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Imaging of juvenile spondyloarthritis. Part I: Classifications and radiographs

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Abstract

Juvenile spondyloarthropathies are manifested mainly by symptoms of peripheral arthritis and enthesitis. By contrast with adults, children rarely present with sacroiliitis and spondylitis. Imaging and laboratory tests allow early diagnosis and treatment. Conventional radiographs visualize late inflammatory lesions and post-inflammatory complications. Early diagnosis is possible with the use of ultrasonography and magnetic resonance imaging. The first part of the article presents classifications of juvenile spondyloarthropathies and discusses their radiographic presentation. Typical radiographic features of individual types of juvenile spondyloarthritis are listed (including ankylosing spondylitis, juvenile psoriatic arthritis, reactive arthritis and arthritis in the course of inflammatory bowel diseases). The second part will describe changes visible on ultrasonography and magnetic resonance imaging. In patients with juvenile spondyloarthropathies, these examinations are conducted to diagnose inflammatory lesions in peripheral joints, tendon sheaths, tendons and bursae. Moreover, magnetic resonance imaging also visualizes early inflammatory changes in the axial skeleton and subchondral bone marrow edema, which is considered an early sign of inflammation.

Introduction

Juvenile-onset spondyloarthropathies (JSpAs) account for 15–20% of all forms of arthritis occurring in the developmental age[1]. They belong to rheumatic diseases with first symptoms, in the form of peripheral arthritis and enthesitis of non-symmetrical localization as well as axial skeleton inflammation, appearing prior to the age of 16. Apart from musculoskeletal symptoms, the disease may also affect the eyes, bowels, skin as well as (although very rarely) heart and lungs[1,2].

The etiopathogenesis of JSpA has not been fully explained. The development of the disease depends on genetic and infectious factors. The presence of HLA–B27 antigen, with its most common subtype HLA-B27*05, is characteristic of JSpA[2]. The IgM rheumatoid factor (IgM-RF) and anitnuclear antibodies (ANA) are not detected in the serum[3]. TNFα cytokine is said to play an important role in the etiopathogenesis. It takes part in neutrophil and lymphocyte activation and upregulation of adhesion molecules, stimulates production of other proinflammatory cytokines and promotes the production of matrix metalloproteinases. All these effects have an impact on bone and cartilage resorption[2]. As in adults, increased intestinal permeability is underlined also in JSpA. It enables transition of enterobacterial antigens that induce arthritis[4]. In the initial phase of the disease, inflammatory infiltrates and vascular changes prevail in the synovium. Later, extensive fibrosis of the joint capsule is observed. The changes within the sacroiliac joints, i.e. inflammatory infiltrates in the subchondral bone tissue, synovitis with subsequent destructive lesions (erosions) of the articular surfaces or syndesmosis inflammation, are identical to those observed in spondyloarthropathies in adult patients. The inflammatory reaction may be observed in only one sacroiliac joint, particularly in the initial stage of the disease, and only later in the other. Inflammation can also involve joints of the spine.

Clinical classifications

Juvenile spondyloarthropathies can be divided into undifferentiated and differentiated forms (Tab. 1).

	Undifferentiated forms
1.	Seronegative enthesopathy and arthropathy syndrome (SEA)
2.	Enthesitis-related arthritis (ERA)
	Differentiated forms
1.	Juvenile ankylosing spondylitis (JAS)
2.	Psoriatic arthritis (PsA)
3.	Reactive arthritis (ReA)
4.	Arthritis associated with inflammatory bowel diseases (IBD)

Tab. 1. *Classification of juvenile spondyloarthropathies[5]*

JSpAs are difficult to diagnose and differentiate particularly from juvenile idiopathic arthritis (JIA). Apart from undifferentiated forms (seronegative ones – absence of rheumatoid factor), which are sometimes initially included in the group of JIA, the symptoms of JSpAs develop gradually in many patients[2]. By contrast with adults with spondyloarthropathies[6,7], the disease in children rarely starts with involvement of the sacroiliac joints or spine. Moreover, children rarely meet the modified New York criteria (for radiographs), used in diagnosing SpA in adults[7].

Currently, there are several classifications and diagnostic criteria for JSpA, including those used in adult patients and validated for children (Amor, ESSG, ASAS criteria for peripheral spondyloarthropathy) as well as criteria prepared specifically for JSpA (SEA, Garmisch-Partenkirchen, ILAR)[2,5,8].

