Case report
Prikaz bolesnika

# CONGENITAL OSTEOCHONDRODYSPLASIA – A CASE REPORT

## PRIKAZ BOLESNICE S KONGENITALNOM OSTEOHONDRODISPLAZIJOM

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**Abstract**

Congenital osteochondrodysplasia is a rare inborn disorder of the development and growth of bone and cartilage. Its incidence in children is 2–3/10,000.

We present the case of a female patient, born in 1952 from an unplanned pregnancy as the fourth child in the family. At her birth the mother was 42 and the father 53 years old. At examination her body height was 152 cm and body weight 87 kg.

She was hospitalized at our clinic because of pain in the spinal and peripheral joints from which she had been suffering since young age. Her father and uncle had similar problems. On physical examination the patient was obese with a large scaphoid calvaria, a very high forehead, a nose with wide base, short trunk and extremities, especially the arms with semi-contractures of the elbow joints and fingers of equal length. There was a contracture of the right hip, the feet were in disproportion with the rest of the body, while Lasegue's test was positive on both sides at 30°. The patient's karyotype was 46 xx. Radiography of the hip joints showed varus deformations and pronounced sclerosis of the femoral head. The knee radiographs were characterized by congenital deformities, and there were clinical and radiographic signs of osteoarthritis. Radiographs of the lumbosacral spine and pelvis showed osteoporosis, hyperlordosis, and a compression fracture of the L5 vertebral body. Total T-score of the hip on DEXA scan was –3.7.

Based on data from the history, physical examination, as well as clinical and laboratory findings, we established the diagnosis of congenital osteochondrodysplasia, a condition which should be considered and diagnosed as soon as possible. Treatment of the disease is multidisciplinary and mainly symptomatic.

**Keywords:** Osteochondrodysplasia – diagnostic image, genetics; Bone diseases, developmental – diagnostic image, genetics; Radiography

**Sažetak**

Kongenitalna osteohondrodisplazija (OCHD C) je rijedak urođeni poremećaj razvoja i rasta kostiju i hrskavice. Incidencija bolesti je 2–3 djece na 10.000 osoba.

Predstavljamo bolesnicu, rođenu 1952. godine kao četvrto dijete nakon nekontrolirane trudnoće. Majka je bila u dobi od 42 godine a otac je imao 53 godine. Bolesnica je u vrijeme pregleda bila tjelesne visine 152 cm i tjelesne težine 87 kg.

Bolesnica je hospitalizirana na klinici zbog bolova u kralježnici i zglobovima, od kojih je patila od mlade dobi. Iste simptome imali su bolesničin otac i ujak. Na pregledu bolesnica je bila pretila, s velikom skafoidnom kalvarijom, vrlo visokim čelom, širokom bazom nosa, s kratkim trupom i ekstremitetima, osobito kratkim rukama s poluflektiranim

zglobovima lakta i prstima ruke, uz jednaku dužinu. Nađena je i kontraktura desnog kuka, stopala su bila velika u odnosu na ostatak tijela, dok je Lasegueov znak bio obostrano pozitivan kod 30 stupnjeva. Imala je osteoartritis koljena, velika stopala (br. obuće 44) koja su bila nerazmjerna s tijelom. Kariotip bolesnice je bio 46xx, Na radiografskim nalazima proksimalni dijelovi femura su bili deformirani u varusu, s izraženom sklerozom glave femura. Radiografija koljena je karakterizirana kongenitalnim deformacijama, dok su nađeni radiografski i klinički znakovi osteoartritisa. Na radiografiji lumbosakralne kralješnice i zdjelice vidi se osteoporoza, hiperlordoza i kompresivna fraktura trupa kralješka L5. T-skor na kuku ukupno mjereno DXA-om je bio –3,7.

Na temelju anamneze, fizikalnog pregleda, kliničkih i laboratorijskih nalaza zaključeno je bolesnica boluje od kongenitalne osteohondrodisplazije. To je bolest o kojoj treba misliti i nastojati postaviti dijagnozu što ranije. Liječenje bolesti je multidisciplinarno i za sad simptomatsko.

