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Case report
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# CORONARY DISEASE AND AORTOPATHY IN ACHONDROPLASIA

## *KORONARNA BOLEST I AORTOPATIJA KOD AHONDROPLAZIJE*

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**Summary**

**Introduction.** Achondroplasia is an inherited autosomal dominant disorder and the most prevalent cause of dwarfism in humans. **Case Report.** A 38-year-old male with achondroplasia required cardiothoracic surgical treatment. Standing at 150 cm, weighing 68 kg, with a body surface area index of 1.68 m², he had a history of diagnosed hypertension and Chiari malformation. A transthoracic echocardiogram five years ago revealed mild aortic regurgitation. In the recent cardiac examination, moderate-to-severe aortic regurgitation, dilation of the Valsalva sinus, and coronary artery disease were observed. The elective cardiothoracic surgery included mechanical aortic valve replacement and myocardial revascularization with a single bypass. Histopathological analysis of the aortic wall indicated mucoid degeneration, atherosclerosis, and focal adventitial hemorrhages. The postoperative course was uneventful, and normal blood pressure values were confirmed with a Holter monitor. **Conclusion.** A comprehensive cardiac evaluation is crucial for patients with achondroplasia, emphasizing the significance of considering echocardiographic parameters in the context of anthropometric characteristics. The proficiency and readiness of adult physicians to consistently provide accurate diagnosis and treatment, especially in urgent interventions or surgical procedures, are essential.

**Key words:** Coronary Disease; Achondroplasia; Aortic Valve Insufficiency; Transcatheter Aortic Valve Replacement; Coronary Artery Bypass

**Sažetak**

**Uvod.** Ahondroplazija je nasledna bolest koja se autosomno dominantno nasleđuje i najčešći je uzrok patuljastog rasta kod ljudi. **Prikaz slučaja.** Muškarac, starosti 38 godina, sa ahondroplazijom, čije lečenje je zahtevalo kardiohirurški tretman. Visina 150 cm, težina 68 kg, indeks telesna mase 1,68 m$^2$, od ranije dijagnostikovana hipertenzija i Kjarijeva malformacija. Transtorakalni ehokardiografski pregled pre pet godina ukazivao je na lako-blagu aortnu regurgitaciju. Pri poslednjem kardiološkom pregledu utvrđena je umereno-teška aortna regurgitacija, dilatacija sinusa Valsalve i koronarna bolest. Elektivna kardiohirurška operacija obuhvatala je zamenu aortne valvule mehaničkom dvolisnom valvulom i revaskularizaciju miokarda jednostrukim bajpasom. Patološko-histološkom analizom zida aorte uočena je mukoidna degeneracija, ateroskleroza i fokalno podlivena krvarenja adventicije. Postoperativni tok je bio uredan. Holterom krvnog pritiska potvrđene su normalne vrednosti. **Zaključak.** Potrebna je uvek kompletna kardiološka obrada kod pacijenata sa ahondroplazijom, uz važnost sagledavanja ehokardiografskih parametara u kontekstu antropometrijskih osobenosti. Neophodna je uvežbanost i spremnost lekara da uvek mogu da pruže adekvatnu dijagnostiku i lečenje posebno u urgentim interventim ili hirurškim procedurama.

**Ključne reči:** koronarna bolest; ahondroplazija; aortna regurgitacija; zamena aortnog zaliska; koronarni bajpas

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## Introduction

Achondroplasia is an inherited disorder transmitted in an autosomal dominant manner, with a 50% chance for newborns to inherit the syndrome if either parent carries it. However, 75% to 80% of patients with achondroplasia may be born to parents of average height due to a de novo dominant mutation in the fibroblast growth factor receptor 3 (FGFR3) gene, which is responsible for this condition [1]. Achondroplasia is the most common cause of dwarfism in humans. Affected individuals typically exhibit short limbs, an enlarged head circumference, and a normal trunk, often accompanied by musculoskeletal and cardiovascular complications. Diagnosing anomalies of the locomotor system prenatally can be particularly challenging, emphasizing the importance of actively searching for them during each prenatal examination. Arterial hypertension emerges as a prevalent risk factor for cardiovascular diseases in this population [2–4]. Reports highlight a tenfold increase in the prevalence of cardiovascular diseases in these patients between the ages of 25 and 35 [5]. In this study, we present the case of a

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***Abbreviations***

| | |
|---|---|
| BSA | – body surface area |
| TTE | – transthoracic echocardiogram |
| LVIDd | – left ventricular internal diameter in diastole |
| LVMI | – left ventricular mass index |
| CT | – computed tomography |
| LAD | – left anterior descending artery |

38-year-old patient at the time of diagnosis, whose treatment required elective cardiothoracic intervention, involving aortic valve replacement with the interposition of a tubular graft and aortocoronary bypass.

