

Sacroiliitis as a mask of neoplasms in childhood: analysis of a clinical case series

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The paper presents a clinical case series that includes 12 children with pelvic bone neoplasms mimicking sacroiliitis, which led to the initial misdiagnosis of enthesitis-related arthritis. It discusses the features of the clinical manifestations and radiation imaging of the tumors and characterizes osteoid osteoma and Hodgkin's lymphoma, which are located in the sacroiliac joints.

Keywords: sacroiliitis; neoplasms; osteoid osteoma; Hodgkin's lymphoma; juvenile idiopathic arthritis; enthesitis-related arthritis.

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The sacroiliac joints (SIJ) are one of the largest joints in the body. Sacroiliitis is an inflammation of the sacroiliac joint, which usually manifests with nonspecific clinical feature – buttock and lower back pain with irradiation to lower extremities. These symptoms also occur during many other pathological processes in this area of the body. During the sacroiliitis pain syndrome varies greatly, and patients describe it differently – pain in one or both buttocks, hip pain, lower back pain, or even more distal pain, for example in femur and leg, and usually it can be described as sharp and dull, acute or stabbing [1].

The clinical picture of sacroiliitis can be observed during various diseases [2], but among adults, sacroiliitis is most often a manifestation of ankylosing spondylitis (AS), and among children it is an enthesitis-associated version of juvenile idiopathic arthritis [3], moreover there is the possibility of both unilateral and bilateral lesion [4]. Symmetric lesions are more common in arthritis which is associated with the HLA-B27 antigen. These are less common in blood diseases (leukemia), oncological (histiocytosis, metastases of the pelvic bones, primary bone tumors) and inflammatory (non-bacterial osteomyelitis) processes, infectious disorders (progressive ossifying fibrodysplasia, hypophosphatasia, Paget's bone disease, etc.). Unilateral lesion of the SIJ is a wide field for differential diagnosis and in case of the above-listed diseases it can be observed with almost the same frequency [5, 6].

The diagnosis of sacroiliitis among children is complicated not only because of its relative rarity, but also because of the variety of clinical manifestations, their severity and localization of the pain syndrome. Approaches to the visualization of sacroiliitis are ambiguous: in pediatrics, preference is given to magnetic resonance imaging (MRI), which allows establishing early signs of

inflammation in this area long before the appearance of x-ray changes. Nevertheless, early detection of osteitis corresponding to inflammation requires careful differential diagnosis in view of its non-specificity. It is no coincidence that in the modified New York AS criteria radiological signs of bilateral sacroiliitis of stage II and higher, or in unilateral sacroiliitis of stage III–IV are included as an obligate symptom, [7], which is due to high requirements for their specificity in order to reduce the likelihood of errors in diagnosis [7, 8].

Among the diseases accompanied by the clinic of sacroiliitis, oncological lesions of bones take a special place. In children, their clinical manifestations, regarded as sacroiliitis, lead to a mistaken diagnosis of enthesitis-associated arthritis, which leads to the prescription of unreasonable treatment and delay in proper therapy, which is specifically important for oncological diseases.

The material we have accumulated regarding bone tumors localized in the SIJ region indicates the need for differential diagnosis in the detection of sacroiliitis in pediatric practice.

As an example of erroneous diagnosis of enthesitis-associated arthritis in the detection of sacroiliitis among children, we present a retrospective analysis of a series of clinical observations for 2006–2018. We analyzed the data of 12 children with tumor lesions of the bones in the SIJ region, which were examined and treated in clinics of St. Petersburg. The ratio of boys to girls was 7:5: under age of 1 year – 1 patient, from 1 to 3 years old – 2 patients, from 3 to 7 years old – 1 patient, from 7 to 11 years old – 4 patients, from 11 to 18 years old – 4 patients, which means 2/3 of the children were at school age. The average age of the onset of the disease was 8 years 6 months; the average diagnosis time was 1.5 years.

