Premature Atherosclerosis and Drug Eluting Stent Restenosis in an Adult with Osteogenesis Imperfecta

Mutlu Gungor, MD¹ Mustafa Aparci, MD² Ali C. Özer, MD³

¹Department of Cardiology, Memorial Hospital, Istanbul, Turkey

²Department of Cardiology, Haydarpaşa Training Hospital, Istanbul, Turkey

³Department of Cardiology, Bayındır Hospital, Ankara, Turkey

Address for correspondence Dr. Mustafa Aparci, MD, Haydarpaşa Training Hospital, Tıbbiye Street, Uskudar, 34668, Istanbul, Turkey (e-mail: maparci@gmail.com).

Int J Angiol 2016;25:e166–e168.

Abstract

Keywords

- ▶ atherosclerosis
- ▶ coronary artery
- ▶ acute coronary syndrome
- ▶ osteogenesis imperfecta
- ▶ percutaneous
- ▶ premature
- ▶ stent

Mild form of osteogenesis imperfecta (OI) may have a normal life span. However, cardiovascular complications including aortic and valvular heart disease, and coronary artery disease may complicate the life period. We presented a patient with mild form of OI and premature coronary atherosclerosis. He had been performed primary percutaneous angioplasty and drug eluting stent implantation to left anterior descending coronary artery ostial lesion. Then he presented with unstable angina pectoris due to the diffuse in-stent restenosis and a highly critical lesion adjacent to previously stented segment. He was suggested coronary artery bypass grafting (CABG), but he preferred coronary angioplasty and was implanted everolimus eluting stent. Control angiography, performed at 9th month, revealed the everolimus eluting stent was satisfactorily patent and the patient was asymptomatic. Numerous genetic defects and histopathological abnormalities of collagen and bone formation that were reported in the etiology of OI may be accounted for premature atherosclerosis in OI. Patients with mild form of OI may present with premature atherosclerosis and acute myocardial infarction. Everolimus eluting stent implantation may be a better choice of drug eluting stent in patients with OI instead of other drug eluting stent or minimally invasive CABG.

Osteogenesis imperfecta (OI) is a heterogeneous genetical disorder of connective tissue in which the collagen synthesis is defective and the diagnosis is generally based on clinical features.¹ Mortality and morbidity are due to cardiovascular complications in mild forms of OI. However, severe forms are characterized with short life span, which terminates at childhood due to trauma and lethal deformations.² Aortic and mitral valvular dysfunctions, aneurysms and dissections of aorta, dilatation of pulmonary artery, and surgical treatment of them are among the frequently reported cardiovascular complications of OI.³ It was mistakenly interpreted that the deaths generally occurred due to an unrelated disease such as myocardial infarction in cases with mild forms of OI (e.g., type I and IV) and a normal life span.⁴

However, we suggest that it is the most important clinical aspect of mild form OI. Herein we presented a 41-year-old male who had mild form of OI and premature atherosclerosis complicated with acute myocardial infarction (AMI) and in-stent restenosis of drug eluting stent in a relatively short, 2-month period.

Case

The patient was a 41-year-old male. He had bluish sclera. He had previously suffered multiple fractures of fingers, metacarpal bones and wrist, anterior arm, and a hip fracture which were completely recovered. He had been previously diagnosed as OI. His medical history was compatible with nondeforming mild form of OI type I.¹ He had been performed

Fig. 1 (a) Infarct related LAD artery and the osteal lesion during the primary angioplasty for acute anterior myocardial infarction. (b) Successful revascularization of LAD artery with TIMI III flow and great patency of lumen without residual stenosis and irregularities. Abbreviations: LAD: left anterior descending coronary artery; TIMI: thrombolysis in myocardial infarction.

primary percutaneous transluminal coronary angioplasty and implanted drug eluting stent to the critically stenotic osteal lesion of left anterior descending coronary artery during acute anterior AMI 2 months ago (►Fig. 1a, b).

Then he presented with acute chest pain, 0.5 mm horizontal ST segment depression on electrocardiogram leads V₄–V₆, and I, aVL, and normal serum levels of cardiac biomarkers (CK-MB, cardiac Troponin I). He was still taking acetylsalicylic acid, clopidogrel, metoprolol, and atorvastatin at that time. The patient was followed up with diagnosis of unstable angina pectoris, a non-ST segment elevation acute coronary syndrome, in a coronary care unit. On his coronary angiography, a concentric in-stent restenosis up to 80 to 90% narrowing and a more severe stenosis up to total occlusion were detected at the osteal segment of LAD artery (►Fig. 2a). It was decided that the coronary artery bypass surgery would be the best option for the treatment of those in-stent restenosis and the next critical stenosis on the LAD artery due to the high risk of restenosis. But the patient did not accept the open heart surgery and we implanted everolimus eluting stent (30 × 18 mm) covering in-stent restenosis and the adjacent critical lesion (►Fig. 2a).

