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科研动态丨华山医院康复医学科新发现：长时程发散式体外冲击波治疗或可逆转脊髓损伤后神经源性异位骨化—病例报道

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Research Trends丨New discovery in the Department of Rehabilitation Medicine of Huashan Hospital: long-term divergent extracorporeal shock wave therapy may reverse neurogenic ectopic ossification after spinal cord injury-case report

Original Li Yun Huashan Rehabilitation Medicine May 19

Research News

Department of Rehabilitation Medicine, Huashan Hospital, Fudan University

The latest case report of the Department of Rehabilitation Medicine of Huashan Hospital Affiliated to Fudan University: the use of long-term divergent extracorporeal shock waves to treat neurogenic ectopic ossification after spinal cord injury can reduce the focus of ectopic ossification and achieve pain relief, Good effect of increasing joint mobility. Previously, conservative treatments for neurogenic heterotopic ossification were all preventive and irreversible lesions. The report provides an emerging non-invasive rehabilitation treatment for this disease, which may reverse the course of the disease. On May 13, 2020, the case was "Long-term radial extracorporeal shock wave therapy for neurogenic heterotopic ossification after spinal cord injury" : A case report), published online in the journal "The Journal of Spinal Cord Medicine" (IF=1.711) in the field of neuroscience.

Introduction

Heterotopic ossification (HO) is a biological process that deviates from normal tissue repair and manifests itself in the formation of mature lamellar bone in soft tissue that does not originally have bone. It can cause painful joint pain and limited joint movement in patients, which can reduce their quality of life. There are many types of HO, such as traumatic, hereditary, joint-derived, burned, etc., one of which is neurogenic, seen after the central nervous system injury.

Neurogenic heterotopic ossification (NHO) is related to central nervous system injury or disease. The incidence of NHO related to spinal cord injury can reach 50%. It usually occurs 1-3 months after injury, and the longest onset time May be 2 years after spinal cord injury. The pathogenesis of NHO is unclear. It is speculated that this may be due to abnormal neural control during the differentiation of mesenchymal cells into osteoblasts, and due to the decrease in tissue oxygenation or abnormal induction and differentiation of pluripotent cells in connective tissue, resulting in bone form. NHO mainly affects large joints, of which the hip joint is the most common, followed by the knee joint and elbow joint. At present, conservative treatment methods mainly play a preventive role, including mild passive joint activities and drug interventions, such as bisphosphonates or nonsteroidal anti-inflammatory drugs, followed by radiation therapy. Surgical resection can be used in cases that seriously affect joint mobility and daily life. It needs to be performed after HO matures, but complications may occur and even cause recurrence.Extracorporeal shock wave therapy (ESWT) is a non-invasive treatment method that uses pulsed sound waves propagating

in three-dimensional space to treat various musculoskeletal diseases, including plantar fasciitis, external epicondylitis of humerus, Shoulder joint calcified tendonitis and fracture nonunion. So far, some case reports and studies have reported the positive effects of ESWT on NHO of the extremities, such as pain relief, joint mobility improvement, and increased muscle strength. However, no literature has reported that ESWT can change the size of HO lesions. Here, we report a case of NHO after spinal cord injury that received divergent ESWT (radial extracorporeal shock wave therapy, RSWT) for 1 consecutive year, and observed changes in the size of NHO lesions.

Case report

Patient information

On September 25, 2017, a 30-year-old woman with no previous medical history developed limb weakness after a car accident. An emergency cervical MRI at a local hospital showed a C6 vertebral compression fracture and an abnormal signal in the corresponding spinal cord segment. The patient then underwent emergency surgery such as C6 decompression, debridement, bone grafting, and internal fixation under general anesthesia. In order to restore motor function, local hospitals were given routine physical therapy after operation. One month later, her left hip appeared swollen and painful, especially the lateral hip, which restricted hip movement. Imaging examination suggested the left hip HO. The local hospital then adopted mild joint loosening treatment to alleviate left hip pain and maintain joint mobility. However, the patient subsequently complained of increased pain and limited joint movement, and the swelling area of the left hip gradually expanded. In January 2018, the patient was referred to the Department of Rehabilitation Medicine of Huashan Hospital for further rehabilitation treatment. In order to control NHO inflammation, meloxicam was given orally for 4 months. After taking the drug, the patient complained of a slight relief of pain, but the size of the imaging ossification block remained unchanged compared with before treatment.