According to ILAR (International League of Associations for Rheumatology), JSpAs are classified as one of JIA entities, called ERA (enthesitis-related arthritis) (Tab. 2). However, this definition excludes cases of reactive arthritis, enteropathy-related arthritis, juvenile ankylosing spodylitis and juvenile psoriatic arthritis[1,2,9].

	JIA category
1.	Systemic arthritis
2.	Oligoarthritis (persistent or extended)
3.	Polyarthritis (RF negative)
4.	Polyarthritis (RF positive)
5.	Psoriatic arthritis
6.	Enthesitis-related arthritis (ERA)
7.	Undifferentiated arthritis

Tab. 2. *International League of Associations for Rheumatology (ILAR) classification of juvenile idiopathic arthritis*

According to the ESSG (European Spondyloarthropathy Study Group), JSpAs are a separate group of diseases, divided into entities as in adult patients. In the initial stage of the disease, most of JSpA cases are classified as undifferentiated, so-called seronegative enthesopathy and arthritis syndrome (SEA). Differentiated forms encompass four entities (Tab. 3). A classification criterion is, according to ESSG, the presence of so-called inflammatory back pain (as in adults) (Tab. 4), but identification of this symptom in children is frequently problematic[1,2,5,9].

JSpA can be diagnosed when the ESSG criteria, listed in Tab. 4, are met. Subsequently, one of the aforementioned forms of JSpA is specified, as shown in Tab. 3.

	Undifferentiated forms
1.	Seronegative enthesopathy and arthritis syndrome (SEA)
	Differentiated forms
1.	Juvenile ankylosing spondylitis (JAS)
2.	Reactive arthritis (formerly including Reiter's syndrome)
3.	Arthritis associated with inflammatory bowel diseases (IBD)
4.	Juvenile psoriatic arthritis (JPsA)[2,3]

Tab. 3. *Juvenile spondyloarthropaties divided into differentiated and undifferentiated forms according to ESSG*

Inflammatory sacral pain or asymmetrical synovitis in the lower extremities plus at least one of the following:	
1.	Positive family history
2.	Psoriasis
3.	Inflammatory bowel disease
4.	Urethritis, cervicitis or acute diarrhea occurring within one month before onset of arthritis
5.	Pain alternating between the right and left buttock
6.	Enthesopathy*
7.	Sacroiliitis**
Exceptions: none	

* Enthesopathy – past or present pain in an enthesis on physical examination.

** Sacroiliitis that meets so-called modified New York criteria[6,10,11].

Tab. 4. *ESSG criteria for the classification of spondyloarthropathies[2,11]*

Seronegative enthesopathy and arthritis syndrome (SEA) was first described in 1982 by Jacobs et al., who found signs of enthesitis in 75% of children with positive HLA-B27 in the serum[1,12]. Other authors demonstrated that this syndrome can reflect initial pauciarticular (oligoarticular) form of reactive arthritis or the onset of childhood arthropathies associated with HLA–B27 antigen. Moreover, Burgos-Vargas et al.[13], reported that 75% of children with an initial diagnosis of SEA developed JAS within 5 years. The diagnosis of SEA in the articles quoted above was based on a clinical examination. At present, such data must be verified in imaging, i.e. by ultrasonography (US) and magnetic resonance imaging (MRI). Coates et al.[14] admitted that clinical assessment of enthesitis (edema and pain at the site of an enthesis subsiding upon mobilization) does not display a sufficient correlation with a US and MR image. Our own observations and prospective studies based on the calcaneal tuberosity in adults[15] did not confirm that US features visible in patients with clinically suspected enthesitis of the Achilles tendon and plantar fascia enable confirmation of the clinical diagnosis of enthesitis. We did not find any signs of increased vascularization of the entheses. Instead there were scars at various levels of organization, delaminated tears, shallow irregularities or erosions and cysts in the bony component of the entheses. In adults, they are usually a sign of chronic microinjuries and degeneration. The spectrum of changes in children has not been published thus far.

Moreover, statistical data on the number of children with a changed diagnosis in the course of the disease are not known either[8]. According to some reports, the verification of the diagnosis from JIA to JSpA takes place in 0–4% to even 36% of patients with chronic peripheral arthritis[8,16]. This results from the fact that most patients with JSpA initially suffer from peripheral arthritis, which is impossible to distinguish from JIA[8]. Such an inflammation is persistent and non-destructive (*persistens non-destructive*)[16]. According to Rosenberg and Petty's hypothesis concerning enthesopathic arthropathy, ERA (i.e. JSpA according to ILAR) and enthesitis in particular, may be a prodromal manifestation of seronegative spondyloarthropathies[17]. This hypothesis is not confirmed by all reports: according to various authors[8], JSpA (or more precisely JAS) was diagnosed in 9% to 92% of cases within 5 years in patients with enthesitis at the onset of the disease.

