CLINICAL IMAGE

Microvascular endothelial dysfunction in a young patient with familial hypercholesterolemia

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Hypercholesterolemia is considered to be the major risk factor for developing a wide spectrum of cardiovascular diseases, including myocardial infarction and stroke. Familial hypercholesterolemia (FH) is an autosomal dominant condition characterized by highly elevated low-density lipoprotein (LDL) cholesterol levels, leading to premature cardiovascular disease and death. Although scientific and methodological progress in genetic investigation have significantly increased its accuracy, most patients with FH still remain underdiagnosed.[1] What is of importance to microcirculation, it has been strongly suggested that development of hypercholesterolemia is firmly associated with endothelial dysfunction.[2] Owing to its accessibility, peripheral microvascular function has been considered as a prognostic and diagnostic biomarker in cardiovascular disease.[3]

Laser-speckle contrast imaging (LSCI) is a recently developed technique based on speckle contrast analysis, which provides a quantitative assessment of microvascular perfusion.[3] Laser-speckle contrast imaging allows for noninvasive, noncontact, and real-time microcirculation imaging over a wide area of the tissue in response to a given stimulus. Importantly, this technology shows very good reproducibility as well as excellent spatial and temporal resolutions.[4] Currently, it is also possible to assess the real-time changes in tissue biochemistry. A brand new technique, known as flow-mediated skin fluorescence (FMSF), is based on monitoring of the intensity of the reduced form of nicotinamide adenine dinucleotide (NADH) fluorescence signal emitted from the epidermis on the forearm in response to blocking and restoring blood flow. Therefore, FMSF enables clinicians to perform a noninvasive evaluation of microcirculation and metabolic regulation. Of note, NADH is an important mitochondrial component and plays a pivotal role in cellular energy metabolism.[5]

A 38-year-old man with an unremarkable medical history was referred to the National Center of Familial Hypercholesterolemia in Gdańsk, Poland, because of a significantly increased LDL cholesterol level of 8.24 mmol/l. He presented with arcus cornealis, which is typical of FH, and had a family history of high LDL cholesterol levels (mother, 9.61 mmol/l; sister, 7.25 mmol/l). Importantly, he had no history of any hypolipidemic therapy. Further genetic testing identified the presence of an LDL-receptor gene mutation (p.Glu140Asp). Transthoracic echocardiography and the carotid intima-media thickness measurements revealed no abnormalities. Therefore, we decided to extend the standard diagnostic protocol and assess microvascular endothelial function.

Here, we present the results of microcirculation measurements assessed simultaneously on the forearm during and following brachial artery occlusion by LSCI (PeriCam PSI System, Perimed, Järfälla, Sweden) and FMSF (Angionica, Ltd., Łódź, Poland). Speckle contrast analysis with colors ranging from blue (low perfusion) to red (high perfusion) showed relatively low basal microvascular perfusion (FIGURE 1A). We also observed a very weak postocclusive reactive hyperemic response (FIGURE 1B), suggesting a low vasodilatation potential, which is mainly endothelium-dependent. Similarly, FMSF revealed a poor endothelium-dependent hyperemic response, while ischemic response, which may reflect tissue sensitivity to hypoxia, remained within normal limits (FIGURE 1C).

To the best of our knowledge, this is the first report on a complex noninvasive assessment of microcirculation in a patient with FH. Although less extensively studied, microvascular disorders may precede endothelial dysfunction in large arteries and the subsequent clinical symptoms.

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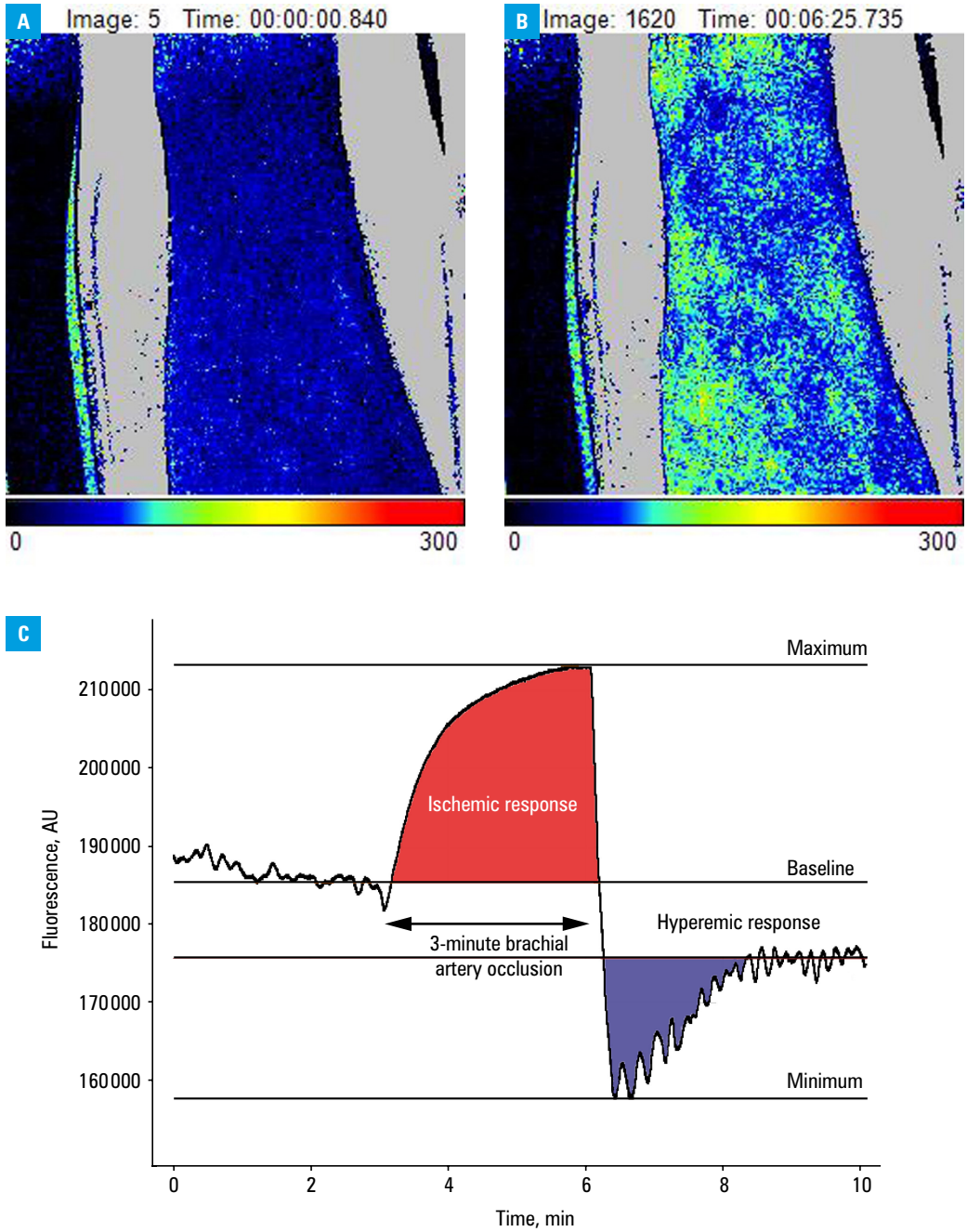

FIGURE 1 Imaging of a patient with familial hypercholesterolemia: **A** – basal microvascular perfusion on laser-speckle contrast imaging with colors ranging from blue (low perfusion) to red (high perfusion); **B** – weak postocclusive reactive hyperemic response with more intense perfusion; **C** – flow-mediated skin fluorescence showing a weak hyperemic response and normal ischemic response

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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