CLINICAL OBSERVATIONS

The disease was initially manifested by symptoms characteristic for sacroiliitis. In addition to pain in the SIJ, most patients complained of pain in the lower back, which intensified while walking and irradiated to the lower limbs. The fact of trauma preceding the onset of pain was noted by 2 patients. In almost a third of cases, pain was accompanied by radicular symptoms, which is not typical for lesion of SIJ in rheumatic diseases.

In all cases, except for observation No. 3 shown below, the diagnosis was established only after a biopsy of the bone lesion area. The table shows the variants for verified tumors. It should be noted that an increase in body temperature and ESR was characteristic only for malignant neoplasms.

Find below three clinical cases that fully reflect the complexity of the diagnosis of tumors in the SIJ field.

CLINICAL CASE No. 1

Patient M., 7 years old, complained of pain in the right knee joint, lameness, morning stiffness for up to 30 minutes, which appeared 4 months after being hit in the right popliteal region.

After 2 months, pain in the projection of the right sacroiliac joined.

According to ultrasonography, radiography and MRI no pathology of the knee joints was detected. Diagnosed enthesopathy of the right knee joint.

On MRI revealed signs of sacroiliitis on the right (bone medulla edema in the region of the lateral mass of the sacrum and ilium on the right). In dynamics, there was an increase in pain in the sacroiliac joints at night. Based on these symptoms, an enthesitis-associated variant of juvenile arthritis was diagnosed, but no HLA-B27 antigen or abnormalities were found in blood tests.

The child received non-steroidal anti-inflammatory drugs, sulfasalazine, but there was no clinical improvement.

On MRI in the dynamics in the zone of edema of the lateral mass of the sacrum, a section of bone destruction is suspected. Therefore, computed tomography (CT) scan of this area was performed, in which changes characteristic of the subchondral osteoid osteoma (or osteoid osteoma; Fig. 1, a–c) were revealed.

Sulfasalazine therapy was canceled, and the child was transferred to the Clinic of Pediatric Surgery of the St. Petersburg Research Institute of Phthisiopulmonology in which the tumor was removed. The pain disappeared after surgery. According to histological examination, osteoid-osteoma is confirmed. Therapy with non-steroidal anti-inflammatory drugs was canceled immediately after surgery. For 2 years after the operation, the child has no complaints.

CLINICAL CASE No. 2

Patient D., 8 years old, was observed for a year with a diagnosis of chronic multifocal osteomyelitis, vertebral form (destruction of the vertebral body LIV). The diagnosis of non-bacterial osteomyelitis was confirmed morphologically in the study of biopsy

material. She received pamidronic acid therapy every 3 months. After the second injection of pamidronate, after 1 month the patient developed pain in the middle third of the leg, which began to intensify at night. The condition was regarded as a possible new focus of osteomyelitis.

Radiography and computed tomography of the bones of the lower leg revealed no pathology. Blood tests are normal. Therapy with non-steroidal anti-inflammatory drugs did not bring improvement, the condition progressively worsened. 3 months after the appearance of these complaints, the patient was hospitalized for pamidronate therapy. MRI of the whole body was performed, pathological foci were not detected. The cause of intense pain in the lower leg remained unclear. On examination, the child had pain in the sacroiliac joint on the side, ipsilateral pain in the lower leg. Made sighting CT scan of the pelvis, to identify the small rounded foci of destruction of the wing of the ilium (Fig. 1d)

With medical and diagnostic purposes performed excisional biopsy hearth histologically established osteoid osteoma. After surgical treatment achieved complete relief of pain. Term postoperative asymptomatic observation of 1.5 years.

CLINICAL CASE No. 3

Patient A., 9 years old, fell ill with acute onset of pain in the left gluteal region, morning stiffness, low-grade fever. According to laboratory examination observed high inflammatory activity (ESR 48 mm/h, CRP 25 mg/l). According to X-ray of the pelvis was determined subchondral sclerosis of the left sacroiliac joint, which was regarded as sacroiliitis. In conjunction with the clinical picture it possible to establish the diagnosis of enthesitis-associated arthritis. The child received antibiotic therapy, non-steroidal anti-inflammatory drugs, sulfasalazine, methylprednisolone was infused once. The patient was also given physiotherapeutic treatment. 2 months after the onset of the complaints joined with pain in the left hip, remained high inflammatory activity. On MRI of the sacroiliac joint - signs of osteitis in the lateral mass of the sacrum and ilium on the left. The diagnosis remained the same, methotrexate was added to therapy. After 4 months, compare to baseline there was lack of positive dynamics, computed tomography (Fig. 2) and MRI of the sacroiliac joints and spine were repeated. On them, a lesion of the destruction of the left iliac bone, lateral mass SI on the left, the appearance of a lesion of the destruction of the Th12. On chest x-ray, three infiltrative lesions in the lungs were determined. Sulfasalazine and methotrexate were discontinued.