Factors of poor prognosis

The predictors of JSpA progression are: involvement of the tarsal joints, presence of HLA-B27 antigen, absence of HLA-DPB1*02, involvement of the hip joint in the first 6 months of the disease and the onset after the age of 8[2]. Flato et al. analyzed data of children registered during the first visit and their records after 10 years from the onset. They demonstrated that risk factors of progression and disability were persistently active disease and polyarticular course 5 years after the first visit ($p<0.05$)[8]. The predictors of erosions (articular destruction) were: elevated erythrocyte sedimentation rate (ESR) persisting for a long time, delayed decision to see a doctor and delayed treatment with so-called disease-modifying antirheumatic drugs (DMARDs)[8]. The analysis revealed that early diagnosis and treatment are significant in disease preventing progression and its complications[8].

Difficulties in early diagnosis

As has been mentioned above, an early diagnosis of JSpA is difficult and frequently delayed by several years (average 8.3 years) due to a different picture in the initial stage of the disease than in ankylosing spondylitis (AS) in adults[13,16,18]. In children, peripheral joints are usually involved whereas axial skeleton involvement prevails in adults[5,19]. Sacroiliitis and spodylitis can be observed in children usually 5–10 years after the onset[5,19]. Typically, joints of the lower extremities are involved. Changes in the upper limbs are rarely observed; in such cases, humeral joint is usually inflamed, and slight joints of the hand are spared[5].

Tarsitis, diagnosed in 1/3 of patients at the initial stage of the disease, is a unique sign of JSpA[5]. Moreover, enthesitis, which is identified in a clinical examination in 60–80% of patients[5], is typical of JSpA. According to clinical data, inflammation usually involves the patellar ligament, Achilles tendon and plantar fascia.

Burgos-Vargas et al.[20] compared the clinical picture of JAS (onset <16 years of age) and AS (onset in adulthood). The involvement of peripheral joints was observed in nearly 90% of children and in merely 37.5% of adults with AS. Enthesopathies were present in $^2/_3$ of children and only in $^1/_3$ of adults. The tarsal joints and feet were involved significantly more frequently in children. All children developed peripheral arthropathies as the disease progressed, and 78.7% developed enthesopathies. It adults, the respective values were: 55% and 47.5%[20].

Another cause of diagnostic pitfalls is a similar clinical picture of JSpA and JIA. In both cases, there are features of

