Four-year imaging follow-up of a homozygous familial hypercholesterolaemia patient: atherosclerosis ingravescence and coronary flow velocity reserve reduced gradually. Case report.

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Abstract

Homozygous familial hypercholesterolemia (HoFH) is a rare heredity disease in which severe cardiovascular atherosclerosis develops from birth due to severe low density lipoprotein-receptor (LDL-R) defects inherited from both heterozygous-carriers of FH (HeFH) parents. This case describes a HoFH patient who underwent medical imaging examination for 4 years over a course of treatment. In addition to the imaging techniques which demonstrated the development of cardiovascular atherosclerosis ingravescents, transthoracic Doppler echocardiography noninvasively and accurately detected the position of atherosclerotic calcifications and evaluated the hemodynamicsof the coronary flow. Analysis showed the patient had a significantly lower coronary flow velocity reserve due to plaques compromising coronary artery ostia.

Keywords: familial hypercholesterolemia, atherosclerosis, echocardiography, coronary flow velocity reserve

Introduction

Familial hypercholesterolemia (FH, OMIM #143890) has become a public health concern throughout the world. Recent direct screening in a Northern European general population detected a prevalence of HeFH of approximately 1/200 [1]. The European Atherosclerosis Society (EAS) FH consensus suggest that the prevalence of HoFH may affect as many as 1 in 160,000-300,000 people [2]. The following case study introduced modern medical imaging technology follow up in a HoFH patient.

Case report

In June 2011, a 13-year-old girl was first sent to Anzhen hospital (Beijing, China) complaining of shortness of breath. Physical examination found multiple cutaneous and tendon xanthomas. Genetic analysis showed disease-causing mutations in LDL-R gene. The patient’s parents also underwent serum lipid tests. Clinical diagnosis of the patient was HoFH and of both parents was HeFH.

From June 2011 to June 2014 we followed up the patient and results of serum lipid tests, electrocardiograms, echocardiography, coronary arteriography (CAG), single photon emission computed tomography (SPECT) and computed tomography angiography (CTA) of large blood vessels were selected and analyzed (table I, fig 1). Simvastatin was given from 2011; the treatment strategy was adjusted according to whether the patient reached the target ≥ 50% LDL-C reduction from baseline [3]. Yearly serum lipid profiles are described in table I.
Four-year imaging follow-up of a homozygous familial hypercholesterolaemia patient

Fig 1. A1) Transthoracic adenosine stress echocardiography detected coronary flow velocity reserve (CFVR=MDVh (mean diastolic velocity in hyperemia) / MDVb (mean diastolic velocity at baseline)) detected in the distal left anterior descending artery (LAD) (CFVR=1.98, 2012); A2) CFVR=1.46, 2014; B1) TTDE detected Aortic Stenosis (mild, AOVmax 320cm/s, PPG 40mmHg, MPG 18mmHg, 2011); B2) Aortic Stenosis (moderate, AOVmax 392cm/s, PPG 61mmHg, MPG 35mmHg, 2014); C1) CTA (Curve Planar Reconstruction) showed that the narrowest place in descending aorta (DAO) is 5.9mm (2012); C2) Narrowest place in DAO is 4.4mm (2014); D1) SPECT myocardial perfusion imaging (MPI) showed myocardial ischemia in the anterior wall (2012); D2) MPI evidenced dilation of LV and myocardial ischemia aggravated (2014); E1) Coronary arteriography (CAG) demonstrated LAD branch displaying 50% stenosis, and the first diagonal branch openings displayed 80% stenosis (2012); E2) CAG showed the left circumflex artery (LCX) had nearly 80-90% stenosis and the right coronary artery (RCA) could not be clearly imaged (2014).

Two-dimensional ultrasonography showed aggravated diffuse thickening of the intima-medium thickness and multiple mixed plaques formations in the peripheral vasculature. Echocardiogram showed left side of the heart significantly dilated and calcified plaques deposited in the valves and the aortic vessel wall. The abnormal segmental wall motion spread widely and the ejection fraction (EF) decreased. The main coronary artery could hardly be detected; adenosine stress echocardiography showed that the CFVR decreased yearly (fig A1, A2). Valves regurgitation and aortic stenosis could be detected (fig B1, B2). CTA showed the whole aorta to be affected by dysplasia (fig C1, C2). SPECT myocardial perfusion imaging (MPI) performed dilation of the left ventricular and myocardial ischemia (fig D1, D2). Coronary arteriography (CAG) displayed coronary artery irregular and stenosis (fig E1, E2).

