneling of the bone marrow cavity (filled by substitutional filler), and marginal bone resection.

**Discussion.** Complex regional pain syndrome is a poorly studied condition, which contributes to the complexity of its diagnosis. In this case, the presence of complex regional pain syndrome can be characterized by tissue injury during surgical intervention as well as by intraoperative injury of the nerve fibers. The stages of complex regional pain syndrome detected in studies may not appear in all patients, and in this case, no staging was observed. By eliminating the obliteration of the medullary canal after segmental resection of the sclerosed portion of the bone, it was possible to reduce the severity of pain, which resulted in the subsequent disappearance of the manifestations of complex regional pain syndrome.

**Conclusions.** This case testifies to the effectiveness of various methods of treating complex regional pain syndrome. The etiology of the specific patient’s pain syndrome should be considered when treating complex regional pain syndrome.

**Keywords:** case report; simple bone cyst; complex regional pain syndrome; beta-tricalcium phosphate.

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**ЛЕЧЕНИЕ КОМПЛЕКСНОГО РЕГИОНАРНОГО БОЛЕВОГО СИНДРОМА ПОСЛЕ ЗАПОЛНЕНИЯ ПОЛОСТИ СОЛИТАРНОЙ КОСТНОЙ КИСТЫ ГРАНУЛАМИ БЕТА-ТРИКАЛЬЦИЙФОСФАТА**

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**Обоснование.** Комплексный регионарный болевой синдром — состояние, характеризующееся множеством клинических проявлений, в первую очередь хронической постоянной болью, связанной с разнообразными повреждениями и анатомически не ограниченной областью иннервации конкретного периферического нерва.
This article presents the treatment of complex regional pain syndrome (CRPS) in a 13-year-old patient, resulting from the surgical treatment of a solitary bone cyst (SBC) in the lower third of the fibula by filling the cavity with beta-tricalcium phosphate granules.

A solitary or single-chamber bone cyst (SBC) is a condition that affects bones. It is characterized by the formation of a single-chamber cavity filled with a clear yellow, straw-colored liquid. In most cases, it has a lining and a connective tissue structure that may contain single giant multinucleated cells [1]. SBCs are among the most common tumor-like bone lesions in children [2]. Most often, they are found in the metaphyseal areas of long bones [3]. A solitary bone cyst leads to the thinning of adjacent sections of the cortical layer of the bone, which can cause a pathological fracture. The main objectives of treatment consist of reducing the risk of a pathological fracture by restoring the organotypical bone structure of the affected bone section. Treatment involves the use of conservative and surgical methods. Despite the many methods described in the literature, there is no single standard for the treatment of patients with an SBC [2].

Complex regional pain syndrome (CRPS) is a condition characterized by many clinical manifestations, primarily chronic persistent pain associated with various injuries and anatomically unlimited areas of innervation by a specific peripheral nerve. There are two types of CRPS, namely type I CRPS, widely known in the 20th century as Sudeck's post-traumatic syndrome (currently the use of this term is considered incorrect), and type II CRPS, designated as causalgia [4]. The syndrome is often accompanied by sensitivity disorders, changes in skin color or temperature, disorders of sweating, tremor, dystonia, local osteoporosis, and others. Various factors can cause CRPS; most often, it occurs after injuries and surgical interventions (in 80%–85% of cases). This syndrome is a relatively rare condition and, therefore, has been studied insufficiently. This limited attention has been because, to some extent, the complexity of its timely diagnosis [5]. CRPS is detected during the first four months after injury in only 3.8%–7.0% of patients.

1. Prolonged pain, not corresponding in intensity to a previous injury or surgery.
2. The history should include at least one of the listed disorders in each of the four categories:
   - sensitivity — hyperalgesia and/or allodynia;
   - vasomotor — data on temperature asymmetry, and/or discoloration of the skin, and/or asymmetry of skin color;
   - sudomotor/swelling — edema, and/or a change in sweating, and/or asymmetry of sweating;
   - motor/trophic — data on a decrease in the amplitude of movements, and/or motor dysfunction (weakness, tremor, dystonia), and/or trophic changes (in the scalp, nails, skin).
3. During the examination of the patient, at least one diagnostic symptom of the following should be recorded:
   • sensitivity — the presence of hyperalgesia and/or allodynia;
   • vasomotor — temperature asymmetry (>1 °C), and/or discoloration of the skin, and/or asymmetry of skin color;
   • sudomotor/swelling — edema, and/or a change in sweating, and/or asymmetry of sweating;
   • motor/trophic — decrease in the amplitude of movements and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (in the scalp, nails, skin).
4. No other diagnosis could explain all symptoms.