## Case Report

A 38-year-old male sought consultation with an internist at a private clinic in early 2021 for an examination due to uncontrolled hypertension, a condition he had been managing since the age of 18. The patient had achondroplasia, standing at a height of 150 cm, weighing 68 kg, and having a body surface area (BSA) index of 1.68 $m^2$. Secondary hypertension had been ruled out in prior assessments. The patient was aware of his Chiari malformation, and his last transthoracic echocardiographic examination (TTE), conducted five years ago, revealed mild aortic regurgitation (AR) without aortic dilation. He reported no subjective complaints, holding a New York Heart Association (NYHA) functional class of 1. His complete blood count (CBC) was within normal range, and the lipid profile showed cholesterol at 7.3 mmol/L, triglycerides at 3.68 mmol/L, and LDL at 4.6 mmol/L. Renal function parameters were within normal limits. Blood pressure measured 160/80 mmHg on both arms, and an electrocardiogram (ECG) indicated sinus rhythm with a heart rate of approximately 70/min, displaying a normal waveform and no signs of ischemia or rhythm disturbances. The TTE revealed slightly increased endocavitary dimensions of the left ventricle (left ventricular internal diameter in diastole (LVIDd) = 5.6 cm, LVIDd/BSA = 3.33 $cm/m^2$), preserved overall systolic function of the left ventricle, and significantly increased mass (interventricular septum thickness in diastole (IVSd) = 1.2 cm/left ventricular posterior wall thickness in diastole (LVPWd) = 1.2 cm, left ventricular mass indexed - LVMI = 174.9 $g/m^2$). The morphology and function of the right ventricle were preserved. Aortic regurgitation (AR) was observed to be moderately severe, qualitatively 3/4+, semiquantitatively with a pressure half-time (PHT) over 260 ms, and holodiastolic flow reversal in the descending aorta (end-diastolic velocity = 36 cm/s). This was associated with sinus of Valsalva dilation measuring 4.7 cm, sinus of Valsalva/BSA = 2.79 $cm/m^2$, and intraintimal dimensions **(Figure 1)**. The patient's therapy was adjusted, and an expert TTE was recommended at the Institute of Cardiovascular Diseases of Vojvodina, where the diagnosis was confirmed. A computed tomography (CT) aortography verified sinus

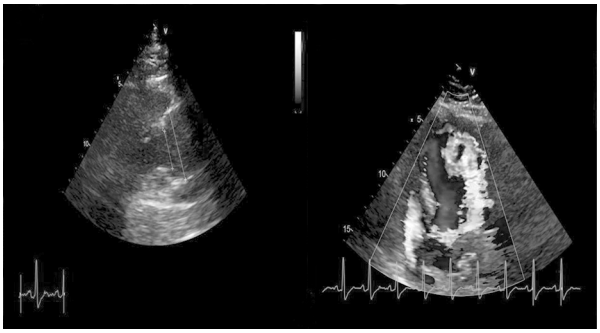

**Figure 1.** TTE – Sinus Valsalva dimensions of 47 mm with color signal of aortic regurgitation
***Slika 1.*** *Transtorakalni ehokardiogram – dimenzije sinusa Valsalve od 47 mm sa kolor signalom aortne regurgitacije*

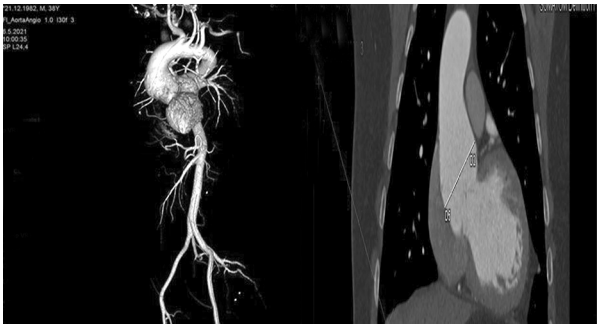

**Figure 2.** CT aortography: Aneurysmal dilatation of the aortic sinus of Valsalva measuring 53 mm
***Slika 2.*** *Kompjuterizovana tomografija aortografija: Aneurizmatsko proširenje sinusa Valsalve aorte 53 mm*

of Valsalva dilation, specifically in the left coronary sinus, measuring 5.3 cm. Other segments of the thoracic aorta displayed normal dimensions **(Figure 2)**. Subsequent CT coronary angiography revealed a borderline significant stenosis in the medial part of the left anterior descending artery (LAD). A preoperative left selective coronary angiography confirmed an 80% stenosis in the medial segment of the LAD. Following the diagnostic procedures, an elective cardiothoracic operation was performed, involving the mechanical bileaflet aortic valve replacement (St. Jude Medical- mechanical heart valves Size 23) with the interposition of an aortic tubular graft (Size 28). Additionally, myocardial revascularization was achieved with a single bypass: left internal mammary artery myocardial revascularization with single bypass. Histopathological analysis of the aortic wall revealed focal adventitial hemorrhage, disrupted media architecture with areas of mucoid degeneration, and pronounced atherosclerosis **(Figure 3)**. The early postoperative course was uneventful, followed by cardiac rehabilitation. Holter blood pressure monitoring confirmed normal values with preserved circadian rhythm. Subsequent echocardiographic examinations post-surgery confirmed the proper functioning of the mechanical aortic valve.

