Chest pain with myocardial ischemia in a child: should we think about coronary slow flow phenomenon?

Bir çocuk hastada miyokart iskemisine bağlı göğüs ağrısı: Koroner yavaş akım fenomenini düşünmeli miyiz?

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Summary– The coronary slow flow phenomenon (CSFP) is an angiographic finding characterized by delayed opacification of epicardial coronary arteries in the absence of stenotic lesion. Herein, we present a 13-year-old boy with recurrent chest pain who was diagnosed with acute ST-segment elevation myocardial infarction associated with CSFP, which has not been reported previously in the pediatric age group. Coronary angiography revealed only the presence of slow flow in the left anterior descending (LAD) coronary artery. Myocardial perfusion scintigraphy revealed a reversible perfusion defect in the LAD territory, which regressed partially at rest and showed complete improvement after dipyridamole infusion. All the symptoms, electrocardiogram abnormalities and cardiac markers returned to normal after dipyridamole treatment during the follow-up. We conclude that CSFP should be kept in mind in the differential diagnosis of chest pain with myocardial ischemia in the pediatric age group.

Özet– Koroner yavaş akım (KYA) fenomeni stenotik lezyon olmaksızın epikardiyal koroner arterlerde opak madde ilerlemesinde gecikme ile kendini gösterir. Burada, tekrarlayan göğüs ağrıları ve çocukluk yaş grubunda daha önce tanımlanmamış olan KYA fenomeni ile ilişkili akut ST-segment yükselmeli miyokart enfarktüsü tanısı konan 13 yaşında bir erkek olgu sunuldu. Hastanın koroner anjiyografi bulguları sol ön inen koroner arterde akım yavaşlaması dışında normaldi. Miyokart perfüzyon sintigrafisinde etkilenen bölgede saptanan perfüzyon defekti dinlenme ile kısmen gerilerken dipiridamol infüzyonu sonrası tamamen kayboldu. Dipiridamol tedavisi başlanan hastanın izlemede yakınmaları düzeldi, elektrokardiyogram bulguları ve kardiyak belirteçleri normale döndü. Sonuç olarak, miyokart iskemisine bağlı göğüs ağrısı ile başvuran çocuk olguların ayırıcı tanısında KYA fenomeninin de akılda tutulması gerektiğini düşünmekteyiz.

The coronary slow flow phenomenon (CSFP) is characterized by delayed opacification of the epicardial coronary arteries in the absence of obstructive coronary disease. The incidence of CSFP is reported as 1-5.5% among adult patients who undergo coronary angiography (CAG) with suspicion of acute coronary syndrome.[1] The presentation pattern of these patients varies widely from vague chest discomfort to myocardial infarction.[1-3] Herein, we present a child who had recurrent chest pain and acute ST-segment elevation myocardial infarction (STEMI) associated with CSFP.

Abbreviations:

CAG	*Coronary angiography*
CSFP	*Coronary slow flow phenomenon*
ECG	*Electrocardiogram*
LAD	*Left anterior descending artery*
STEMI	*ST-segment elevation myocardial infarction*
TIMI	*Thrombolysis in myocardial infarction*

CASE REPORT

A 13-year-old boy was admitted to an outpatient clinic with complaints of severe chest pain, described as pressure-like, together with diaphoresis and dyspnea. Since the patient's symptoms and laboratory findings were consistent with myocardial ischemia, a treatment including metoprolol, oral nitrate and acetyl salicylic acid was administered, and he was then referred to our hospital. His chest pain was recurrent, both at rest and