The child examined in oncohematological, two bone marrow punctures and an iliac trepanbiopsy were performed - evidence for the systemic blood diseases not obtained: biopsy specimen showed a granulation inflammatory reaction, single giant cells of the Langhans type; immunohistochemical study on S-100 protein negative. Mycotic invasion has been suggested. Ultrasound of the abdominal cavity revealed splenomegaly.

The structure of verified tumors

Morphological version of the tumor	DF	KHE	OB	SBC	ABC	OO	HL	ES
Number of observations	1	1	1	1	2	2	2	2

Note. DF – desmoplastic fibroma; KHE – kaposiform hemangioendothelioma; OB – osteoblastoma; SBC – solid bone cyst; ABC – aneurysmal bone cyst; OO – osteoid-osteoma; HL – hodgkin's lymphoma; ES – ewing's sarcoma

CLINICAL OBSERVATIONS

In connection with the suspicion of tuberculosis and invasive mycosis, bronchoscopy was performed. Microscopy of bronchial washings revealed round-shaped cells with signs of phagocytosis, and the culture was negative. Received lincomycin, fluconazole. Advise phthisiologist - low probability of tuberculosis infection. When the control computer tomography sacro-iliac joint is marked as a negative trend of increasing size destruction zone left iliac retaining periosteum. 6 months after the onset of the disease, he entered the clinic of St. Petersburg State Pediatric Medical University. An examination revealed an increase in the cervical and right cervical-supraclavicular lymph nodes, which upon palpation were of a dense consistency, painless. Clinically there was pain in the left sacroiliac joint.

The inflammatory activity remained high (ESR 62–86 mm/h, CRP up to 30 mg/l), iron deficiency anemia was added. Consulted by a hematologist, oncologist. Computed tomography of the neck, chest, abdomen and pelvis, skull was performed; osteoscintigraphy. Multiple foci of destruction in the sacrum, ilium, vertebrae, conglomerates of the cervical lymph nodes, multiple lung infiltrates were found. To clarify the diagnosis performed incisional biopsy of the cervical lymph node. The results of histology and immunohistochemistry indicated lymphogranulomatosis, nodular sclerosis. Started chemotherapy with a positive effect, and a remission of the disease has been achieved.

DISCUSSION

In spite of differences within skeletal neoplasms we would like to make an accent on two conditions, which are considered to be the hardest in diagnostic process: there are Hodgkin lymphoma and osteoid osteoma. Osteoid osteoma is the third in prevalence of skeletal benign tumours (about 11–14%) after osteochondroma (48%) and enchondroma (23%) [9].

Osteoid osteoma looks like a little focus with oval or round form (also called 'nidus' (nest)), sometimes includes osseal particles ('nucleus' of osteoid osteoma) and has zone of perifocal osteosclerosis or hyperostosis [10]. Usually the tumor does not exceed 1.5 cm in diameter [11]. First of all it hits the long tubular bones (femur, tibia), than – vertebra column, wrists and feet [12], but not pelvis and ileosacral joints (rare localization). Osteoid osteoma is diagnosis of childhood and young adulthood, usually we see it in the age of 5–20 years, and about 50% cases occur in period 10–20 years. Men get sick 1.6–4 times more often than women [12]. The most typical clinical symptom is local pain, especially in the rest and in the night. Salicylates have good and rapid analgetic effect, sometimes other

NSAID help [13]. Pain can irradiate to closely-related joints, imitate arthralgia and can be a precursor of local symptoms, which create difficulties in diagnostic process [9,13,14] how it was demonstrated in clinical case No. 2. Paraarticular localization imitates picture of active arthritis with limitation of movements, morning stiffness and explained mistakes in diagnosis [15].