Treatment of CRPS includes medications, regional peripheral nerve blockade, rehabilitation measures, and psychotherapy [7]. The appropriateness of using some treatment methods is quite controversial [8]; therefore, there is no absolute standard for therapeutic measures of this syndrome. However, the therapy should be etiopathogenetically substantiated; but in this case, only positive results are possible [9].

Beta-tricalcium phosphate (β-TCP) is a biocompatible, biodegradable synthetic material used as a biological filler to replace damaged bone tissue. According to most studies, β-TCP in the practice of orthopedists has proved itself as a material with osteoplastic characteristics necessary to replace post-resection defects [10].

Usually, a complete or almost complete restoration of the bone structure occurs several years after the use of this osteo-replacing material [10]. The β-TCP substitution rate depends on many factors, such as the amount of implantable material, type of bone, and age of the patient. Relapses of cysts and osteomyelitis were registered in only a few cases when using this material [10]. However, when analyzing the sources in PubMed and eLibrary databases, there were no clinical cases associated with atypical resorption of the bone-replacing material when filling the cavity formed after the marginal excision of a neoplasm.

Clinical case

After an ankle joint injury in a 13-year-old patient, an X-ray examination revealed an aggressive lesion in the lower third of the right fibula oval, which was 1.9 × 0.8 cm in size (30.11.2012) (Fig. 1). X-ray control was recommended every six months. One year later, the size of the cavity increased to 2.2 × 1.0 cm as determined on the image. The patient complained of a mild transient pain syndrome (2–3 points according to a visual analog scale (VAS)), which intensified during physical exertion (according to a VAS, up to 5–6 points).

Three months after repeated X-ray examinations (January 20, 2014), surgery was performed. of the procedure entailed marginal excision of the affected part of the right fibula with electrocoagulation of the cyst walls and plastic surgery of the post-resection bone defect with β-TCP granules (Chronos, Switzerland). The pathologically altered region of the lower third of the fibula was accessed externally. Intraoperatively, after removal of the cortical layer, 2.0 ml of hemorrhagic contents were detected and evacuated. The endosteal surface of the preserved cortical walls was treated with a small curette. The radiograph after surgery revealed that the cavity had been filled with granules of osteoplastic material. According to the histological examination, there was a solitary bone cyst.

Walking with crutches with a graduated weight load on the operated lower limb was allowed on day
14 after surgery. On day 21, after surgery, a fracture of the preserved cortical layer of the fibula without displacement occurred in the area of the bone cyst resection (Fig. 2). The lower right leg and foot were not immobilized during the post-fracture period.

Two weeks after the fracture, the patient experienced burning pains, estimated by him as 5–7 points according to a VAS, in their presence, episodes of fulgurant pains also occurred (7–9 points according to a VAS). A clinical test revealed neuropathy of the peripheral nerves of the lower leg, *n. suralis* and *n. peroneus*. Diagnostic blockades were performed using lidocaine, which allowed short-term pain relief.

On September 30, 2014, a surgical intervention was performed in the form of neurolysis, *n. suralis*. In the early postoperative period, the characteristic pain syndrome was absent, but on day 5, it reappeared. Stimulation electroneuromyography was conducted and in the study of the motor fibers *n. peroneus*, *n. tibialis*, on both sides, the pathology was not detected.

Body temperature increased to subfebrile; this condition was noted for two years. A course of treatment was prescribed, including ipidacrine 10 mg twice a day, pregabalin 75 mg 2 twice a day, and B vitamins for one month.

In the future, no positive dynamics were seen, which led to the assumption of a pronounced involvement of *n. suralis* in cicatrical-adhesive processes and the need for repeated revision or resection of this nerve.