**Ključne riječi:** Osteohondrodisplazija – dijagnoza, genetika; Razvojne koštane bolesti – dijagnostički prikaz, genetika; Radiografija

## Introduction

Congenital osteochondrodysplasia is an inborn disorder of the development and growth of bone and cartilage. This disease is rare with an incidence in children of 2–3/10,000.

It occurs in two forms, lethal and non-lethal. Nowadays the disease can be diagnosed before birth by ultrasound or DNA analysis of fetal cells (1, 2).

The nonlethal form includes: 1) disorders of long bone and spinal cord growth, 2) increased anarchic fibrous tissue and bone cartilage, and c) decreased and increased bone density.

Non-lethal osteochondrodisplasia can be presented in three major forms: short extremities, short body and extremities, and curved bone pathology.

In the past there were several classifications of these disorders regarding their causes, etiology, and prognosis. One of the most commonly used classifications is the one based on genetic changes in the previously mentioned three clinical forms (Tables 1–3) (3).

In the case of achondrodysplasia, the genetic disorder involves a derangement of the gene composition of the 3rd fibroblast growth factor, while in the other forms mutations of the gene for collagen II and different mutations in the same gene occur, causing various defects and disorders of bone and cartilage. Inheritance runs through dominant and recessive pathways. The disorder starts in the embryonic stage and often has a lethal outcome before, during, or immediately after birth. At birth it can be observed that the head is increased by dysmorphism, showing the typical pronounced craniocephalic neurocranium with a high forehead, irregular root of the nose, and a relative progenia. Other prominent features of the disease are consequences of the growth disorder causing reduced growth of long bones and vertebrae. Most affected are the extremities, especially the femur and humerus, which lag in development, resulting in a disproportion

Table 1 Osteochondrodysplasia with short limbs (according to reference No 3)
*Tablica 1. Osteohondrodisplazija s kratkim udovima (prema referenciji br. 3)*

| Type of osteochondrodysplasia | Mode of heredity* |
|---|---|
| 1. Achondrodysplasia | AD |
| 2. Diastrophic dysplasia | AR |
| 3. Chondrodisplasia with epiphysis | AR,XVD,XVR |
| 4. Metatropic dysplasia | AD |
| 5. Omodysplasia | AD,AR |
| 6. Mesomelic dysplasia | AD,AR |
| 7. Acromesomelic dysplasia acromesomelica | AR |
| 8. Grebe dysplasia | AR |
| 9. Other micromelic dysplasias | SP |

**Mode of heredity: AD – autosomal-dominant, AR – autosomal--recessive, XVD – autosomal-dominant inheritance related to X, XVR – related recessive X, and SP – with sporadic appearances.*

Table 2 Osteochondrodysplasia with short body and extremities (according to reference No 3)
*Tablica 2. Osteohondrodisplazija s kratkim udovima i trupom (prema referenciji br. 3)*

| Type of osteochondrodysplasia | Mode of heredity |
|---|---|
| 1. Spondyloepiphyseal congenital dysplasia | AD |
| 2. Hypochondrogenesis | AD |
| 3. Kniest dysplasia | AD |
| 4. Spondyloepiphyseal dysplasia | AD |
| 5. Pseudodiastropic dysplasia | AR |
| 6. Immunoosseous dysplasia | AR |
| 7. Opsismodysplasia | AR |
| 8. Spondyloepiphyseal dysplasia with laxity | AR |
| 9. Spondyloepiphyseal dysplasia with abnormal calcification | AR |

Table 3 Osteochondrodysplasia with curved bones (according to reference No 3)
*Tablica 3. Osteohondrodisplazija sa zakrivljenim kostima (prema referenciji br. 3)*

| Type of osteochondrodysplasia | Mode of heredity |
|---|---|
| 1. Campomelic dysplasia | AD |
| 2. Kyphomelic dysplasia | AR |
| 3. Stuve-Wiedemann dysplasia | AR |

between the extremities and the trunk. Thus the dominant clinical presentation is rhizomelic dwarfism. Often there is a decreased range of motion, with restricted extension and pronation in the elbows.