Computer tomography is the best way to visualize osteoid osteoma, especially when it is too little or when X-ray examination is not informative (for example, when we examine massive bone structures (spine or pelvis)) [16]. The typical signs on MRI are microcirculation disturbances in the bone tissue (bone swelling) which area is bigger than tumors' nest and it is also leads for false diagnosis. Using drug analgesia is not sufficient and can provide side effects [17] and because of this surgical resection or percutaneous radiofrequency ablation is used in treatment. The main symptom of osteoid osteoma in our clinical cases was intensive pain in ileosacral region without any inflammation in the blood.



Fig. 1. Computed tomogram of the pelvic bones with osteoid osteoma of the lateral sacrum mass on the right (arrows) in patient M., 7 years old (clinical case No. 1; a–c) and in the posterior part of the wing of the right iliac bone (arrow) in patient D., 8 years old (clinical case No. 2; d)

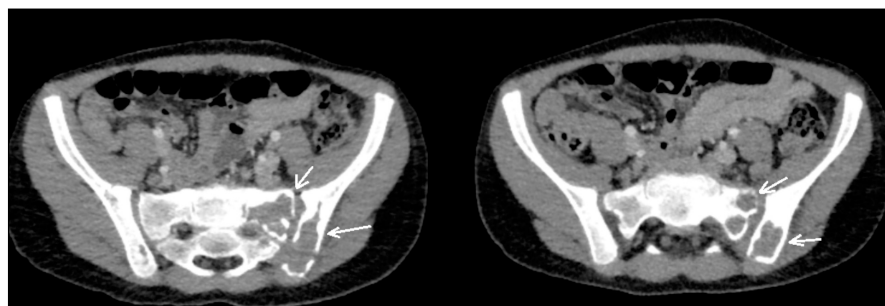


Fig. 2. Computed tomogram of the pelvic bones with foci of destruction in the sacrum, ilium (arrows) with Hodgkin's lymphoma in patient A., 9 years old (clinical case No. 3)

CLINICAL OBSERVATIONS

Hodgkin lymphoma is frequent malignancy of lymphoid tissue which mostly hits teenagers and young adults in the age of 15–34 years [18]. Morphological picture presents by malignant hyperplasia of lymphoid tissue of spleen and lymph nodes. Metastases disseminate everywhere, but lung and bone injury say about terminal stage of disease (IV) [19]. Skeleton involvement is not a major symptom of Hodgkin lymphoma and in combination with not specific morphological picture of different tissue biopsies prolonged the process of verification of diagnosis in clinical case No. 3. The evolution of disease with 'classical' hyperplasia of lymph nodes (especially supraclavicular and cervical) allowed to get correct biopsy, found specific changes and confirm the diagnosis.

So, the bone tumors can manifestate with rheumatic symptoms and underline difficultness in differential diagnosis in clinical practice. When we have unilateral sacroiliitis, first of all, we should exclude neoplastic diseases. It is important to remember that osteitis in MRI is not-specific symptom and demands computer tomography examination or repeating MRI.

Finally, computer tomography is the optimal route to visualize destructive bone process and gives evidence for diagnostic biopsy.

Transparency of the study

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Declaration of Financial and Other Relationships