Assessment

Upon admission, the patient had muscle atrophy on both limbs, pain in the left hip, and a marked raised area. The critical muscle strength of the bilateral key muscles above the C8 level (muscle strength level 3) is level 5, and the tactile sensation and acupuncture sensation decrease below the bilateral T5 level. Sensation in the anal area decreases, spontaneous contraction of the anus and deep anal pressure exist. Tendon reflexes in both lower extremities were positive, and the Pap sign was positive. The patient can walk with the aid of a walker. The diagnosis was: incomplete C8 spinal cord injury, ASIA grade D. During the follow-up period, ultrasound examination and CT scan were used to assess the size of the ossified mass, measure the range of motion (ROM) of the left hip joint of the patient in the supine position, use VAS to assess the degree of pain, and determine the marker of bone formation-serum The level of serum alkaline phosphatase (sALP).

RSWT intervention

One week before RSWT treatment, meloxicam was discontinued. The patient was placed in a supine position and the left hip was completely exposed during RSWT intervention. A qualified physiotherapist trained by RSWT performs rehabilitation treatment. He applies the coupling agent to the skin of the raised area of the patient's left hip and slides the shock wave probe on the surface (MP100, Storz Medical Masterplus, Tagerwilen, Switzerland)). RSWT treatment parameters: 4000 shocks, frequency 8 Hz, pressure 1.0 bar (1 bar=0.1 MPa=0.1 N/mm^2), causing skin depression of about 1 cm. The treatment frequency is once a day, five times a week, a total of nearly 1 year. At the same time, conventional physical therapy is performed. There were no obvious side effects such as tingling, pain, redness, bruising, edema or hematoma during the course of treatment.

Result

From May 2018 to May 2019, patients underwent routine physical therapy, RSWT treatment

and follow-up in the undergraduate program. The evaluation intervals during treatment were 1.5 months, 3 months, 7 months and 11 months after the first intervention. Ultrasound examination showed that the size of hyperechoic lesions gradually decreased from 45mm*25mm to 18mm*16mm (Figure 1). CT scans showed that the ossified masses were reduced in cross section of ilium, ischium and femur. Three-dimensional reconstruction CT further confirmed that after one year of treatment, the volume of ossified mass was significantly reduced compared with the first RSWT intervention (Figure 2). Passive ROM of the hip joint was severely restricted in the early stage of NHO and gradually improved during the treatment of RSWT. After 1.5 months of treatment, the VAS score decreased from 8 to 1 and was maintained for 5 months. The patient's pain disappeared at the final stage of treatment. After the first course of treatment, sALP decreased from 184 IU/L to 126 IU/L, and remained stable for about 5 months, and finally further decreased to 86 IU/L (Table 1).