Thoracolumbar kyphosis is another sign in these patients. There is muscle hypotonia and arcual kyphosis, and when the child begins to walk there are also hyperlordosis, disc herniation, and other changes consistent with osteoarthritis, which may result in spinal cord compression. Another feature of the disease is an early appearance of various deformities of the extremities, and osteoarthritis of the peripheral joints, mainly hips and knees, are found at an early age. Obesity and osteoporosis with high levels of blood lipids and sugar are also seen early in life (4). Cardiovascular involvement is one of the extraskeletal manifestations of osteochondrodysplasias, manifested as valvular insufficiency, foramen ovale, patent ductus arteriosus, and other associated congenital heart malformations.

## Case presentation

The female patient that we are presenting here was admitted to our Rheumatology Clinic for the first time because of spinal and joint pain. She had been feeling pain from a very young age. She was occasionally treated on an outpatient basis. For over 10 years she could not walk without the aid of another person, and recently she could not stand on her own.

The patient was born from an unplanned pregnancy, the fourth child in the family. At the time of her birth the mother was 42 and the father 53 years old. Her height was 152 cm and body weight 87 kg. The father and uncle also had "rheumatic and bone problems" in their young age. On physical examination the patient was conscious, oriented to time, space, and people, subfebrile, eupneic, anicteric, acyanotic, obese, with visible skin and mucosa of normal appearance. She took a passive position in bed. Regarding the appearace of the head and neck, the following features were observed (Figure 1): reduced pilosity (for her age), high forehead, scaphoid form of the skull, and signs of average progenia. The neck was characterized by limited movement (lateral flexions and both rotations). During the examination there was pain and sensitivity to palpation at all vertebral spinous process levels, with a positive "ring sign" at the L4 l and L5 levels. Pain sensitivity on palpation of all long bones was also expressed. Short arms with semi-contractures of both elbows and the fingers of the hand were present, too. There was a flexion contracture of the right hip joint and pain during motion of both knee joints, with aches, movement restriction, and Baker's cysts in the right knee. The feet were large (European size 44) and in disproportion with the rest of the body. There was a positive bilateral straight leg test (Lasegue's test) at 30°. Decreased superficial touch sensation was found from the knees below.

Figure 1 General appearance of the patient
*Slika 1. Opći izgled bolesnice*

Laboratory findings were as follows: ESR 25/1h, alkaline phosphatase 170 UI/L , Ca 5.3, PCR- 12.9 mg/L, uric acid 353.1 μmol/L. Urine culture 3 times was negative.

Brucella agglutination test, AST-O, and Wraight's test were also negative. The patient's karyotype was 46 xx.

Chest radiography showed an increased shadow of the aortic knob, increased transparency in both pulmonary areas, an elevated diaphragm (due to obesity), and changes consistent with osteoporosis and right scoliosis of the thoracic spine (Figure 2). Radiographs of the lumbosacral region in two standard projections and the pelvic region including the hips showed reduced mineralization, a compressive fracture of the L5 vertebral body, hyperlordosis, congenital malformation of the hips in the form of coxa vara, with deformations and pronounced sclerosis of the femoral head (Figures 3 and 4). Radiographs of the knee joints were characterized by congenital deformations and osteoarthritic changes as well (Figure 5). A total hip DEXA scan showed a T-score of –3.7.

As it is known that osteochondrodysplasia is associated with aortic valve insufficiency, standard 2-dimen-

