

## Case Report

# Aseptic necrosis of the femoral and humeral heads in a patient who has received a course of cell therapy.

### ABSTRACT)

**Aims:** The article is devoted to the problem of complications of pulse therapy and long-term use of corticosteroids in patients with multiple sclerosis.

**Presentation of case:** There was described a case of aseptic necrosis of the femoral and humeral heads in a patient suffering from multiple sclerosis after a course of cell therapy.

**Discussion & Conclusion:** This case is interesting not only because the patient got aseptic necrosis of the femoral as well as humeral heads but also due to possible role of stem cell therapy applied after intensive course of corticosteroids.

*Keywords: aseptic necrosis, multiple sclerosis, femoral bone, humeral bone, stem cell therapy*

## 1. INTRODUCTION

Osteonecrosis (aseptic necrosis) of the tubular bone heads is one of the most severe complications of multiple sclerosis (MS) pulse therapy. It is known that every third case of non-traumatic osteonecrosis is associated with prolonged use of corticosteroids, and, in turn, from 3-20% of patients receiving high doses of glucocorticoids are at risk of developing aseptic necrosis [1-3]. Currently, there is no clear understanding of what doses and what duration of therapy lead to osteonecrosis, however, compared with other nosofoms, the incidence of osteonecrosis of the heads of the tubular bones in MS remains low [1, 3, 4-7]. So, Sahrajan MA et al. (2012) for 5 years of observation at the University Hospital of Tehran revealed only 5 cases of osteonecrosis after pulse therapy with methylprednisolone in a dose of 5 to 15 g per course [4]. Another study showed that in patients with MS, the frequency of osteonecrosis after pulse therapy is 15.5% [5]. Italian researchers consider the occurrence of osteonecrosis as a result of the influence of several factors: increased blood clotting, impaired lipid metabolism and fatty embolism of small-caliber vessels, increased peripheral vascular resistance, and activation of osteocytes apoptosis.

To date, Ukraine has no statistics on the prevalence of osteonecrosis in patients with multiple sclerosis. At the same time, the number of patients with multiple sclerosis has increased in recent years, which may, under the conditions of limited use of disease modifying therapy lead to an increase in the number of cases of osteonecrosis after pulse therapy.

## 2. PRESENTATION OF CASE

This publication is devoted to the clinical case of aseptic necrosis of the heads of the humeral and femoral bones in patient B., born in 1982, who received repeated courses of pulse therapy with methylprednisolone in preparation for cell therapy in one of Moscow's clinics (Russia).

The patient has suffered from MS since 2003, when, after a stressful situation in the conditions of the maritime transition, there was a dysfunction of the pelvic organs, a clinic of central prosoparesis, lower paraparesis. The flow is steadily progressive with temporary spontaneous disturbance. According to MRI of the brain without contrast, in 2003, MS was diagnosed, courses of nootropic therapy were conducted. In 2007–2008, there was a restriction of movement due to weakness in the legs (EDSS 5.0–6.0); in 2010, another deterioration was noted in the form of a decrease in motor activity (EDSS 6.0–6.5). Further deterioration occurred in 2011, the patient spent a long time in bed, sitting wheelchair, walking for short distances (EDSS 7.0. In 2012, she was examined and consulted at the National Medical and Surgical Center named after NI Pirogov (Moscow, Russia). Passed a course of high-dosage immunosuppressive therapy (pulse therapy with solyudrol - 6000 mg per course) with the support of autologous hematopoietic cells, a course of robotic kinesitherapy. For a long time, she received consolidation therapy with mitoxantrone, Zofran (Latran) as a support therapy. In the spring of 2014, after a regular course of kinesitherapy, pain occurred in the shoulder and tazoberdorine joints. In May 2015, the diagnosis of aseptic necrosis of the heads of the humerus and femur was diagnosed. The patient received vazoprostan, denozumab (prolia), calcium supplements, vitamin D3 but her condition was not improved.

In October 2018, the patient passed the re-examination. At the time of the survey she complained of pain in the hip and shoulder joints, had restrictions on walking, numbness of the left leg, reduced visual acuity. Blood pressure was 135/80 mm Hg on the right hand, 130/80 mmHg on the left hand. HR - 82 beats per minute.

On examination, the palpebral fissures were equal, the pupils were equal, photoreactions were alive, ophthalmodynamics was in full range, the adjusting nystagmus was present when looking to the right, weakness of convergence from two sides, more to the left. Muscle strength was reduced, more to the left (4 points). Eendon and periosteal reflexes in hands were raised without a clear difference of the parties. Positive reflexes of Jacobson-Laske, Zhukovsky and Wenderovich were positive in both sides, more pronounced on the left. Knee reflexes were reduced without a clear difference of sides, the Achilles reflex on the right was missing, on the left it was reduced.

