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*Prikaz slučaja /*
*Case report*

# PLATYPNEA-ORTHODEOXIA SYNDROME - A RARE CAUSE OF PERIPHERAL CYANOSIS IN CHILD

# PLATIPNEA-ORTODEOKSIJA SINDROM - REDAK UZROK PERIFERNE CIJANOZE DETETA

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*Key words*
orthodeoxia, peripheral cyanosis, intracardiac shunt, right to left shunt

*Ključne reči*
ortodeoksija, periferna cijanoza, intrakardijalni šant, desno-levi šant

*Abstract*

**Introduction**: Platypnea-orthodeoxia syndrome is a rare clinical entity manifesting with arteriosus desaturation when a patient is in upright position, and retreats when a patient is lying. We are presenting a case of a 3-month old child with the symptoms of peripheral cyanosis in upright position caused by a rare platypnea-orthodeoxia syndrome. **Case Report**: In the clinical picture beside marmorized skin peripheral cyanosis was visible in upright position along with the bluish sclerae. Laboratory analyses (except for the increased lactates and D dimers), Chest X ray, Ultrasound of Abdomen, CT Thorax and Abdomen and electroencephalogram were normal. Echocardiographic finding showed the presence of a secundum defect in the interatrial septum and right-to -left shunt. **Discussion**: The causes of peripheral cyanosis are numeral and all of them must be carefully inspected within a differential diagnosis. The most common causes are intracardiac shunt, pulmonary parenchymal ventilation /perfusion mismatch, and pulmonary arteriovenous shunts. **Conclusion**: Peripheral cyanosis is a part of a clinical picture of different diseases, but its manifestation only in upright position can indicate a rare entity of platypnea- orthodeoxia syndrome detected within a differential diagnosis.

## *INTRODUCTION*

Platypnea-orthodeoxia syndrome (POS) is an uncommon condition of positional dyspnea (platypnea) and hypoxemia -arterial desaturation (orthodeoxia). The symptoms occur when the patient is upright and resolve quickly with recumbency [(1)]. The precise cause of the syndrome is unclear but patients develop right to left intracardiac shunting in the presence of normal right sided cardiac pressures [(2)] . Cyanosis is an abnormal bluish discoloration of the skin and mucous membranes; it is caused by high levels of deoxygenated (reduced) hemoglobin (or its derivates) circulating within the superficial dermal capillaries and subpapillary venous plexus [(3)]. Peripheral cyanosis is the blue tint in fingers or extremities, due to an inadequate or obstructed circulation. The blood reaching the extremities is not oxygen-rich and when viewed through the skin a combination of factors can lead to the appearance of a blue color [(4)]. We are presenting a case of a 3-month old child with symptoms of peripheral cyanosis in upright position caused by the rare disorder of platypnea orthodeoxia syndrome.

## *CASE REPORT*

This case report refers to the third child from the fourth regularly controlled pregnancy ended within the term as a vaginal delivery. Somatometric parameters were at the level of the referent values for that age (birth weight 3.700 grams, birth length 50 cm) and Apgar Score was 9/10. The infant has been regularly vaccinated and without allergic reactions to food and medicaments. The child was making progress in body mass index and was fed by the adapted infant formula. In the family anamnesis was only specific that the child's elder sister had the cyanotic episodes around the lips when she was 6 months to year and a half old.

A 3-month old male infant was admitted to our hospital due to peripheral cyanosis which appear during the shift of

body position when the child is put into upright position and which deteriorated while crying and being exposed to the cold. The difficulties have been present for a month and a half, while other difficulties were not perceived. The child was not getting tired while taking food.

On admission he was conscious and alert, afebrile, eupneic, normocardiac with oxygen saturation of 98 % on room air, heart rate of 120 per minute. On examination beside marmorized skin, peripheral cyanosis and bluish sclerae were specific. All other physical findings were normal. The initial analysis only showed slightly increased inflammatory marker (CRP 11mg/L) whereas complete blood count was within the reference range (r.r) including the values of methemoglobin and fetal hemoglobin. Acid-base status and the analysis of the gases in the arterialized capillary blood were within the reference range. The laboratory analyses showed the elevated lactate 3,05 mmol/L (r.r 0,5-2,2) and elevated D dimer 540 ng/ml (r.r <240).

Chest X ray was nonspecific, only the shadow of upper mediastinum seemed wider due to enlarged shadow of thymus. The ultrasound of abdomen was performed and it was completely normal. As an additional step in the diagnostic CT of chest and abdomen were done natively and after the application of contrast and they were without any detected pathological changes. Within a wider evaluation electroencephalogram (EEG) was carried out and it did not reveal any unusual electrical activity in the brain. During a detailed echocardiographic examination, the signs of lung hypertension were dismissed. In the morphological finding, a cardiologist spotted a secundum defect (hole) with the diameter of 4,5 mm in the interatrial septum. While the child was in the vertical suspension, a slight peripheral cyanosis appeared and it was located mostly on the legs. From the subxiphoid position echocardiographic was detected a periodical right- to-left shunt on the atrial septal defect.