Control angiography that was performed at the 9th month following the last drug eluting stent implantation revealed that the everolimus eluting stent was satisfactorily patent with only a 10 to 20% focal in-stent restenosis (►Fig. 3). As the patient did not have any sign or symptom of ischemia, he was planned for follow-up.

Discussion

It was reported that patients with milder forms of OI, type I and IV, had a normal life span and died of unrelated illnesses such as AMI, respiratory disease, and malignancy. Of the 41 patients with type I and IV OI, 8 (19.5%) (mean age 56.8,

Fig. 2 (a) Diffused type in-stent restenosis and a more severe critical lesion adjacent to previously stented segment. (b) Complete revascularization and patency of left anterior descending coronary artery ostium by everolimus eluting stent which comprised the regions of previously stented and de novo distal lesion.

range 48–70 years) had died of due to myocardial infarction and coronary artery disease.⁴ However, the rate of deaths due to AMI is significantly high, which could not be ignored. Premature atherosclerosis and increased mortality during third and fourth decades in those patients with mild forms of OI may be a significant clinical issue to be evaluated as in our case. Sedentary lifestyle and highly calorogenic and atherogenic dietary contents may promote atherosclerosis in those patients who generally avoid physical activity. Active or passive smoking may contribute to premature atherosclerosis. Co-existence of hypertension,

Fig. 3 (a) Visualization of coronary stent image by a coronary angiography performed at 9th month. (b) Everolimus eluting stent was satisfactorily patent with a focal stenosis of 10–20%.

hyperlipidemia, and hyperglycemia may worsen the cardiac complications in OI patients.⁵ Since type I OI has an autosomal dominant inheritance,¹ their siblings may be at risk for premature atherosclerosis in association with presence of OI. Thus coronary risk management gains importance for patients with type I and IV OI and also for their siblings.

Progressive nature of premature atherosclerosis may be complicated not only with AMI at third or fourth decades, but also with the failure (e.g., in-stent restenosis and re-infarction) of bare metal or drug eluting stent implantation as in our case. Favorably, we observed that everolimus eluting stent continued to be patent at the 9th month. We concluded that the everolimus eluting stent could be an option alternative to surgical treatment or implantation of other drug eluting stents in patients with OI. Despite the possible complications due to brittleness and friability of bones, there are several cases which had been successfully treated with aortocoronary bypass grafting and sternotomy.^{6,7} A ministernotomy approach which was successfully performed for the aortic valve replacement in a patient with OI can be proposed as an alternative option.⁸ Coronary dissection during coronary angiography had been developed and resulted with emergency aortic valve replacement and coronary bypass grafting in a patient with OI.⁹ Thus coronary angiogram or angioplasty should be performed cautiously in those patients.

Since OI is a clinical consequence of various histopathological abnormalities caused by numerous genetic mutation or defects of collagen, bone morphogenic protein, and transcription factors, etc.,¹⁰ identification of the certain mechanism which is accounted for premature atherosclerosis may be difficult. Fibromuscular dysplasia (FMD) may be an explanatory mechanism for in-stent restenosis of first DES. FMD may be one of the components of familial syndromes characterized with hypertension, bone fragility, brachysyndactyly, and multiple arterial narrowings (e.g., renal, cerebral, carotid, abdominal, and coronary).¹¹ However, Davies et al reported that patients who had been treated with stent implantation to renal artery stenosis due to FMD had satisfactorily higher patency rates at long-term period.¹² Osteocalcin, one of the bone formation markers, is significantly increased in patients with OI.¹³ Osteocalcin expressing mononuclear cells and endothelial progenitor cells are associated with early coronary atherosclerosis, plaque destabilization, and vascular calcification.^{14–16} Higher osteocalcin level is also associated with carotid atherosclerosis in type 2 diabetes.¹⁷ Furthermore, bone morphogenetic protein variants which are defective in OI patients may be associated with the premature atherosclerosis.^{18,19}

In the conclusion, patients with nondeforming mild form of OI may develop acute cardiovascular events due to premature atherosclerosis which has not been identified yet probably due to complex interactions of various genetic and histopathological defects. But those patients should be managed according to the primary prevention standards of atherosclerotic cardiovascular disease. Everolimus eluting stent implantation either in acute coronary syndrome scene or in stable coronary artery disease may be first-line revascularization option.