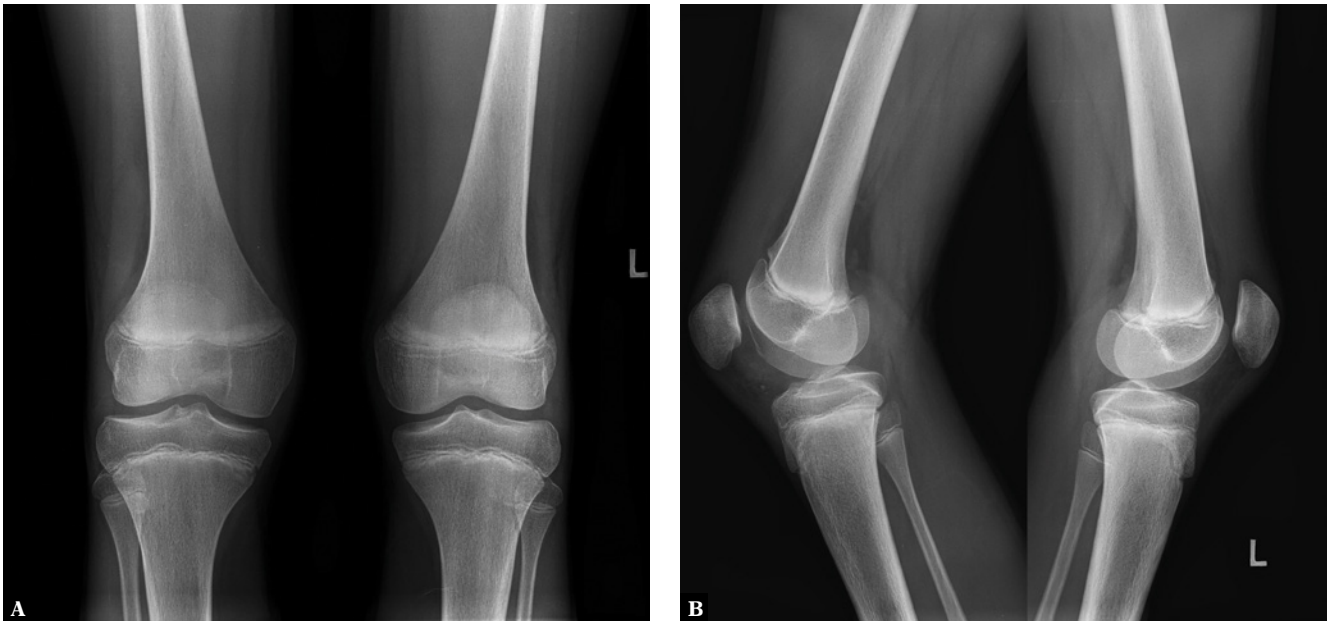

Fig. 1. *AP* **(A)** *and lateral* **(B)** *radiographs of the knee joints in a 16-year-old boy: increased density of periarticular soft tissue with lesions prevailing on the right side and hypertrophied epiphyses of the right knee joint*

peripheral arthritis, tenosynovitis, enthesitis or SEA. The disease is usually classified as one of JIA forms, most often as type 2 (pauciarticular juvenile rheumatoid arthritis, JRA) [18]. Spondylitis and sacroiliitis as well as progression of SEA to AS are observed in most children 5–10 years after the onset[18]. Compared with adults, the axial skeleton is rarely involved in the first year after the onset[18]. In JSpA, the disease rarely progresses to the radiographic forms of bilateral sacroiliitis that fulfil the New York criteria for adults[17].

Based on these observations, 2 types of JAS onset have been defined: 1) the aforementioned SEA syndrome – the involvement of peripheral joints and entheses with progression to AS several years after the onset, and 2) a rarer form resembling adult AS in which the axial skeleton becomes involved shortly after the onset[18].

Burgos-Vargas et al.[3] identified features of the disease that enable the differentiation of early JAS from early JIA in the first year after the onset. They are: pauciarthritis/oligoarthritis, enthesitis in the lower extremities, tarsitis, presence of HLA-B27 antigen and rare involvement of the joints of the upper extremity (which, in turn, is typical of JIA)[3]. The inflammation of the knee, ankle and interphalangeal joints was observed in both forms with a similar frequency. In the material of Burgos-Vargas et al., the hip joint became involved several years after the onset whereas other authors report its involvement in the early stage of JAS[3].

Imaging of juvenile spondyloarthritis

The contemporary diagnostic process of axial spondyloarthropathies (sacroiliitis and spondylitis) in adults is based on an plain radiography and MRI, in accordance with the ASAS criteria (*Assessment of Ankylosis Spondylitis*) from 2009[6,10,21]. Imaging is conducted in patients with so-called chronic or inflammatory back (spinal) pain[6,10,21].

As has already been mentioned, the identification of this sign in children and adolescents is difficult since it rarely occurs in this age group in the initial stage of the disease or is not reported by children[5,22]. This probably refers to the youngest patients since large population-based studies among adolescents have demonstrated that nearly a half of them experience severe back pain. The frequency of this ailment increases with age and is associated with the sedentary lifestyle and a low level of physical activity. SpA is diagnosed in over 40% of children and adolescents that report to the doctor, which is a greater percentage than in adults in whom mechanical back pain is usually diagnosed[23].

Another reason for diagnostic problems in children and adolescents with suspected SpA is a difficulty in interpreting radiographs, which are often negative in early stages of the disease due to a greater quantity of cartilage than in adults. As in adults, a certain diagnosis of sacroiliitis based on radiography is possible after several months or even years after the onset. Similarly, early inflammatory lesions in the spine are invisible on radiography and usually develop later than sacroiliitis[24].

If, however, radiographic changes in the sacroiliac joints are visible (so-called radiographic form), the consecutive grades of sacroiliitis (according to New York criteria) are not distinct from one another, which results in an uncertain diagnosis of the grade of the disease. Moreover, interpretation of radiographs depends on additional factors: the quality of a radiograph, technique in which it is taken, experience of a radiologist and individual variability in the shape of the sacroiliac joints[25].

As in adult patients with SpA, early stages of sacroiliitis are localized in the subchondral bone tissue, which is visible only on MRI. According to the ASAS criteria, MRI is conducted in adults if radiography is negative, grade 1 sacroiliitis is diagnosed or grade 2 is identified unilaterally[6]. There are no such criteria for children and adolescents with SpA. By contrast with adults with spondyloarthropathies, single existing reports concerning patients with JSpA indicate low specificity of inflammatory back pain. Moreover, there are no critical papers on the diagnostic value of radiography of the sacroiliac joins or publications confirming the usefulness of MRI[22,26].