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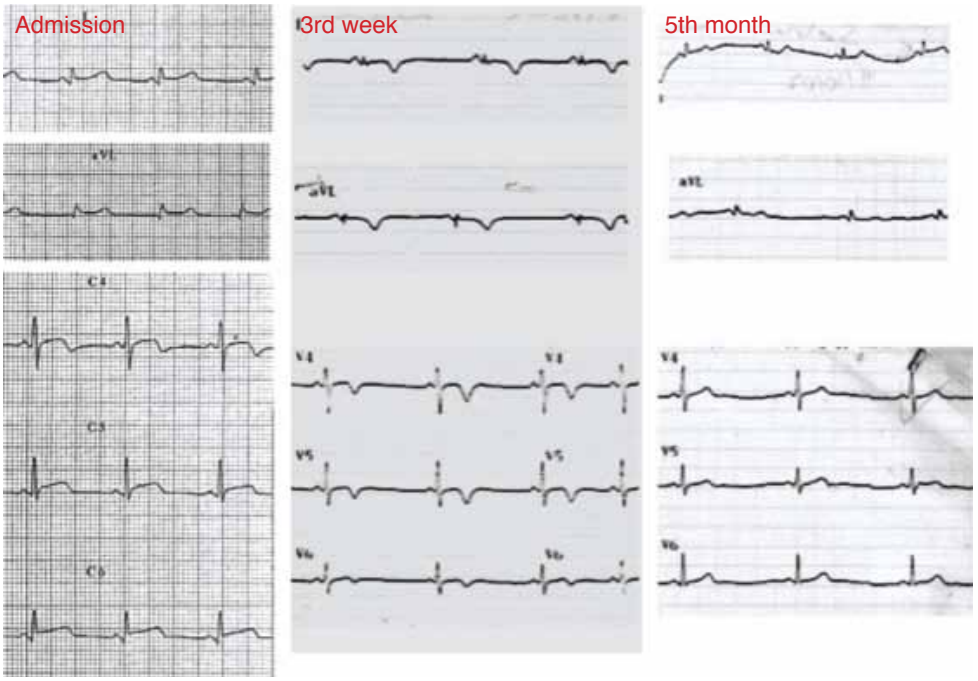

Figure 1. ECG findings of the patient in leads DI, aVL and V4-6 at admission and during follow-up.

on exertion, lasting more than 30 minutes. He was otherwise healthy, and his medical history was unremarkable. At presentation, the patient's electrocardiogram (ECG) revealed ST-segment elevation in the leads DI, aVL and V4-6 (Fig. 1). Cardiac markers were found elevated: creatinine kinase-MB was 66 U/L (N: <25 U/L) and troponin I was 6.9 ng/ml (N: <0.04 ng/ml). The physical examination and echocardiography did not reveal any pathological findings. Chest X-ray showed a normal cardiac silhouette with clear lung fields. Serum cholesterol, triglyceride and other laboratory tests including C-reactive protein and erythrocyte sedimentation rate were also normal. Serological tests were negative for the most common viruses

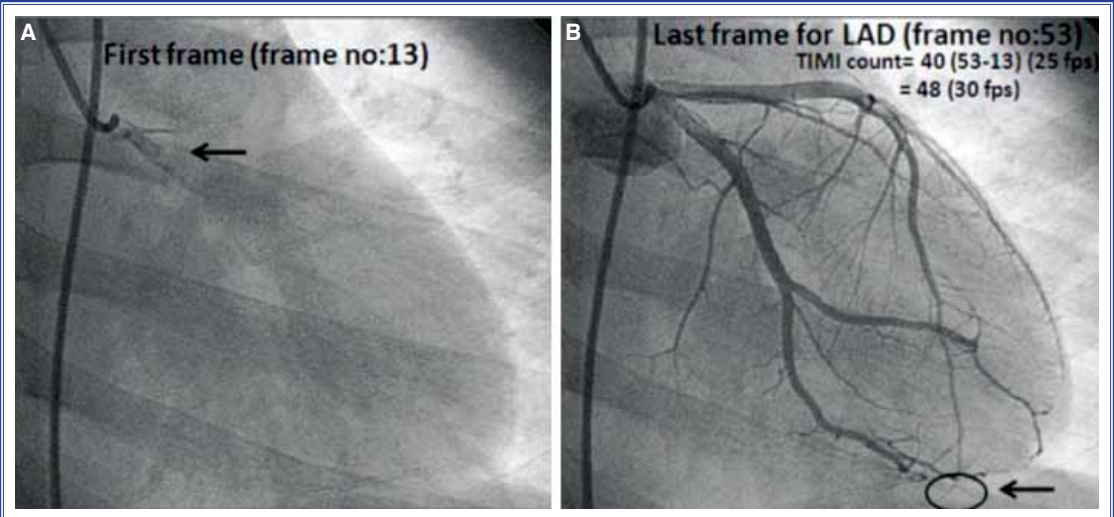

Figure 2. Definition of CSFP in the left anterior descending artery (LAD). **(A)** Representing the first frame in which dye fully enters the artery (arrow). **(B)** Representing the last frame in which distal landmark of the LAD (the moustache) first becomes opacified (arrow). **Supplementary video files associated with this case can be found in the online version of the journal.*