During the hospitalization that lasted 9 days arterial tension and oxygen saturation were monitored every day with a pulse oximeter on all four extremities in horizontal and vertical position and they were mostly within the referent range. Peripheral cyanosis appeared periodically in vertical position and the oxygen saturation was in the range of 85%-98% on the lower extremities. The general health condition of the child was good, with normal vital parameters with preserved digestive function and urination and his body mass improved. The child was regularly controlled by a cardiologist without any therapy and the consultation of a cardio surgeon was indicated at the age of 6 months.

## *DISCUSSION*

The first case of POS was reported by Burchell et al. in a patient in 1949 with post traumatic intrathoracic arteriovenous shunt. The terms "platypnea" and "orthodeoxia" were coined by Altman et al. and Robin et al 1969 1978 respectively [5]. Descriptions of cyanopathia or *Morbus caeruleus* (cyanosis) have been reported in medical literature since the time of Hippocrates, but the pathophysiology of cyanosis was depicted only in 1749 [3]. There are not any relevant data how often orthodeoxia syndrome was present in general population or infancy. It is considered that one of the most common causes is a congenital defect in heart development (especially patent foramen ovale, but also atrial septal defect), which is, according to some facts, present in about 25% of the population without any symptoms. In addition, for a number of patients with POS, varying between 13% and 47% depending on different authors, the etiology cannot be identified with certainty, i.e.,orthodeoxia occurs without identifiable lung or heart disease [6].

A diagnosis of POS requires two of the following criteria: orthodeoxia, platypnea, presence of an interatrial communication, right-to-left shunt and absence of pulmonary arterial hypertension or right atrial hypertension. POS can originate in the heart, lungs, abdomen, or elsewhere due to either an intracardiac (cardiac POS) or intrapulmonary shunt, or a ventilation-perfusion mismatch [7] . Generally, in clinical picture patients with POS suffer from dyspnea and/or hypoxemia that arises in the upright position and is also present in the sitting position. These symptoms are usually attenuated or disappear within a few minutes by assuming a lying position [8]. This drop in saturation is defined as a drop in Pa $O_2$>4mmHg or $SaO_2$>5% from supine to an upright position [5].

In cardiac abnormalities with right-to- left shunts oxygen poor blood gets from the right half of the heart into the left side and thus into the systematic circulatory system. Congenital defects can lead to right-to-left shunting immediately after birth such as persistent truncus arteriosus (minimal cyanosis), transposition of great vessels, tricuspid atresia, Tetralogy of Fallot (pulmonary stenosis, ventricle septum defect, overriding aorta, right ventricular hypertrophy), total anomalous pulmonary venous return [9].

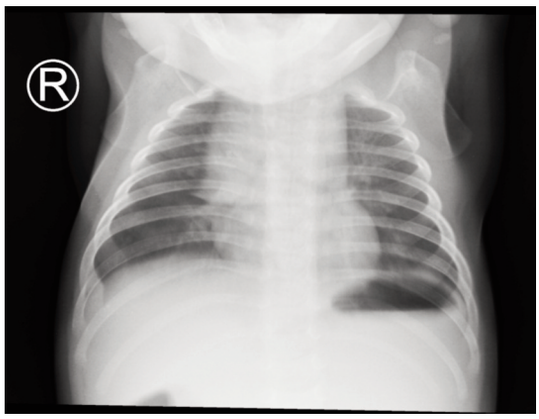
In the majority of cases, the syndrome is caused by the coexistence of an anatomical heart defect, especially patent foramen ovale (PFO), but also atrial septal defect (ASD) or atrial septal aneurysm (ASA) with septal fenestration, combined with structural or functional abnormalities or other thoracic or abdominal organs [10]. POS can be a manifestation of hepatopulmonary syndrome (HPS), defined as a triad of liver disease, inadequate oxygenation, and pulmonary vasodilation [11]. The prevalence of HPS in cirrhotic patients varies depending on various criteria used in the literature varying between 4% and 32% in some reviews, and 25.6 among liver transplant candidates [12].