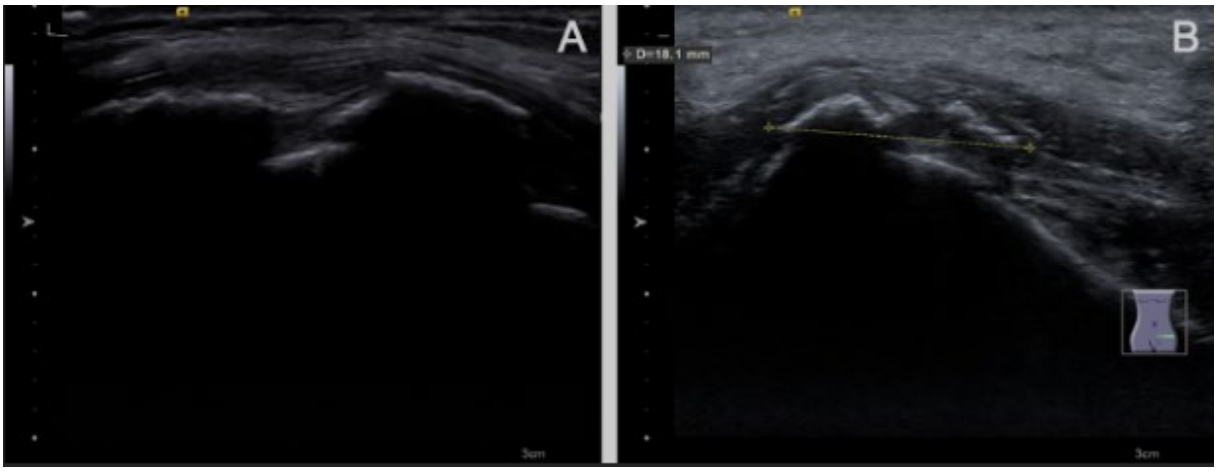

Figure 1 Ultrasound image taken at the maximum diameter of the same part of the left hip joint. A. Before RSWT intervention, the ultrasound image showed a hyperechoic lesion with no sound shadow at the back (maximum diameter: 45mm). B. After 1 year of treatment, the hyperechoic lesion on the ultrasound image becomes smaller

(maximum diameter: 18mm).

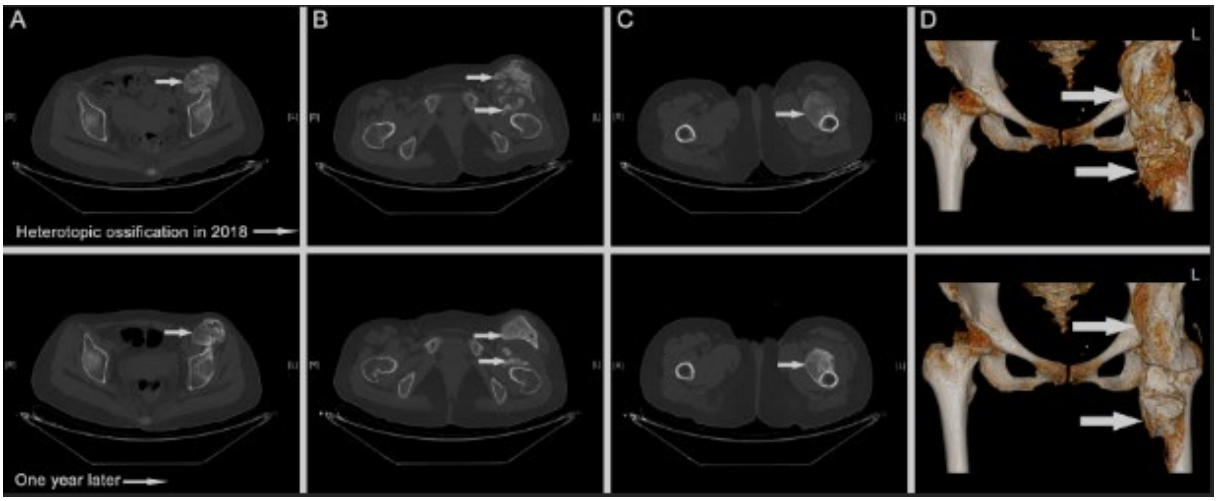

Figure 2 CT of hip joint. In 2018, neurogenic heterotopic ossification (NHO) of the left hip was distributed in the ilium and femur, and it shrank after 1 year (lower picture). A. NHO on the iliac cross section. B. NHO on the cross section

of the ischium. C. NHO on the cross section of the femur. D. Three-dimensional reconstruction CT showed that NHO lesions were significantly reduced. White arrows indicate ossified masses.