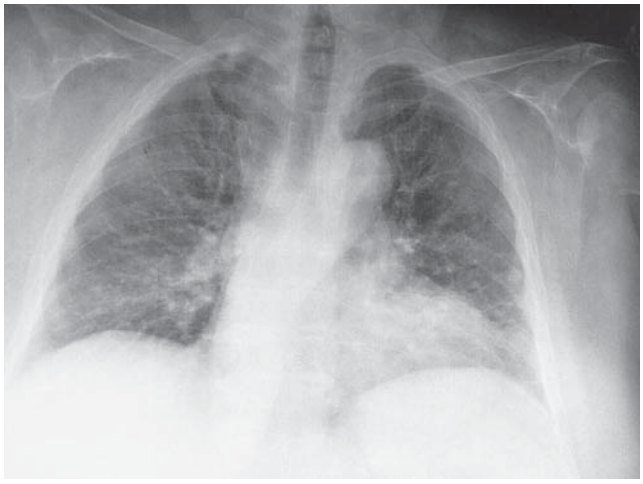

Figure 2 Chest radiograph
*Slika 2. Radiografija intratorakalnih organa*

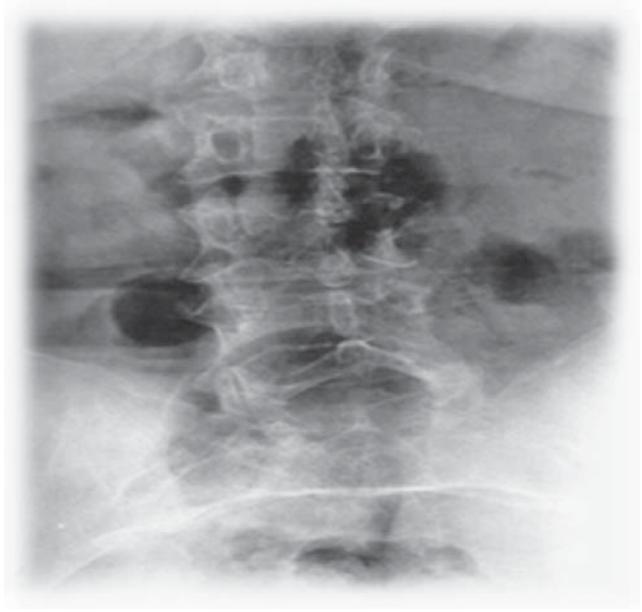

Figure 3 Radiograph of the lumbosacral spine
*Slika 3. Radiografija slabinske kralježnice*

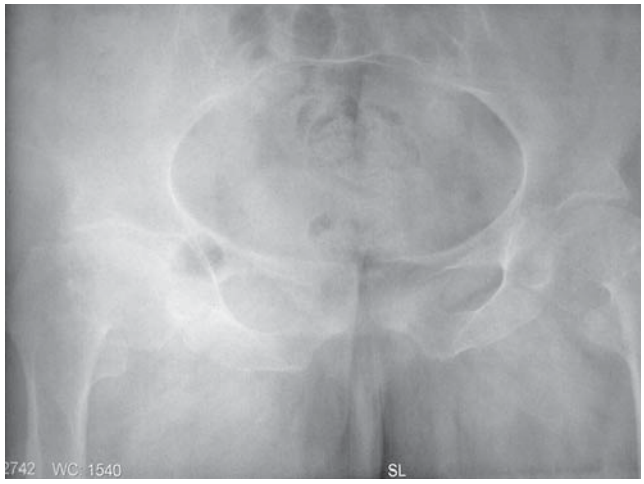


Figure 4 Pelvic radiograph
*Slika 4. Radiografija zdjelice*

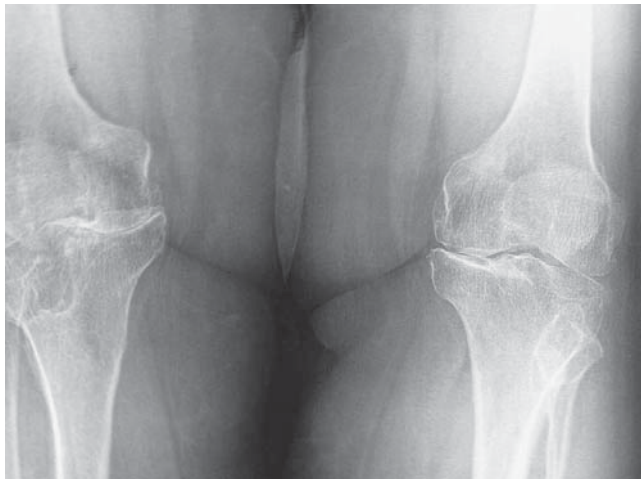

Figure 5 Radiograph of the knees
*Slika 5. Radiografija koljena*

sional echocardiography, M-mode, color Doppler, and pulsed Doppler echocardiography were done. Impairment of the diastolic function was found, with reduced E wave velocity, E/A ratio, and isovolumetric relaxation time (IVRT), while the E wave deceleration time was increased. Based on measurements of the aortic annulus, sinotubular junction, ascending aorta, descending aorta, and correcting for body surface area (BSA), mild aortic valve insufficiency was established.