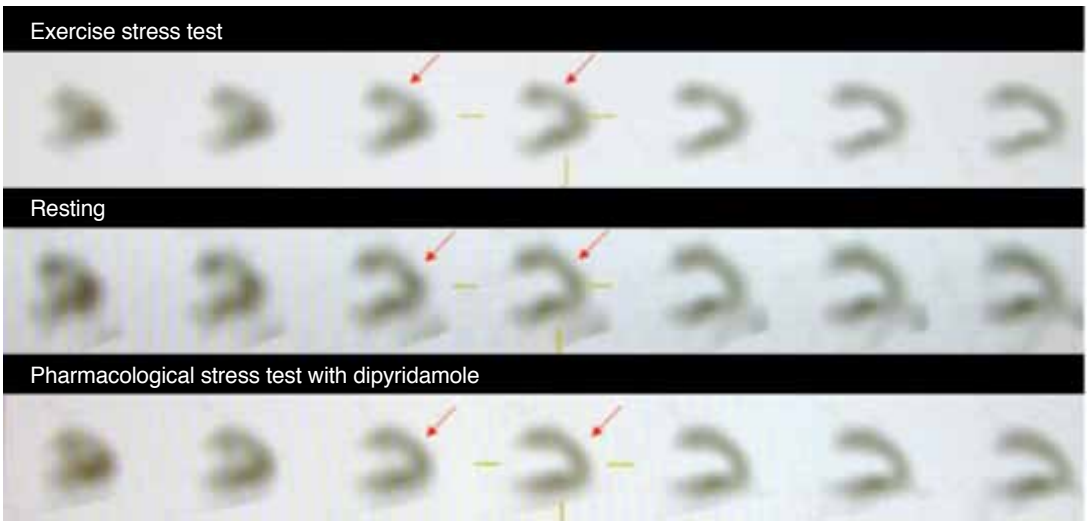

Figure 3. Vertical long-axis myocardial perfusion images showing anteroseptal reversible perfusion defects (upper and middle line). After the dipyridamole stress test, normal myocardial perfusion was observed (lower line).

affecting the heart. He underwent selective CAG and left ventriculography on the second day of hospitalization. The left ventriculography revealed slight hypokinesis in the anterolateral wall, and CAG revealed no stenosis, ectasia, fistulae, or abnormal origin of the coronary arteries. However, the presence of slow flow in the left anterior descending (LAD) coronary artery was observed (Video 1*). Thrombolysis in myocardial infarction (TIMI) frame counts of the coronary arteries were calculated according to Gibson's method.[4] The frame rate of the patient's images (25 frames/s) were multiplied by 1.2 in order to obtain the values for 30 frames/s, as described previously. Consequently, the TIMI frame count for LAD was 48 frames (normal values, 36.2±2.6) (Fig. 2). Frame counts greater than +2 standard deviations (SD) from the published range are considered to be abnormal and indicative of slow flow.[4] However, TIMI frame counts for both the circumflex and right coronary arteries were within normal ranges. Subsequently, myocardial perfusion scintigraphy revealed a reversible perfusion defect in the LAD territory, which regressed partially at rest and showed complete improvement after dipyridamole infusion (Fig. 3). Screening for inherited thrombophilic disorders was negative (including protein C, protein S, and antithrombin deficiencies, fibrinogen, homocystine, and plasminogen activator inhibitor-1 levels, activated protein C resistance, and mutations for factor V Leiden, methylenetetrahydrofolate reductase, and prothrombin). We started dipyridamole treatment (4 mg/kg/day, TID), and all the ECG abnormalities and cardiac markers returned to normal gradually (Fig. 1). He has not experienced severe chest pain or any findings of myocardial ischemia under dipyridamole treatment during the follow-up.