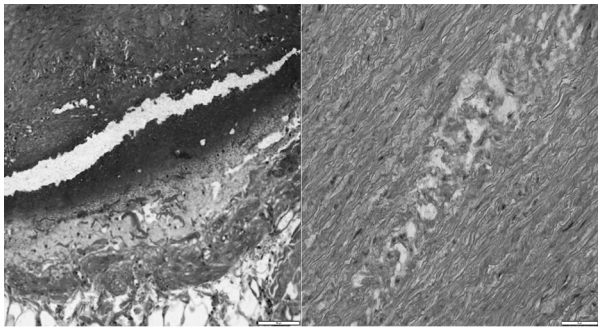

**Figure 3.** Ph analysis of the aortic section. **Left image** - 20x H&E, showing adventitia stained with blood. **Right image** - 40x H&E. Aortic wall with areas of disrupted elastic fibers and regions of mucoid degeneration. ***Slika 3.*** *Patohistološka analiza isečka aorte.* ***Leva slika*** *– 20 x HE gde se vidi krvlju podlivena adventicija.* ***Desna slika*** *– 40 x HE. Zid aorte sa delom raskidanih elasičnih vlakana i područijima mukoidne degeneracije.*

## Discussion

We presented a case of a young patient with achondroplasia who, amidst the challenges of the coronavirus-19 pandemic, also exhibited cardiac weakness. Despite the difficulties of the time, a relatively swift and comprehensive non-invasive cardiac diagnostic assessment was conducted, enabling timely and adequate treatment and resulting in significant improvement in cardiac morphology and function [6]. Verstraeten A. et al. in a 2020 publication, explained the association between achondroplasia and thoracic aortic aneurysms. The underlying cause of the disease lies in a pathological variant resulting in the heightened function of the fibroblast growth factor receptor 3 gene. They noted that dysregulations of the extracellular matrix, abnormal transforming growth factor-beta (TGF-β), and endoplasmic reticulum stress are common substrates for these diseases [7]. From the perspective of aortic pathology, although the abdominal region is more frequently affected, thoracic aortic diseases are more commonly associated with hereditary conditions. Over 20 gene bases for this have been identified so far, yet they account for less than 30% of the total cases [8]. Georgios and Tagarakis, et al., in a 2010 publication, illustrated the peculiarities of elective cardiothoracic revascularization, specifically aortocoronary bypass (CABG), in patients with achondroplasia. The patient, aged 41, was diagnosed with a three-vessel disease (90% stenosis of the proximal left anterior descending artery, 70% stenosis of the first obtuse marginal branch of the ramus circumflex artery, and 90% stenosis of the right coronary artery) before the decision for the planned operation. Despite his young age, he had no significant family comorbidities, and aside from high-normal blood pressure values, he had no other major risk factors that would be particularly relevant at his age. Echocardiography and ventriculography were normal. The operation proceeded without complications, involving a triple bypass, mammary artery to the proximal LAD, and two venous grafts to the other two diseased coronary vessels [9]. Sukhvasi et al.conducted a retrospective study analyzing outcomes of cardiothoracic surgical and interventional non-surgical cardiological procedures in patients with achondroplasia. Out of a total of 5274 identified articles, 14 met the criteria for inclusion in the analysis. Among the included cases, 53.8% (7/13) exhibited coronary artery disease, and 30.8% (4/13) of patients had a history of myocardial infarction. Among eight patients who underwent heart surgery, 37.5% (3/8) underwent multivessel coronary artery revascularization, 37.5% (3/8) had aortic valve replacement surgery, 25% (2/8) underwent surgery for type A aortic dissection, and the remaining 12.5% (1/8) had pulmonary thromboendarterectomy. Six patients underwent percutaneous coronary intervention. In 16.7% (1/6) of patients, an interventional procedure on the aortic and pulmonary valves was performed, and a pacemaker was implanted in another 16.7% (1/6). The mean size of arterial cannulas was 20.0 Fr. (French). Despite the small number of patients in this analysis, it precisely defined the cardiac substrate of this entity [10].

## Conclusion

Given the increased prevalence of cardiovascular comorbidities in individuals with achondroplasia, a comprehensive cardiac assessment is imperative. Echocardiographic parameters should be consistently evaluated, taking into account anthropometric characteristics, with particular attention to the body surface area index. Adult physicians must demonstrate proficiency and readiness to consistently deliver accurate diagnosis and treatment, especially in urgent interventions or surgical procedures.

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