PREMATURE CORONARY ARTERY DISEASE IN IDENTICAL MALE TWINS

M. DEĞERTEKİN, M.D,
M. GENÇBAY, M.D,
Y. EVCİMEN, M.D,
B. YAYMACI, M.D
İ. DİNDAR, MD,
Y. BAŞARAN, MD.
F. TURAN, M.D,

Studies on coronary artery disease in identical twins might provide an answer to the question of whether atherosclerotic coronary artery disease is caused by genetic or environmental factors.
In the present report, we described laboratory findings of two male identical twins with coronary artery disease demonstrating angiographic similarities of coronary atherosclerotic lesions.

Key words: identical twins, coronary artery disease

From: Koşuyolu Heart and Research Hospital, Kadıköy, İstanbul

Adress for reprints:
Muzaffer Degertekin, MD
Kosuyolu Heart and Research Hospital
81020
Kadıköy,Istanbul,Türkiye
Phone: 90 216 326 69 69
Fax: 90 216 339 04 41

Whether heredity or environment is prominent in etiology and natural history of coronary artery disease is a controversial issue. Considering the complex pathophysiology of atherosclerosis and long latent period before any arterial lesions producing the clinical disease arise, it is difficult to decide on relative importance of these two main factors. Studies on incidence of coronary heart disease in identical twins is an important part of the research on atherosclerosis.
In the present report, we documented clinical and selective coronary arteriographic findings of identical male twins with coronary artery disease and reviewed the prior identical twin reports including selective coronary arteriographies.

CASE REPORT

Twin I

B.Ö., a 32-year-old male patient was admitted to the hospital with the complaint of recent onset of retrosternal chest pain.

Physical Examination:

He was 174 cm tall and weighed 73 kg. His blood pressure was 110/70 mm Hg. Examination of cardiovascular system and other systems revealed no abnormal findings.

Laboratory findings :
ECG revealed a ST segment depression of 1.5 mm in V5 and V6 precordial derivations. Blood glucose level and chest x ray were normal. Total serum cholesterol was 334 mg/dl, while HDL was 32mg/dl, LDL was 185 mg/dl, LP(a) was 90mg/d, and Apo E genotype was found to be 3/3. Oral glucose tolerance test and fasting blood insulin levels were in normal limits. ANA, LE cell (slide test) and RF were negative. Two dimensional echocardiographic study showed a normal left ventricular wall motion (Table 1).

History:
He had no history of diabetes mellitus and hypertension. He has smoked a package of cigarettes for 17 years.

Coronary Angiography:
Left anterior descending artery had 90%, 70% and 80% stenosis after septal I,II and diagonal II branches, respectively. Obtus margin II branches of circumflex had proximal stenosis of 25 % with normal distal vessels (Figure 1A). Right coronary artery system was normal and dominant. Left ventricular end diastolic pressure (LVEDP) and left ventricular segmental wall motion was normal (Figure 1B) (Table II).

CABG was recommended to the patient.

B.Ö. underwent CABG surgery, receiving LIMA graft to the LAD artery. After the operation, a lipid lowering diet and to stop smoking was recommended. Two months after the first post operative visit B.Ö. was

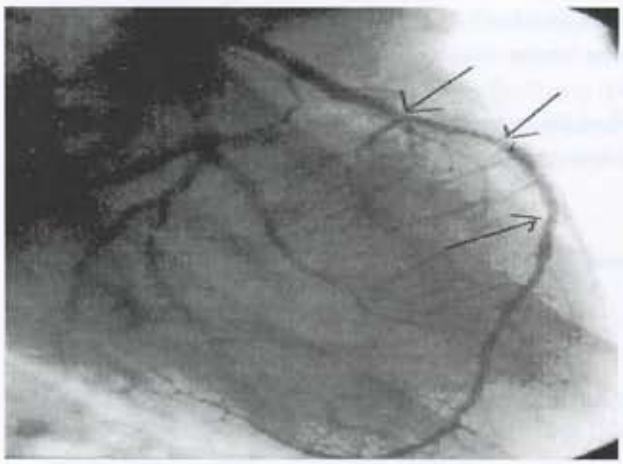

Fig 1 A. Coronary angiogram of twin I, showing extensive disease in LAD.

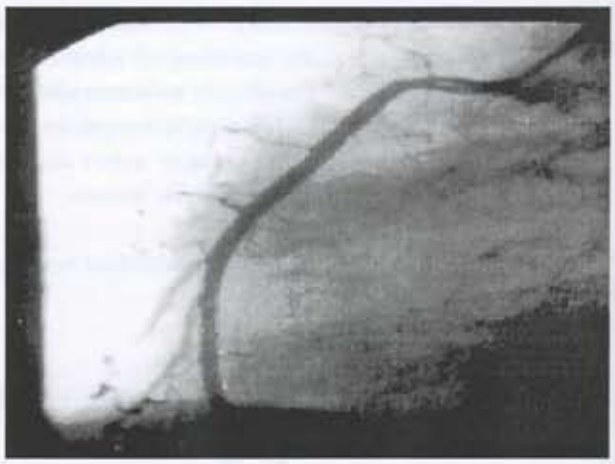

Fig 1 B. Normal and dominant right coronary system

Table I: Clinical data of the twins with coronary artery disease

	Twin 1 (B.Ö.)	**Twin 2 (S.Ö.)**
Age at onset (years)	32	32
Weight (kg)	73	74
Height (cm)	174	172
Diabetes Mellitus	–	–
Hypertension	–	–
Cigarete smoking (day /year)	20/17 years	40/14 years
Total Cholesterol (mg/dl)	334	345
LDL (mg/dl)	185	183
HDL (mg/dl)	32	30
Lipoprotein (a)	90	56
Apo E genotype	3/3	3/3
Anti-nuclear antibody (ANA)	–	–
Rheumatoid factor	–	–
Erythrocyte and leukocyte antigens	Identical	Identical

asymptomatic. The treadmill exercise test, thallium scintigraphic examination and serum cholesterol levels were normal.