In spite of the discovery of this rare disease, doctors' lack of experience with it, as well as the lack of specialized teams for diagnosis and treatment, the genetic damage that causes this disease is transmitted from generation to generation (5). This was the case with our patient as well. The disease itself does not affect the intellectual aspect and the patient's ability to experience life like everyone else. This should be taken in consideration, too.

If the disease is suspected at birth, follow-up during the growth period is essential, especially taking into consideration the longitudinal body measures and anthropometric measurements (height, weight, limb size, distance between fingertips at arms apart, length and width of the head). The measures should be compared to the growth age and sex percentile (6). Since collagen is one of the main structural components of the connective tissues, this disease can have various extraskeletal clinical manifestations. Collagen disorders in osteochondrodysplasia patients affecting the connective tissue of the heart are responsible for valvular heart diseases and aortic disorders (7–9).

Patients with this disease require specialized and trained teams (involving pediatricians, orthopedic surgeons, genetics specialists, psychiatrists, endocrinologists, psychologists, rheumatologists, cardiologists, and rehabilitation medicine specialists) to reduce the

consequences of the disease as much as possible. This kind of care was not available for our patient during her years of growth; she had to cope with just counseling about how to make her life as easy as possible in the circumstances.

Diagnosis of patients with congenital osteochondrodysplasia is challenging because the disease starts during the fetal period. Skeletal changes are early findings and their prevention is of the greatest importance for the prognosis and quality of life of these patients. Treatment of these patients is multidisciplinary and lifelong. At the first presentation of suspicious individuals with short limbs and body it is essential to exclude or confirm the diagnosis of congenital osteochondrodysplasia.

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## LITERATURE

1. Ligutić I, Barišić I, Antišević D, Vrdoljak J, Primorac D. Osseous dysplasia- specific medical care for children with chondrodysplasia (Koštane displazije – specifična zdravstvena skrb djece s hondrodisplazijama). Paediatr Croat. 2001;45:19–26. [article in Croatian]
2. Rasmussen SA, Bieber FR, Benacerraf BR, Lachamn RS, Rimoin DL, Holmes LB. Epidemiology of osteochondrodysplasias: changing trends due to advances in prenatal diagnosis. Am J Med Genet. 1996;61:49–58.
3. Lachman RS. Introduction and overview. Pediatr Radiol. 1998; 28:735–6.
4. Kornblum M, Stanitski DF. Spinal manifestations of skeletal dysplasias. Orthop Clin North Am. 1999;30:501–20.
5. Thompson M, Hecht JT, Bohan TP, et al. Neuroanatomic and neuropsychological outcome in school-age children with achondroplasia. Am J Med Genet. 1999;88:145–53.
6. Fowler ES, Glinsky LP, Reiser CA, Horton VK, Pauli RM. Biophysical bases for delayed and aberrant motor development in young children with achondroplasia. J Dev Behav Pediatr. 1997; 178:143–50.
7. Migliaccio S, Barbaro G, Fornari R, et al. Impairment of diastolic function in adult patients affected by osteogenesis imperfecta clinically asymptomatic for cardiac disease: casuality or causality? Int J Cardiol. 2009;131(2):200–3.
8. Weis SM, Emery JL, Becker KD, McBride DJ Jr, Omens JH, McCulloch AD. Myocardial mechanics and collagen structure in osteogenesis imperfecta murine (oim). Circ Res. 2000;87(8):663–9.
9. Ligutić I, Strinović B. Dystrophic nanism (Distrofični nanizam). Arh Zast . 1970;14:3–12. [article in Croatian]