A catheter was inserted (for one month) for prolonged analgesia using 0.2% ropivacaine to relieve pain in the middle third of the lower right leg. During the action of a local anesthetic, the pain was significantly reduced to two points, according to a VAS. The patient independently regulated the drug administration through a microinfusion pump with an adjustable flow rate. The best way to relieve the pain was an infusion for 2 h at a rate of 4 ml/h 4–5 times a day when necessary.

On January 19, 2015, revision surgery of the neurolysis of *n. suralis* was performed. During the postoperative period, an improvement was first noted (0–1 point, according to a VAS). However, after two days, fulgurant pains appeared along the nerve branch (up to 9 points according to a VAS). A course of treatment was prescribed, including amitriptyline, at a dose of up to 50 mg/day for two months to stop the neuropathic pain.

Within three months, the pain focus was centered in the form of an increased dull, bursting pain in the region of the affected area of the bone (up to 6–8 points according to a VAS) with a significant increase at night and during exertion. The roentgenogram revealed obliteration of the bone marrow cavity; magnetic resonance imaging showed cicatrical adhesion of the soft tissues of the lower third of the leg (Fig. 3). There was a slight restriction of the range of movement in the right ankle joint, slight swelling, and temperature asymmetry (a local increase in temperature of the corresponding skin area).

On April 28, 2015, surgery was performed in the region of the tunneled site of the lower third of the fibula, represented by reconstructing the osteoplastic material. During the postoperative period lasting 2–3 months, the intensity of the pain decreased (up to 4–6 points according to a VAS), then it reached the previous level (8 points according to a VAS). A computer tomogram six months after the surgery showed a round defect, a break in the cortical layer with uneven areas of bone sclerosis of the distal fibula, and a lack of visualization of the bone marrow cavity at this level.

On August 15, 2015, percutaneous cold plasma ablation with an Arthrocare Quantum 2 was performed using the Topaz Microdebrider nozzle to block pain reception temporarily. The effect of the procedure was insignificant (6–8 points, according to a VAS).

Reinstallation of the catheter (for two weeks) in the middle third of the lower right leg for prolonged analgesia with 0.2% ropivacaine was also ineffective (4–6 points according to a VAS during the infusion).

The pain syndrome, up to 4–5 points according to a VAS, was registered when taking flupirtine maleate at a dose of 200 mg, or etoricoxib 90 mg, or with intramuscular injections of ketorolac tromethamine 30 mg.

Based on clinical data (prolonged pain, impaired sensitivity, temperature asymmetry, the decreased amplitude of movements), taking into account the ineffectiveness of the treatment and the absence of an identified disease that would explain the above complaints, a diagnosis of CRPS was established.
In January 2016, to treat CRPS, 5 mg of zoledronic acid was prescribed in combination with the intake of calcium preparations at a dose of 1000 mg and vitamin D at a dose of 10,000 IU. A course of gabapentin 300 mg 2 times a day was performed with a gradual increase to 300 mg 3 times a day, and a course of duloxetine, starting from 30 mg/day and then increasing the dose to 60 mg/day after one week. The course of treatment was three months.

Persistent pain syndrome (up to 6–8 points according to a VAS), a decrease in surface sensitivity along the posterolateral surface of the lower right leg, and anesthesia of the dorsal and plantar surfaces of the outer part of the right foot, starting from the lateral surface of the finger III, were noted. The patient walked with crutches. If the foot was not supported when trying to step on the affected limb, then the pain intensified noticeably. The exacerbation of the pain syndrome occurred in the evening and at night (up to 8–10 points according to a VAS). The pain was noted on palpation on the lateral ankle of the lower right leg. The range of motion of the right ankle joint was limited due to pain. Swelling and hyperthermia periodically appeared in the affected area.

At the level of the distal metadiaphysis of the right fibula, computed tomography revealed a deformity and osteosclerotic bone changes over 29.0 mm with endosteally located areas of high density. The bone was slightly swollen locally, through channels were noted after tunneling, notching and cystic restructuring of the posteroexternal surface of the right talus bone, thickening of the adjacent parts of the joint capsule of the right ankle joint in the posteroexternal parts due to slight edema, and the amount of synovial fluid was slightly increased (Fig. 4).