References

- 1 Van Dijk FS, Sillence DO. Osteogenesis imperfecta: clinical diagnosis, nomenclature and severity assessment. *Am J Med Genet A* 2014;164A(6):1470–1481
- 2 Radunovic Z, Wekre LL, Diep LM, Steine K. Cardiovascular abnormalities in adults with osteogenesis imperfecta. *Am Heart J* 2011; 161(3):523–529
- 3 Lamanna A, Fayers T, Clarke S, Parsonage W. Valvular and aortic diseases in osteogenesis imperfecta. *Heart Lung Circ* 2013;22(10): 801–810
- 4 McAllion SJ, Paterson CR. Causes of death in osteogenesis imperfecta. *J Clin Pathol* 1996;49(8):627–630
- 5 Migliaccio S, Barbaro G, Fornari R, et al. Impairment of diastolic function in adult patients affected by osteogenesis imperfecta clinically asymptomatic for cardiac disease: casualty or causality? *Int J Cardiol* 2009;131(2):200–203
- 6 Passmore JM, Walker WE, Fuentes F. Successful aortocoronary bypass in osteogenesis imperfecta. *J Am Coll Cardiol* 1987;9(4): 960–963
- 7 Reguillo F, De La Llana R, Castañón J, et al. Osteogenesis imperfecta and coronary artery surgery. A case report. *J Cardiovasc Surg (Torino)* 1996;37(6):621–622
- 8 Izzat MB, Wan S, Wan IYP, Khaw KS, Yim APC. Ministernotomy for aortic valve replacement in a patient with osteogenesis imperfecta. *Ann Thorac Surg* 1999;67(4):1171–1173
- 9 Eskola MJ, Niemelä KO, Kuusinen PR, Tarkka MR. Coronary artery dissection, combined aortic valve replacement and coronary bypass grafting in osteogenesis imperfecta. *Interact Cardiovasc Thorac Surg* 2002;1(2):83–85
- 10 Forlino A, Marini JC. Osteogenesis imperfecta. *Lancet* 2015. doi: 10.1016/S0140-6736(15)00728-X
- 11 Grange DK, Balfour IC, Chen SC, Wood EG. Familial syndrome of progressive arterial occlusive disease consistent with fibromuscular dysplasia, hypertension, congenital cardiac defects, bone fragility, brachysyndactyly, and learning disabilities. *Am J Med Genet* 1998;75(5):469–480
- 12 Davies MG, Saad WE, Peden EK, Mohiuddin IT, Naoum JJ, Lumsden AB. The long-term outcomes of percutaneous therapy for renal artery fibromuscular dysplasia. *J Vasc Surg* 2008;48(4): 865–871
- 13 Cundy T, Horne A, Bolland M, Gamble G, Davidson J. Bone formation markers in adults with mild osteogenesis imperfecta. *Clin Chem* 2007;53(6):1109–1114
- 14 Collin J, Gössl M, Matsuo Y, et al. Osteogenic monocytes within the coronary circulation and their association with plaque vulnerability in patients with early atherosclerosis. *Int J Cardiol* 2015; 181:57–64
- 15 Zhang H, Wang LJ, Si DL, et al. Correlation between osteocalcin-positive endothelial progenitor cells and spotty calcification in patients with coronary artery disease. *Clin Exp Pharmacol Physiol* 2015;42(7):734–739
- 16 Reyes García R, Rozas Moreno P, Muñoz-Torres M. Osteocalcin and atherosclerosis: a complex relationship. *Diabetes Res Clin Pract* 2011;92(3):405–406
- 17 Sheng L, Cao W, Cha B, Chen Z, Wang F, Liu J. Serum osteocalcin level and its association with carotid atherosclerosis in patients with type 2 diabetes. *Cardiovasc Diabetol* 2013;12:22
- 18 Syx D, Guillemin B, Symoens S, et al. Defective proteolytic processing of fibrillar procollagens and procollagen due to biallelic BMP1 mutations results in a severe, progressive form of osteogenesis imperfecta. *J Bone Miner Res* 2015;30(8): 1445–1456
- 19 Simões Sato AY, Bub GL, Campos AH. BMP-2 and -4 produced by vascular smooth muscle cells from atherosclerotic lesions induce monocyte chemotaxis through direct BMPRII activation. *Atherosclerosis* 2014;235(1):45–55