	Pre-treatment	Post-treatment			
Date	05/15/18	1st session 07/04/18	2nd session 08/24/18	3rd session 12/07/18	4th session 04/11/19
Size(mm).	45*25	41*25	40*18	38*25	18*16
Flexion	0	15°	25°	32°	46°
Extension	0	5°	15°	15°	20°
Abduction	0	20°	25°	33°	42°
Adduction	0	5°	12°	15°	18°
Internal Rotation	0	0	0	5°	10°
External Rotation	0	0	0	5°	10°
Pain(VAS)	8	1	1	1	0
sALP/IU/L	184	126	126	124	86

Note: VAS, visual analogue scale; sALP, serum alkaline phosphatase.

Table 1 Related measurement results before and after treatment (lesion size, passive ROM, pain and sALP level)

discussIn this case, we reported the efficacy of RSWT on NHO in a spinal cord injury patient. This patient has received non-steroidal anti-inflammatory drugs and conventional physical therapy, but has not achieved significant clinical benefits. Our report suggests that RSWT can be used to treat NHO, which can reduce pain and improve ROM, and may reduce the size of the lesion.Several cases have reported that ESWT treatment of HO has shown pain relief and functional improvement (such as continuous wheelchair sitting time, affected joint ROM, etc.), but no effect of lesion reduction has been observed. According to the different output energy waveforms, ESWT can be divided into two main types: focused extracorporeal shock wave therapy (FSWT) and RSWT. Compared with FSWT, RSWT has a lower intensity, less pain, less cost, a lower incidence of side effects, a shallower effect site, but a wider range. Thanks to these characteristics, the use of RSWT treatment does not require anesthesia, and does not require periodic refocusing of the probe. Therefore, RSWT is more suitable and acceptable in the clinical application of HO. However, in the currently reported cases of treating HO, RSWT is rarely used and FSWT is mostly used.It is generally believed that the soft tissue around HO is compressed by ossification foci, resulting in ischemic injury, inflammatory response and tissue necrosis (occupation effect). The three main mechanisms by which FSWT treats HO can be summarized as follows: (1) Regulation of angiogenesis: related to the early release of angiogenesis-related factors, thereby improving blood supply, aerobic metabolism, and promoting tissue and nerve regeneration; (2) anti-inflammatory: That is to regulate the secretion of inflammatory substances; (3) Pain relief: It is related to the reduction of excitatory nociceptive media and the reorganization of pathological memory.The specific mechanism of RSWT treatment of HO is still unclear. It is speculated that RSWT oscillates in tissues, which can improve microcirculation and metabolic activity, leading to micro-damage mediated by cavitation effects, which can lead to pain relief and neovascularization. In this case, we first observed that RSWT intervention reduced NHO lesions. The process of HO maturation is similar to normal bone reconstruction, and spontaneous osteolysis may occur in children with diseases related to hereditary bone