On April 11, 2017, because conservative and surgical treatments were ineffective, a subperiosteal segmental resection of the sclerotic area of the lower third of the right fibula within unchanged bone tissue was performed. The size of the resected bone site was 1.5 × 3.0 cm. According to the histological data, the site of osteosclerosis was determined. A plaster cast was applied for eight weeks (Fig. 5).

In the postoperative period, the severity of pain decreased (up to 4–6 points according to a VAS). Intensive rehabilitation measures were performed.
Four months after resection of the sclerotic area of the lower third of the fibula, the heterogeneity of the structure and blurring of the contours of the distal metadiaphysis of the fibula with the formation of a bone callus were determined on a control X-ray (Fig. 6). The full load on the limb was recognized as appropriate. At the six-month post-surgical examination, the pain was absent (0 points according to a VAS), and there was a loss of sensitivity in the dorsum of the foot. The subsequent examination 12 months after the resection showed the absence of pain or other clinical manifestations. According to computed tomography, there was a clear tendency to restore the organotypical bone structure of the lower third of the fibula in the surgical area (Fig. 7).

Discussion

Complex regional pain syndrome is a rare condition, which determines the complexity of its diagnosis. Therefore, clinicians do not immediately identify it. Establishing the root cause for the occurrence of this syndrome and its type also presents a problem. As mentioned above, there are two types of CRPS, I and II. CRPS I is provoked by tissue damage because of a limb injury, and CRPS II is caused by nerve damage. In the case described, the occurrence of CRPS can be associated with both tissue injury during surgery (marginal resection of the affected part of the fibula), and intraoperative damage to nerve fibers. In addition, it is difficult to establish the exact time of occurrence of the first manifestations of CRPS, since the physical load on the limb was limited because of recovery during the postoperative period.

At this stage, it is impossible to state with full confidence whether the restructuring of the osteoplastic material, accompanied by the osteosclerotic process, affected the further development of CRPS. This distinction is difficult since a similar radiological picture was noted after the onset of the main disease symptoms. Alternatively, atypical repair of bone tissue, manifested by obliteration of the medullary cavity, was noted in the case of CRPS, possibly because of the neurotrophic disorder.

The question of the sensitivity disorder remains unresolved, manifested by hyperalgesia in the lateral ankle and loss of sensitivity of the dorsal and
Conclusion

The above example demonstrates the following:
1) The complexity of the diagnosis, interpretation of the data, and the choice of the therapeutic approach for CRPS;
2) A short-term effect or lack of a result when applying symptomatic methods of treatment to CRPS, both conservative and surgical;
3) The importance of knowledge of pain etiology in the treatment of CRPS.

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References


Plantar surfaces of the outer part of the foot. This symptom can be interpreted because of the damage to the integrity of the nerve because of surgical intervention, which explains the sensitivity disorders after the disappearance of the pain syndrome during the subsequent examination, and as a manifestation of CRPS, one of the diagnostic criteria of which is a loss of sensitivity.

The stages of CRPS stages established in the study may not appear in all patients [6], and in this case, we did not record a certain staging, which also hindered the diagnosis.

The use of standard methods, both non-surgical (antidepressants, antipsychotics, anticonvulsants, bisphosphonates), and surgical (cold plasma ablation, revision, and neurolysis of n. suralis) treatment in the case under study did not provide a lasting positive result. Nevertheless, a temporary effect was noted with the use of regional blockades, prolonged conduction analgesia, neurolysis of n. suralis, and tunneling of the site of the lower third fibula, as represented by reconstructing the osteoplastc material. It was possible to reduce the severity of pain and the subsequent disappearance of CRPS manifestations by eliminating the bone marrow cavity after the segmental resection of the sclerotic section of the fibula.

**Conclusion**

The stages of CRPS stages established in the study may not appear in all patients [6], and in this case, we did not record a certain staging, which also hindered the diagnosis.

The complexity of the diagnosis, interpretation of the data, and the choice of the therapeutic approach for CRPS;

A short-term effect or lack of a result when applying symptomatic methods of treatment to CRPS, both conservative and surgical;

The importance of knowledge of pain etiology in the treatment of CRPS.
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