Still, radiography of the axial skeleton and peripheral joints is the basis for JSpA diagnosis in children. In peripheral spondyloarthropathies, pediatricians base their assessment on a clinical examination of joints and entheses for arthritis and enthesitis. There are no criteria or standards that would include US or MRI in diagnostic schemes of early inflammatory changes; such criteria are already in use with respect to adult patients[6,10,21].

Below, we present radiographic pictures of individual entities belonging to the group of juvenile spondyloarthropathies, according to the ESSG classification[27]. Subsequently, in the second part of that paper, we will discuss the usefulness of US and MRI in the diagnosis of early inflammatory changes in the course of JSpA.

Plain radiography

Juvenile ankylosing spondylitis (JAS)

Juvenile ankylosing spondylitis (JAS) usually begins with acute, subacute or primarily chronic inflammation in a single joint, typically in the lower extremity (knee, ankle or hip joint). Also, inflammation of the first metatarsophalangeal joint and the first interphalangeal joint is typical of the initial stage of the disease. One or both sternoclavicular articulations can be involved. In merely 10–20% of cases, the disease begins with inflammatory back pain.

Radiographic changes are observed in a late stage of the disease when cartilaginous and bony components of peripheral joints or joints of the axial skeleton are already being destroyed. In the axial skeleton, one can observe features of sacroiliitis, which can initially be unilateral. By contrast with AS in adults, children do not usually develop complete ankylosis of the sacroiliac joints (grade IV of sacroiliitis) or the spine. Squaring of the vertebral bodies and syndesmophyte formation are rare. Destructive changes in the body–disk–body complex (spondylodiscitis) are sporadic, and the cervical spine involvement is exceptionally rare.

Peripheral joints (Fig. 1):
- Usually, lower extremity joints are involved, such as: knee, hip, ankle, the first toe; sometimes joints of the upper extremities.
- Changes are usually unilateral.
- Osteoporosis or cysts are visible.
- Erosions are identified extremely rarely; destruction is not extensive.

Entheses (Fig. 2):
Enthesopathic lesions of tendons, aponeuroses and capsuloligamentous complexes are visible as ossifications of various shapes (band-like, linear, cloud-like) and erosions in the bony component of an enthesis. Typical lesions are seen in the entheses of the calcaneal tuberosity.

Sacroiliac joints (SIJs) (Fig. 3):
- Both the cartilaginous (symphysis and synchondrosis types) and syndesmotic parts of the joint can be involved.
- The iliac part of the SIJs becomes involved earlier, probably due to mechanical and anatomic factors.
- Initially, articular margins are blurred (loss of the linear margin of the cortical bone); there are shallow erosions and areas of subchondral sclerosis.
- With increasing number of erosions, the bone surface becomes markedly serrated and the joint space unevenly dilated. Subsequently, segmental narrowing of the joint space with bony bridge formation is observed. Ankylosis in children is very rare (mainly in young adults). Usually, grade I, II or III of sacroiliitis (according to the New York Criteria) is diagnosed[7].

Spine (Fig. 4):
- Lesions in the cervical spine, in the form of vertebral body destruction with subsequent osseous regeneration in the later stage of the disease, may also appear and be the only change within the spine.
- Squaring of the vertebral bodies and syndesmophyte formation are very rare and can develop many years after the onset.
- Sporadically, other lesions, typical of adult AS, may develop: ankylosis of sacroiliac and lumbosacral ligaments, ankylosis of the costovertebral articulations and intervertebral joints, spondylodiscitis and lesions in the atlantoaxial joint.
- Lesions typical of adult patients with AS, such as ankylosis on several levels of the spine and the formation of a "bamboo spine" do not develop.

Moreover, the clinical picture includes eye inflammation, sometimes being the first sign of JAS.

Juvenile psoriatic arthritis (JPsA)

The radiographic image in children is not different from that in adults. However, sacroiliitis and spondylitis are not as common in children. Moreover, the full spectrum of radiographic lesions typical of JPA is rarely observed. Boys more frequently develop sacroiliitis (usually asymmetrical) and spondylitis (C1/C2 subluxation and syndesmophytes are rare). In girls, peripheral arthritis prevails.