DISCUSSION

Chest pain is a common complaint and is a leading cause of visits to pediatric cardiologists and emergency rooms among children. Although the majority of the etiological factors are non-cardiac and benign in nature, several cardiac conditions can cause chest pain and myocardial ischemia or infarction in the pediatric population. STEMI in subjects with normal coronary arteries is quite a rare entity, especially in children and adolescents. Although the underlying mechanism is not clearly understood, it is considered that concealed atherosclerosis, coronary vasospasm, coronary embolization, inflammation, thrombosis, or hypercoagulable state may play a significant role alone or within a combination. Our patient presented with a history of recurrent episodes of chest pain, ECG abnormalities and elevated cardiac markers, which were suggestive of myocardial ischemia. However, there was no coronary abnormality on the angiography. Screening for the common causes of viral myocarditis and inherited

thrombophilic disorders was unremarkable. He had no systemic febrile illness or upper airway tract infection prior to presentation. He also had no history of smoking, drug or substance abuse or addictions. Both CAG and myocardial perfusion scintigraphy were consistent with CSFP in our patient. TIMI frame count for LAD was found to be >2 SD from the normal range. Despite the fact that TIMI frame counts have been derived from a study consisting of adult patients with longer coronary arteries than children, both CAG and myocardial perfusion scintigraphy were consistent with CSFP in our patient, for the LAD. Nevertheless, further studies are needed to obtain normal values and to define CSFP in children.

Angina pectoris and ST-segment elevation after treadmill exercise testing have been reported in patients with CSFP.[2] Recently, CSFP has been documented in adults who had anginal chest pain with elevation in the ST segment.[1,5] Doğan et al.[6] reported a 15-year-old boy who had acute STEMI and anatomically normal coronary arteries. However, they described multiple prothrombotic gene polymorphisms, unlike in our patient, and considered that these polymorphisms might have contributed to the development of acute STEMI. Yetkin et al.[7] reported that patients with myocardial infarction and normal coronary arteries had increased TIMI frame counts compared with patients without myocardial infarction. Thus, they suggested that decreased coronary flow rate might be a common step in the pathogenesis of myocardial infarction with normal coronary arteries. However, the underlying mechanisms and clinical implications of CSFP are still not completely understood. Cellular edema, fibromuscular hyperplasia, myofibrillary disorganization, and microvascular thickening with luminal narrowing of the coronary arteries are major pathological findings in these patients.[1,8] Elevated resting coronary microvascular tone and endothelial dysfunction have been introduced as the most responsible etiological factors for this phenomenon.[1,7] Increased levels of plasma homocysteine, increased endothelin-1 release and reduced nitric oxide bioactivity have been reported in patients with CSFP, suggesting impaired endothelial function.[1,7-10] Functional obstruction of microvessels seems to be relieved by dipyridamole infusion in the affected arteries.[2,3,8,9] Moreover, improvement of the perfusion defects on the myocardial perfusion scintigraphy has been shown after dipyridamole infusion in these patients.[9] Kurtoglu et al.[10] observed that coronary flow returned to normal levels in 70 of 75 vessels with oral dipyridamole treatment in patients with CSFP. Further, atypical anginal complaints disappeared in 68% of the patients in their study and decreased in frequency in one-third of the remaining patients. Similarly, in our patient, we achieved regression of the symptoms and laboratory findings under dipyridamole treatment without severe chest pain or myocardial ischemia during the follow-up.

In conclusion, although chest pain is a common symptom in children, fortunately, myocardial ischemia and infarction occur very rarely, unlike in adults. On the other hand, there are well-known congenital or acquired causes in the pediatric population due to various etiological factors. However, to the best of our knowledge, this is the first case of STEMI associated with CSFP in this age group.

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****Supplementary video file associated with this article can be found in the online version of the journal.***

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Key words: Blood flow velocity; chest pain; child; coronary circulation; myocardial ischemia.

Anahtar sözcükler: Kan akım hızı; göğüs ağrısı; çocuk; koroner akım; miyokart iskemisi.