Peripheral cyanosis was observed as a specific clinical entity in this case. The basic classification of cyanosis is that it can be central or peripheral. The most important causes of the central type of cyanosis come from central nervous system (intracranial hemorrhage, drug overdose, tonic-clonic seizure), respiratory system (pneumonia, bronchiolitis, bronchospasm, pulmonary hypertension, pulmonary embolism, hypoventilation, chronic obstructive pulmonary disease), cardiovascular disease (congenital heart disease, heart failure, valvular heart disease, myocardial infarction), blood (methemoglobinemia, polycythemia, congenital cyanosis). Apart from these causes which can be in the base of both central and peripheral cyanosis, there are high altitude (>2400m) hypothermia and obstructive sleep apnea. As the potential causes of periphery cyanosis in the literature are mentioned reduced cardiac output (e.g. heart failure or hypovolemia), cold exposure, arterial obstruction, (e.g. peripheral vascular disease, Raynaud phenomenon) and venous obstruction (e.g. deep vein thrombosis).

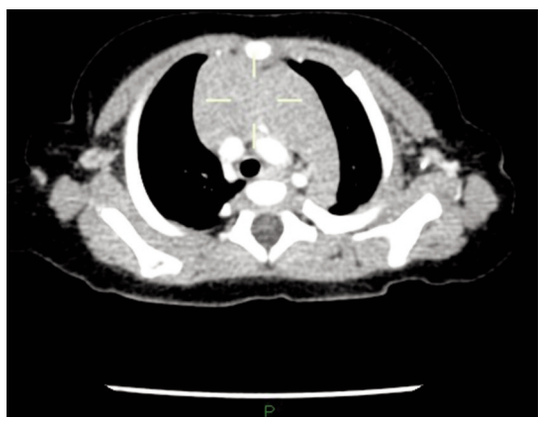
In our case a thorough laboratory and radiological diagnostic was conducted (Chest X ray, Ultrasound of Abdomen, CT of Thorax and Abdomen) as well as electrophysiological examination (EEG). In making a diagnosis and the examination of morphology and functionality of the heart and great blood vessels the most important was echocardiographic examination. It showed a secundum defect between right and left cardiac atrium as well as the existence of right-to left shunt, which was the cause of peripheral cyanosis. Slightly lower values of oxygen saturation measured with a pulse oximeter present when the infant was in upright position indicated a rare orthodeoxia syndrome. Higher values of lactate and D dimer were caused by hypoperfusion and following blood track on the periphery. Monitoring of oxygen saturation with oximeter as well as the arterial pressure (tension) on all four extremities are important because of the assessment of circulation and dismissing potential diseases such as coarctation of aorta.

*CONCLUSION*

Peripheral cyanosis is a part of clinical picture of different diseases, but its manifestation only in the upright position can indicate a rare entity of platypnea orthodeoxia syndrome considered within differential diagnosis. The examination of all potential causes of peripheral cyanosis is crucial in well-timed diagnostic and treatment. The key role in making a diagnosis played echocardiographic examination which indicated the existence of right-to -left shunt and a defect in the interatrial septum that contributed the development of specific clinical picture. The treatment of choice is surgical closure of the intracardiac (usually interatrial) communication, which may result in dramatic symptomatic and hemodynamic improvement [2].




***Picture no. 1**. PA chest X ray - Enlargement of the cardiac silhouette due to enlarged hymus*



***Picture no. 2.** Axial CT scan if thorax-detected only enlarged thymus without other pathological findings*


## *Sažetak*

**Uvod:** Platipnea-ortodeoksija sindrom je redak klinički entitet koji se manifestuje arterijskom desaturacijom kada je pacijent u uspravnom položaju, a povlači se u horizontalnom. Prezentujemo Vam slučaj deteta uzrasta 3 meseca sa perifernom cijanozom u uspravnom položaju u čijoj osnovi je bio redak poremećaj-platipnea ortodeoksija sindrom. **Prikaz slučaja:** U kliničkoj slici pored mramorizovane kože, bila je uočljiva periferna cijanoza u uspravnom položaju i plavičaste sklere. Laboratorijske analize (izuzev povišenih laktata i D dimera), rendgensko snimak pluća i srca, ultrazvuk abdomena, CT grudnog koša i abdomena i elektroencefalogram su bili uredni. Ehokardiografskim nalazom detektovano je prisusutvo u interatrijalnom septumu secundum defekta i desno-levog šanta. **Diskusija**: Brojni su uzroci periferne cijanoze i svi moraju biti pažljivo razmotreni u okviru diferencijane dijagnoze. Najčešće je u osnovi intrakardijalni šant, poremećaj odnosa ventilacija/perfuzija u plućnom parenhimu i plućni arterijsko-venski šant. **Zaključak**: Periferna cijanoza je deo kliničke slike različitih bolesti, ali njena manifestacija samo u uspravnom položaju diferencijalno dijagnostički može da uputi na redak entitet platiinea ortodeoksija sindrom.

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