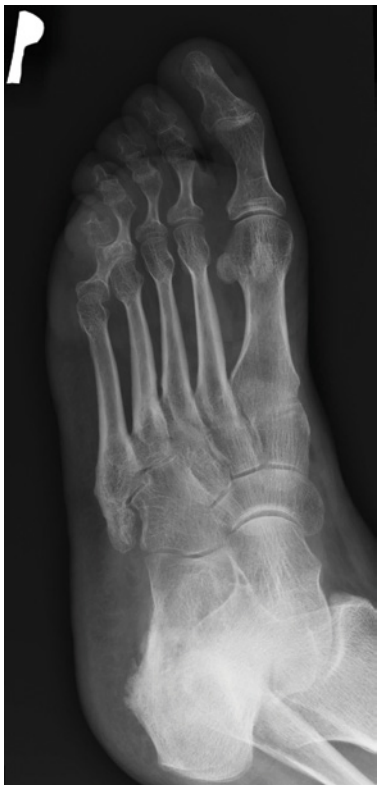

Fig. 2. *Oblique radiograph of the right foot in an 18-year-old boy: enthesopathic changes in the plantar fascia attachment to the calcaneus*

Entheses:

- Enthesopathic lesions are frequently the only sign for a long time.
- Enthesopathic lesions of tendons, aponeuroses and capsuloligamentous complexes are visible as ossifications of various shapes (band-like, linear, cloud-like) and erosions in the bony component of an enthesis (typically in the region of the calcaneal tuberosity).

Peripheral joints (Fig. 5):

- The image is initially normal, or periarticular osteoporosis is present.
- The disease usually begins with inflammation in a single joint (typically the knee) or several articulations (knee, ankle, hip, foot). The further course is in most patients polyarthritic with asymmetrical lesions involving joints of the upper and lower extremities.
- Periosteal thickening (periostitis) on the phalanges, metacarpal and metatarsal shafts is typical.
- Acroosteolysis of the distal phalanges is characteristic.
- Sometimes, osteolysis and ankylosis are observed in the same hand and foot.
- Inflammation of distal interphalangeal joints in the hands and feet with simultaneous destruction (geodes, erosions) and proliferative lesions are typical.
- Joint space narrowing.
- The image of so-called "sausage digits" in the course of tenosynovitis of flexor digitorum tendons or inflamma-

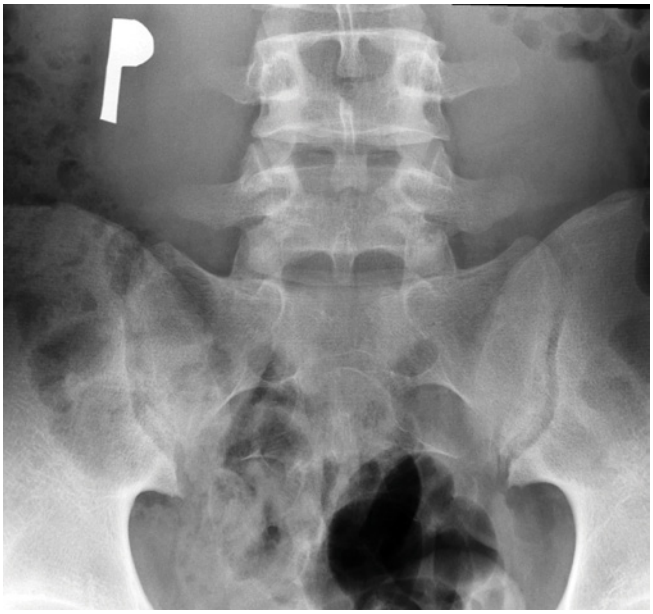

Fig. 3. *AP radiographs of the sacroiliac joints in an 18-year-old girl diagnosed with sacroiliitis in the early period: unclear outline of the sacroiliac joints with changes prevailing on the right side and subchondral bone sclerosis in the right sacroiliac joint*