development abnormalities. However, adult HO lesions often gradually expand and stabilize. As of now, the only disease that has been proven to shrink through RSWT is calcified tendonitis of the shoulder joint. It is speculated that the pressure of the shock wave may cause the cracking and cavitation inside the calcification foci, leading to the disintegration of the sediment, and the sediment may be swallowed locally and absorbed into the surrounding soft tissue. Whether RSWT has a similar mechanical effect on NHO remains to be further explored.For HO, RSWT has no optimal parameter settings. In the reported cases, RSWT applied different parameters: 2500 to 4000 shocks, frequency 3 to 12 Hz, and pressure 2 to 5 bar. The frequency of RSWT treatment is once a week or 5 times a week for 3-7 weeks. Both can improve limb function and reduce pain, and the efficacy can last for 12 weeks. Different from previous studies, the duration of treatment in this case was nearly 1 year. Not only did pain, ROM, and sALP levels improve, but the size of NHO lesions also declined significantly. No previous reports have been reported. It is known that the following factors determine the clinical efficacy of ESWT: the sound wave energy per unit area per pulse is the energy flux density (EFD), and the number and frequency of impacts. An in vitro study showed that the total energy dose (TED) of each treatment can be calculated by multiplying the EFD by the total number of shocks, which can be regarded as a simple algorithm for the clinical study of shock wave dose. Therefore, the difference in efficacy in different cases may be caused by different TED and treatment courses. In this case, the energy accumulation of RSWT may also be one of the causes of NHO lesion shrinkage.ROM limitation is considered to be one of the most common clinical manifestations in HO. ESWT improved ROM, presumably related to pain reduction and fibrosis changes in ossification site. After treatment in this case, a pseudo-joint was formed across the hip joint between the iliac bone and the proximal femur, which may lead to limited ROM improvement. In addition, although we can not measure the actual bone mass of ossified foci, we did observe the shrinkage of NHO lesions by ultrasound and CT. In theory, it may help increase the ROM.**limitation**In this case, we did not detect the level of serum C-reactive protein, which is a marker of HO inflammatory activity after spinal cord injury. In addition, the RSWT parameters we used are based only on past cases and clinical experience. In the future, long-term follow-up observation is needed to record its long-term efficacy, as well as possible complications and recurrence.**in conclusion**Combined with the results of case reports, we believe that long-term RSWT has the potential to treat NHO, but its late efficacy and

reduction effect on NHO lesions need to be further confirmed.

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Chief physician Li Fang comments:

Our department Li Yun, Zhu Yulan, Xie Zhen, Jiang Congyu made a very meaningful clinical report: One year of diffuse extracorporeal shock wave treatment dramatically reduced the volume of hip neurogenic ectopic ossification lesions, and Improves pain and joint mobility. The high-energy shock wave treatment applied to urinary calculi can thicken the iliac bone, while the low-energy divergent extracorporeal shock wave treatment reduces the volume of ectopic ossification lesions. After the thinking process not written in this article, I think there is a possibility that the entire lesion will shrink due to the collapse of immature bone tissue inside the heterotopic ossification lesion. This patient had a high level of serum alkaline phosphatase when initially receiving divergent extracorporeal shock wave therapy. Although neurogenic ectopic ossification was approaching maturity for more than 6 months, this case was clearly not mature. One possible mechanism of neurogenic ectopic ossification is the decrease of tissue oxygenation, which is exactly the treatment target of divergent extracorporeal shock wave, which is also the solver of the soft tissue problem. If bone synthesis is interrupted, new normal tissue replaces part of immature bone tissue, collapse and shrinkage may occur. Unfortunately, the sound shadow behind the strong bone echo prevents us from exploring the deep part, and CT's ability to distinguish soft tissues is not sufficient. If

combined with MR and isotope imaging, the pathology and treatment mechanism of the entire neurogenic heterotopic ossification may be more clear.
Case reports cannot provide a strong evidence-based basis, but it provides a potential direction. Perhaps the door to successful treatment of neurogenic heterotopic ossification in the immature stage opens. And this needs to be confirmed or denied by further randomized controlled studies.This case report was initiated and completed by colleagues such as Li Yun and Zhu Yulan. I only gave some academic suggestions when writing.
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About the Author

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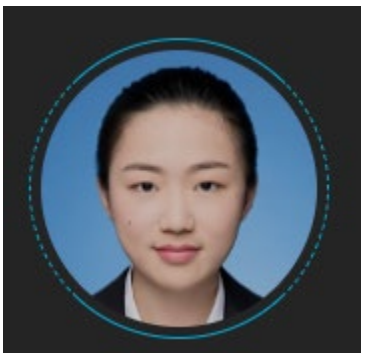

Li Yun, a resident standardized training student at the 2017 Huashan Hospital Rehabilitation Medicine Base, Master of Rehabilitation Medicine and Physiotherapy (Scientific Research Type), Fudan University, current research direction: rehabilitation of bone and joint system diseases, published as the first author in Chinese core journal papers 1 And 2 papers included in SCI (1 of which has been accepted for publication).