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Л И Т Е Р А Т У Р А

- Buchanan BK, Varacallo M. Sacroiliitis. In: StatPearls. Treasure Island: StatPearls Publishing; 2019.
- Slobodin G, Hussein H, Rosner I, Eshed I. Sacroiliitis – early diagnosis is key. *J Inflamm Res.* 2018 Sep 10;11:339-344. doi: 10.2147/JIR.S149494. eCollection 2018..
- Petty RE, Laxer RM, Lindsley CB, Wedderburn L. Textbook of Pediatric Rheumatology. Saunders; 2015.
- Adams TL, Marchiori DM. Arthritides. In: Marchiori DM, editor. Clinical Imaging: With Skeletal, Chest, & Abdominal Pattern Differentials. 3rd edition. Elsevier Mosby; 2014. P. 476–624.
- Antonelli MJ, Magrey M. Sacroiliitis mimics: a case report and review of the literature. *BMC Musculoskelet Disord.* 2017 Apr 22; 18(1):170. doi: 10.1186/s12891-017-1525-1.
- Slobodin G, Rimar D, Boulman N, et al. Acute sacroiliitis. *Clin Rheumatol.* 2016 Apr; 35(4):851-6. doi: 10.1007/s10067-016-3200-6. Epub 2016 Feb 4.
- Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum.* 1984 Apr;27(4):361-8.
- Эрдес ШФ, Ребров АП, Дубинина ТВ и др. Спондилоартриты: современная терминология и определения. *Терапевтический архив.* 2019;91(5):84-8. [Erdes ShF, Rebrov AP, Dubinina TV, et al. Spondylarthritides: modern terminology and definitions. *Терапевтический архив.* 2019; 91(5):84-8. (In Russ.)].
- Orth P, Kohn D. Diagnostik und Therapie des Osteoidosteoms. *Orthopade.* 2017 Jun; 46(6):510-521. doi: 10.1007/s00132-017-3428-0.
- Deferm JT, Steens SC, Vriens D, et al. Chronic temporomandibular joint pain: two cases of osteoid osteoma and a review of the literature. *Int J Oral Maxillofac Surg.* 2017 Sep;46(9):1130-1137. doi: 10.1016/j.ijom.2017.03.036. Epub 2017 May 8.
- Iyer RS, Chapman T, Chew FS. Pediatric Bone Imaging: Diagnostic Imaging of Osteoid Osteoma. *AJR Am J Roentgenol.* 2012 May;198(5):1039-52. doi: 10.2214/AJR.10.7313.
- Boscainos PJ, Cousins GR, Kulshreshtha R, et al. Osteoid Osteoma. *Orthopedics.* 2013 Oct 1;36(10):792-800. doi: 10.3928/01477447-20130920-10.
- Miyazaki M, Arai Y, Myoui A, et al. Phase I/II Multi-Institutional Study of Percutaneous Radiofrequency Ablation for Painful Osteoid Osteoma (JIVROSG-0704). *Cardiovasc Intervent Radiol.* 2016 Oct; 39(10):1464-70. doi: 10.1007/s00270-016-1438-7. Epub 2016 Aug 4.
- Ebrahimzadeh MH, Ahmadzadeh-Chabock H, Ebrahimzadeh AR. Osteoid osteoma: a diagnosis for radicular pain of extremities. *Orthopedics.* 2009 Nov;32(11):821. doi: 10.3928/01477447-20090922-23.
- Asik M, Ersen A, Polat G, et al. Arthroscopic excision of acetabular osteoid osteoma in a 7-year-old patient. *Knee Surg Sports Traumatol Arthrosc.* 2015 Nov;23(11):3432-5. doi: 10.1007/s00167-014-2978-5. Epub 2014 Apr 9.
- Radcliffe SN, Walsh HJ, Carty H. Osteoid osteoma: the difficult diagnosis. *Eur J Radiol.* 1998 Aug;28(1):67-79.
- Temple MJ, Waspe AC, Amaral JG, et al. Establishing a clinical service for the treatment of osteoid osteoma using magnetic resonance-guided focused ultrasound: overview and guidelines. *J Ther Ultrasound.* 2016 May 20;4:16. doi: 10.1186/s40349-016-0059-6. eCollection 2016.
- Gomez-Almuguer D, Gonzalez-Llano O, Jimenez-Antolinez V, Gomez-De Leon A. Treatment of classical Hodgkin's lymphoma in children and adolescents. *Expert Opin Pharmacother.* 2019 Jul;20(10):1227-1234. doi: 10.1080/14656566.2019.1606212. Epub 2019 Apr 25.
- Tang F, Min L, Ye Y, et al. Classic Hodgkin lymphoma in pelvis. *Medicine (Baltimore).* 2017 Sep;96(39):e8196. doi: 10.1097/MD.00000000000008196.

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