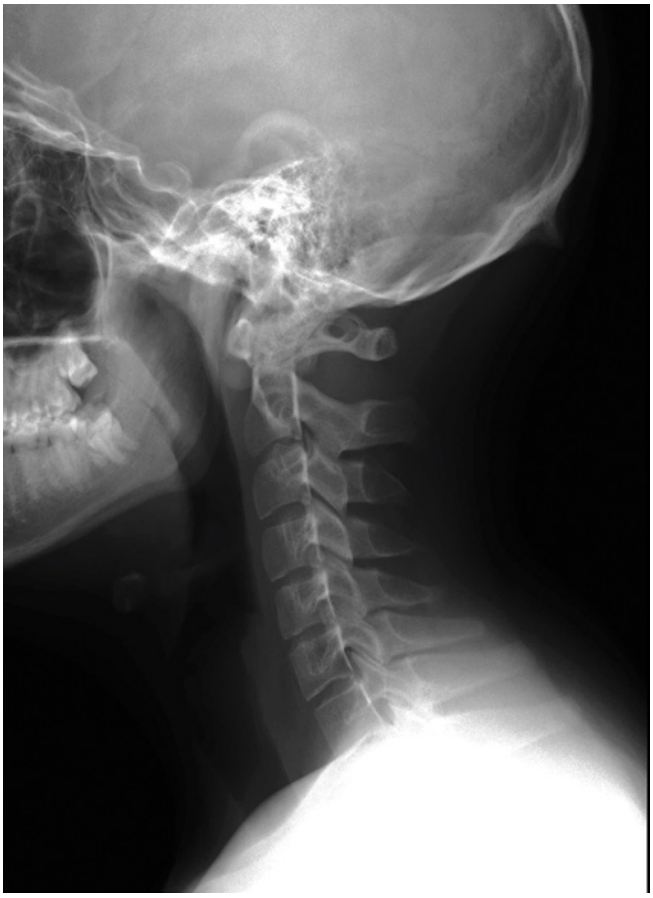

Fig. 4. *Lateral radiograph of the cervical spine in a 16-year-old patient with AS: loss of cervical lordosis and the concave line of anterior parts of the cervical vertebral bodies*

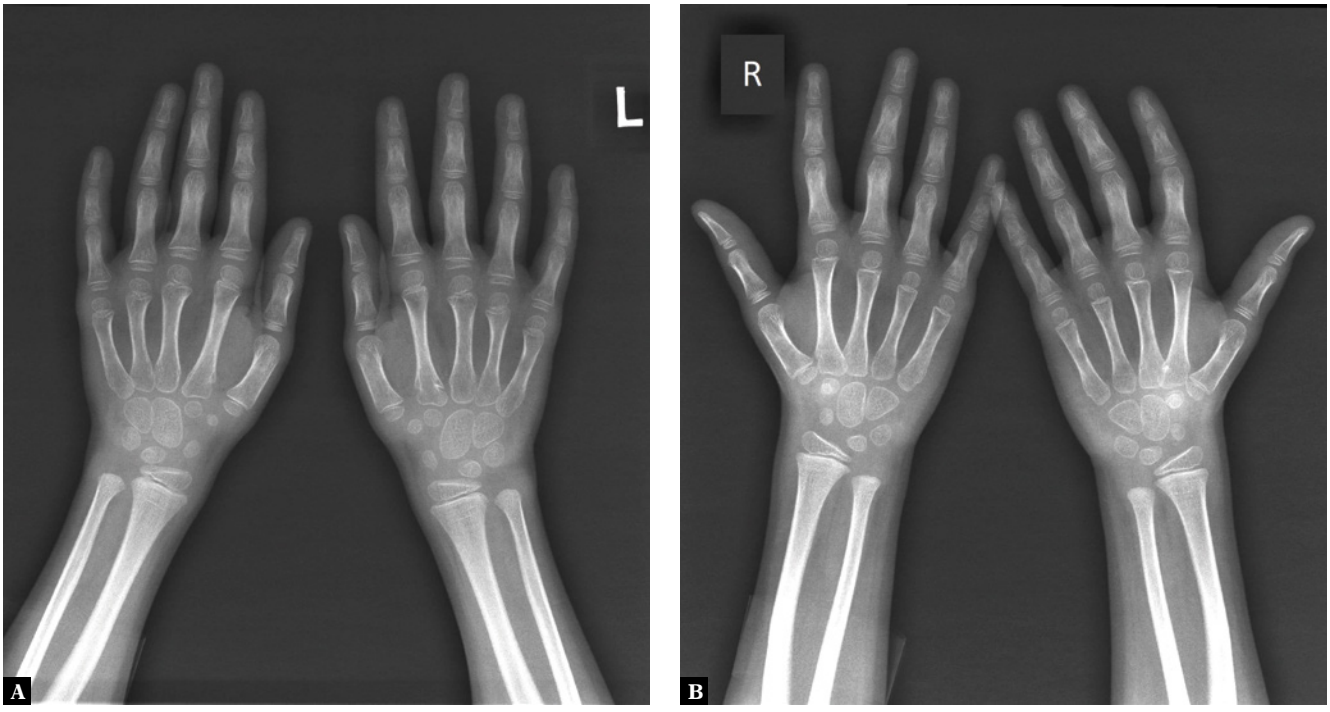

Fig. 5. *AP* **(A)** *and oblique* **(B)** *radiograph of the hands in a 6-year-old girl: periarticular osteoporosis of the hands, periosteal buildup/thickening along the 2nd and 3rd distal phalanges of both hands*

tion of soft tissues of a digit, or as a result of synovitis of the proximal and distal interphalangeal joints.
- Inflammatory changes are more symmetrical than in JIA.