Discussions

Based on the widespread prevalence of FH [1], there are approximately 10 million worldwide and 2.6 million potential FH patients in China. Medical guidelines recommend the use of imaging techniques to diagnose and manage FH subjects [4]. In theory, the basic pathogenesis of FH is a typical progression of arteriosclerosis mainly affecting the arterial system, and it is an idealized model of current and developing arteriosclerosis. The treatment of patients with FH has improved in recent years, but limitations remain. Our study showed that combined drug therapy could not keep the HoFH patient’s LDL cholesterol level below the target value.

Aortic root calcification and aortic supravalvular stenosis are typically characteristic of HoFH. CTA could

Table I. Transthoracic Doppler echocardiography and serum lipid results from 2011-2014

<table>
<thead>
<tr>
<th>Year</th>
<th>Age</th>
<th>LVDd (mm)</th>
<th>LVSD (mm)</th>
<th>IVS (mm)</th>
<th>AAO (mm)</th>
<th>EF (%)</th>
<th>AOVmax/PPG/MPG</th>
<th>CFVR</th>
<th>TC (mg/dL)</th>
<th>LDL-C (mg/dL)</th>
<th>TG (mg/dL)</th>
<th>HDL-C (mg/dL)</th>
</tr>
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<tbody>
<tr>
<td>2011</td>
<td>13</td>
<td>46</td>
<td>31</td>
<td>12</td>
<td>19</td>
<td>58</td>
<td>320/40/18</td>
<td>2.15</td>
<td>16.28</td>
<td>12.81</td>
<td>1.43</td>
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<tr>
<td>2012</td>
<td>14</td>
<td>56</td>
<td>45</td>
<td>10</td>
<td>17</td>
<td>45</td>
<td>337/45/20</td>
<td>1.98</td>
<td>16.79</td>
<td>12.75</td>
<td>1.46</td>
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<tr>
<td>2013</td>
<td>15</td>
<td>60</td>
<td>48</td>
<td>9.5</td>
<td>16</td>
<td>43</td>
<td>378/57/34</td>
<td>1.76</td>
<td>15.27</td>
<td>12.68</td>
<td>1.31</td>
<td>0.53</td>
</tr>
<tr>
<td>2014</td>
<td>16</td>
<td>65</td>
<td>52</td>
<td>9</td>
<td>15</td>
<td>40</td>
<td>392/61/35</td>
<td>1.46</td>
<td>13.29</td>
<td>12.63</td>
<td>0.87</td>
<td>0.42</td>
</tr>
</tbody>
</table>

LVDd (mm): left ventricle end diastolic diameter; LVSD (mm): left ventricle end systolic diameter; IVS (mm): interventricular septum; AAO (mm): ascending aorta; EF (%): ejection fraction; AOVmax (cm/s): maximum velocity of aorta; PPG (mmHg): peak pressure gradient; MPG (mmHg): mean pressure gradient; CFVR: coronary flow velocity reserve; TC: total cholesterol; LDL-C: low density lipoprotein cholesterol; TG: triglyceride; HDL-C: high density lipoprotein cholesterol; (*4 year variation rate of serum lipids of TC, LDL-c, TG, HDL-c is 18.37%, 1.41%, 39.16%, and 71% respectively)
display the dysplasia and degree of stenosis of the whole aortic curve. Dual-source computed tomography could visualize plaque in both the aorta and coronary artery; however, it was unable to evaluate the coronary flow.

TTDE demonstrated the coronary heart disease and imaged the size of the calcification, while estimating the degree of stenosis in the aortic valve and measuring coronary flow hemodynamics. CFVR is detected by adenosine stress echocardiography, defined as the ratio of mean diastolic velocity in hyperemia (MDVh) to mean diastolic velocity at baseline (MDVb), CFVR under 2.0 is suggestive of coronary artery stenosis [5]. TTDE showed that when calcification is involved in the proximal of the main trunk of the coronary artery or near the coronary ostia, CFVR is lower in HoFH than HeFH and HoFH’s where there is no calcification proximal to the coronary (the latter two CFVR is usually between 2 and 3). The reason for this is that in HoFH the plaque in the coronary ostia results in a decreased coronary flow. CFVR could be used as a parameter to assess the extent of the FH patient’s coronary artery disease and the clinical efficacy of the lipid-lowering treatment.

Imaging techniques could be used as the preferred method for follow-up observation in FH patients. Color Doppler ultrasound techniques, especially echocardiography, should be used routinely in the diagnosis and help monitor clinical lipid-lowering treatment in FH patients.

References