Gait was severely impaired, she had paraparesis, more pronounced on the left. Active and passive movements in the shoulder and hip joints were limited - flexion in the shoulder 60-70 °, right abduction - 80 °, left - 60 °. Pathological foot reflexes of Babinsky, Pussep, Rossolimo were positive on both sides.

Coordinator tests were performed uncertainly from 2 sides, with intention tremor. Decrease in sensitivity on the left in the Th9-Th10 innervation zone was found. There were signs of constant incontinence. Meningeal signs were negative, no fasciculations were detected. The patient was emotionally labile, asthenized, the phenomenon of acrohyperhidrosis was determined.

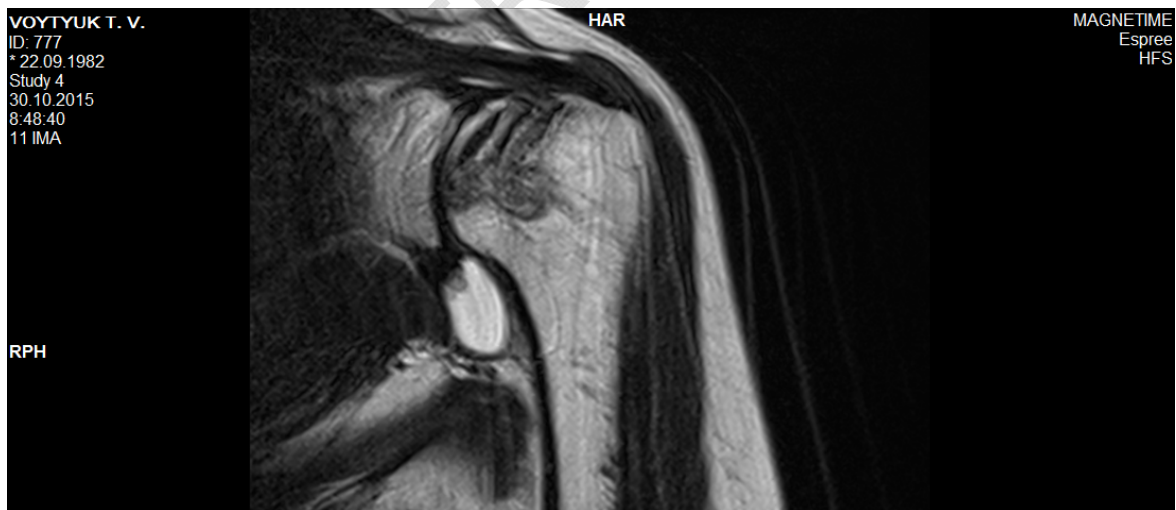
The MRI signs of pronounced avascular necrosis of the femoral heads, the deformation of the left femoral head, an excess amount of fluid in the joints, more to the left were determined (Fig. 1). In addition, signs of avascular necrosis of the lateral femoral condyles on both sides were identified. MRI signs of avascular necrosis of the heads of both humerus bones and fluid in the joint cavity were identified also.



a)



b)\*



c)

Fig. 1 Manifestations of aseptic necrosis (a - heads of the femurs, b - lateral condyles of the femurs, c - heads of the humerus)

Multiple demyelination foci were defined in the brain, non-accumulating contrast, in the white matter of both hemispheres, in the legs of the brain, in the pons, in the medulla, in the corpus callosum, in the cerebellar hemispheres, in the cranial spinal cord, with a nominal diameter of 0.3 cm up to 2.8 cm, periventricular drain character. Cyst-like extensions of subarachnoid spaces in all areas of the brain, moderate expansion of the ventricular system, expansion of cerebellar sulci were determined. Cleavage of the posterior parts of the transparent septum was identified.

### 3. DISCUSSION AND CONCLUSION

Considering the pronounced dysfunction and the absence of regress of symptoms, the patient was recommended surgery for prosthetic hip joints, however, in the current socio-economic conditions of Ukraine, this intervention could not be performed - waiting in line for a free prosthetic may take years. At the same time, the delay significantly worsens the prognosis and may lead to a further aggravation of the clinical picture.

This case is interesting not only because the patient got aseptic necrosis of the femoral as well as humeral heads but also due to possible role of stem cell therapy applied after intensive course of corticosteroids. There are no publications of such cases in the literature. However stem cell therapy was recommended for treatment of avascular necrosis by some authors [7]. Further investigations could help to clarify if such approach is safe and efficient.

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NONE TO DECLARE

### COMPETING INTERESTS

Authors have declared that no competing interests exist

### AUTHORS' CONTRIBUTIONS

All authors provide clinical guidance for the patient authors read and approved the final manuscript."

### ETHICAL APPROVAL (WHERE EVER APPLICABLE)

The manuscript was approved by an Institutional Ethical Committee of the Center of Reconstructive & Renovative Medicine of Odessa National Medical University.

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