Reactive arthritis (ReA)

This form of the disease is rare in children. It is characterized by enthesopathies of the calcaneal tuberosity.

Peripheral joints are usually asymmetrically involved. Similarly to JPsA, this concerns several or numerous large joints of the lower extremity (often the knee and ankle, rarely the hip joint). Sometimes, small joints of the foot are involved as well (sausage toes).

Sacroiliitis, usually symmetrical and bilateral (rarely unilateral), is observed. The lesions in the SIJ are similar to those in JAS.

Peripheral joints:
- Thickening and increased density of periarticular soft tissue – identical to JAS.
- Periarticular osteoporosis appears during an acute attack; in chronic inflammation, it can be invisible or poorly marked.
- Erosions are initially marginal and subsequently subchondral; joint space narrowing.

Entheses:
- Compared to adults with ReA, enthesopathies occur more rarely.

Spondyloarthritis in the course of colitis ulcerosa and Crohn disease (enteropathic JSpA)

JSpA is found in approximately 10% of children with inflammatory bowel diseases, more often in those with Crohn's disease than ulcerative colitis. Arthritis may pre-

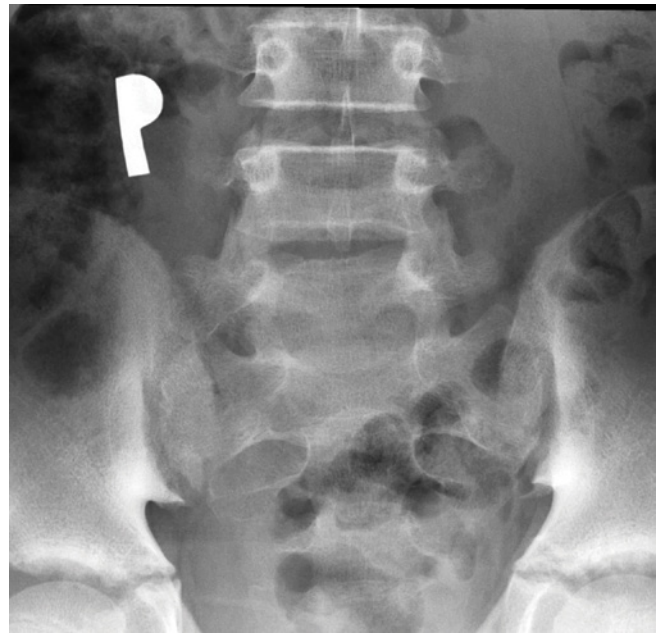

Fig. 6. *AP radiograph of the sacroiliac joints in an 18-year-old patient with Crohn disease: uneven and obscure lines of the right sacroiliac joint*

cede bowel disease, but usually develops in the course of eneropathy (Fig. 6).

There are two forms of this JSpA: a peripheral form with peripheral arthritis and a rarer axial form with sacroiliitis and spondylitis.

Peripheral joints:
- In the peripheral form, large joints of the lower extremity are usually involved (typically the knee and ankle). The wrist, hand and glenohumeral joints are involved more rarely, sometimes asymmetrically.
- Thickening and increased density of periarticular soft tissue.
- Periarticular osteoporosis.
- Usually, there are no features of bone destruction.

Entheses:
Typically, enthesopathic lesions of the Achilles tendon and plantar aponeurosis up to the calcaneal tuberosity.

Axial skeleton:
- Involvement of the spine and sacroiliac joints is rare in children; these changes develop in adulthood.
- The radiological picture resembles JAS. The sacroiliac joints are usually involved symmetrically, the involvement of the spine with squaring of the vertebral bodies and syndesmophyte formation is less common.

Conclusion

Plain radiography still remains a standard in the diagnostic process of early inflammatory changes in the course of JSpAs. Its role is, among others, to rule out malignancies, trauma or specific inflammations of bones and joints. In early stages of JSpAs, radiographs are usually negative or reveal features of osteoporosis, increased radiodensity and extended shadow of soft tissues or hypertrophic epiphyses. Depending on the clinical suspicion, the next examination is ultrasonography or magnetic resonance imaging in order to diagnose early inflammatory lesions in peripheral joints, tendon sheaths, bursae or entheses, or abnormalities in the course of axial spondyloarthropathies. Changes seen in these examinations will be discussed in the second part of the publication.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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