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Severe coronary artery disease secondary to graft versus host disease after bone marrow transplantation in a 24-year-old woman

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A 24-year-old woman with the history of aplastic anemia treated with an autogenic bone marrow transplantation (BMT, at the age of 4) and acute myeloid leukemia treated with allogenic BMT (at the age of 9) with graft derived from unrelated donor (8/10 human leukocyte antygen matched and ABO mismatched). The preparative regimen comprised 14,3 Gy total body irradiation (TBI) and standard chemotherapy. On day 1 after BMT graft versus host disease (GVHD) occurred and it was responsive to corticosteroids. At the age of 17 she underwent bilateral total hip arthroplasty due to aseptic necrosis of both femoral heads following high-dose steroid treatment. Patient was admitted to the cardiology department as a matter of urgency due to suspicion of myocarditis. On presentation she complained of fatigue and slight limitation in physical activity in the form of moderate exertion. Her medical treatment included methylprednisolone due to GVHD (2mg-2mg-4mg), escitalopram 7.5 mg and hormone replacement therapy consisted of estrogen and progesterone. Electrocardiogram revealed sinus rhythm 86 beats/min, pathologic Q waves in II, III, aVF leads and QS complexes in V1-V3. Akinesi of apex and apical segments of left ventricle (LV) with ejection fraction (EF) of 30% was found in echocardiography. Biochemistry findings showed hypercholesterolemia (total cholesterol: 8.77mmol/L, LDL-cholesterol: 5.30 mmol/L, triglycerides: 2.64 mmol/L), while troponin was within norm. Cardiac magnetic resonance (CMR) revealed subendocardial scar of apex and apical segments (> 75% of wall thickness) of LV and medial segments of intraventricular septum and inferior wall (25-75% of wall thickness) typical for ischemia with severe reduced EF (29%); no signs of myocarditis were found (Fig.1A). Furthermore, coronary angiography was performed and it showed advanced coronary artery disease (CAD): chronic total occlusion (CTO) of the left anterior descending artery (LAD) with poor collateral flow, CTO of right coronary artery (RCA) with good collateral flow and critical stenosis of the circumflex artery (LCx, Fig.1B). Due to the lack of distal LAD target for bypass grafting the patient underwent percutaneous coronary intervention (PCI) of LCx with successful drug-
eluting stent implantation (Fig.1C). Also, PCI of totally occluded RCA was planned as the next stage of percutaneous revascularization. Optical coherence tomography (OCT) of the treated vessel revealed multiple atherosclerotic lesions (Fig. 1D-F). Significant coronary artery stenosis in a young woman has been reported previously [1]. However, CAD rarely occurs as a late complication of GVHD after BMT. Thus, the pathogenesis and morphology of coronary lesions are barely known. Nevertheless, there are many potential risks factors after BMT related to premature CAD, such as TBI, chemotherapy, corticosteroids treatment, local inflammation in the setting of GVHD. In addition, elevated LDL-cholesterol concentration and premature CAD indicate that the familial hypercholesterolemia (FH) cannot be excluded with certainty (FH possible). However, the non-typical features for atherosclerotic plaque, such as increase intima proliferation with an enhanced fibrosis revealed in the OCT imaging suggest that the chronic inflammation play a crucial role in lesions formation in this patient (Fig.1D-F). To the best of our knowledge, CAD associated with GVHD after BMT has been documented seven times in the literature [2-5]. Among them, two patients underwent PCI with stent implantation and these two patients survived [2-3].

Reference:


Figure

1A. CMR short axis, late gadolinium enhancement. Subendocardial scar of medial segments of intraventricular septum and anterior wall.

1B. LAO caudal angiographic view before PCI. Critical stenosis of LCx in proximal segment.

1C. LAO caudal angiographic view after PCI of LCx.

1D. OCT scan. Thrombus attached to the arterial wall (red arrow).

1E. OCT scan. Fibroatheroma with organized fibrotic thrombus.

1F. OCT scan showing a thin-capped lipid-rich plaque (red arrow).