Twin II

S.Ö. a 32-year-old male patient who is the identical twin brother of B.Ö (case 1) had no complaints and symptoms of a CAD when he was invited to the hospital in order to investigate whether he had the risk factors and CAD.

Physical Examination:

He was 172 cm tall and weighed 74 kg. His blood pressure was 120/80 mm Hg. Examination of cardiovascular system and the other systems revealed no abnormal findings.

Laboratory findings:

ECG, fasting blood glucose level and chest x ray were normal. Total serum cholesterol level was 345 mg/dl, while HDL was 30 mg/dl, LDL was 183 mg/dl and LP(a) was 56 mg/dl. Apo E genotype was found to be 3/3. OGTT and fasting blood insulin level were in normal limits. ANA, LE cell (slide test) and RF were negative. His ECG, treadmill exercise test, cardiac scintigraphy, stress echocardiography and 24 hour Holter monitoring findings were also normal. The twin pair was tested for red cell and human leukocyte antigens (Table 1). All types were found identical. Although identical twin brother was asymptomatic and laboratory test did not show any ischemic findings, coronary angiography was

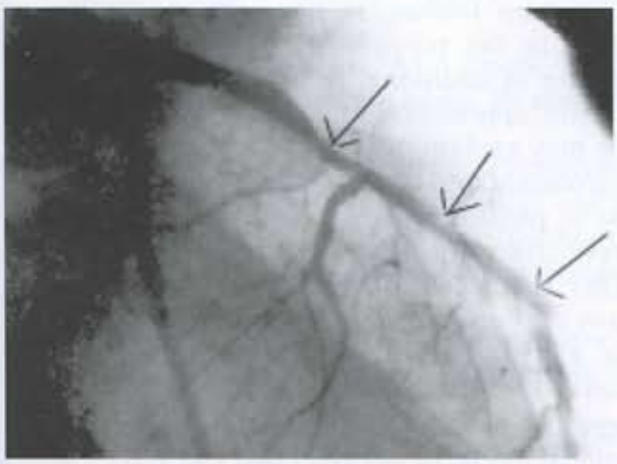

Fig 2 A. Coronary angiogram of twin II, showing extensive disease in LAD.

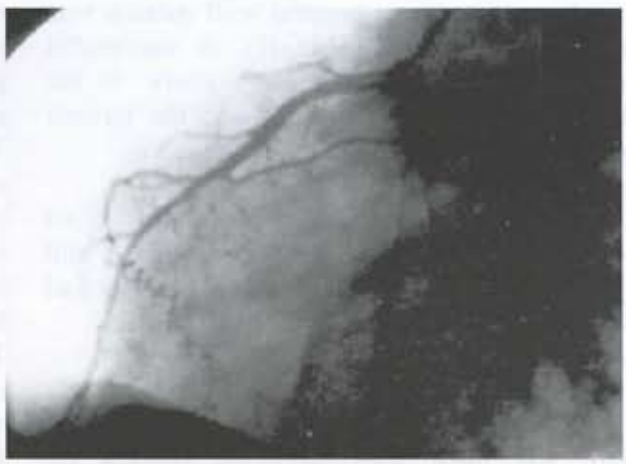

Fig 2 B. Normal right coronary system

Table II: Comparison of coronary angiographies.

	TWIN 1	**TWIN 2**
LMCA	Normal	Normal
LAD (% stenosis)		
After septal branch I	90	60
After septal branch II	70	70
After Diagonal branch	80	60
Cx (% stenosis)		
Obtuse margin I	N	N
Obtuse margin II	N	N
RCA (% stenosis)	N	N
Dominance	RCA	Balanced
Segmental Wall motion	N	N

LMCA: Left main coronary artery, LAD: Left anterior descending artery, Cx: circumflex artery, RCA: Right coronary artery.

recommended and performed 2 months after his brother's operation.

History:

He had a smoking history of 10 cigarettes a day for 14 years. (Number of cigarettes per day was lower than his brother) He had no history of diabetes mellitus and hypertension. He had lived in the same place with his brother until the diagnosis of the disease.

Coronary Angiography:

Coronary arteriography showed three consecutive stenoses, 60%, 70% and 60%, respectively after the first diagonal branches of LAD. Left circumflex artery revealed only 25% stenosis in the proximal part of the second obtus marginale artery (Figure 2A). Right coronary artery system was normal and coronary circulation was balanced. LVEDP and left ventricular segmental wall motion was normal (Figure 2B, Table II). A successful percutaneous transluminal angioplasty to the LAD lesions was performed, and the patient had no cardiac symptoms since then.

Family History:

The patients' mother had coronary heart disease, NIDDM diabetes mellitus and hyperlipidemia. Their father, older brother and sister had no history of CAD.

DISCUSSION

There has been four previous reports on selective coronary arteriography performed in twin pairs. In identical twins with coronary heart disease, similarities in both the anatomy of coronary vessels and the localization of the coronary lesions were also previously reported. Angiographically documented appearance of coronary anatomy, the location and the degree of the stenoses have been shown to be similar in identical twins in three of these reports (1-3). Schilling reported that all of the twin pairs had similar lesions and similar coronary anatomies in their coronary arteriographies (4) (Table III). Despite Schilling's report and identical genetic and environmental influences, there were marked differences in coronary anatomy and nature of coronary atherosclerotic disease in the present identical twins. The sister of the identical twins as well, had a normal, but different pattern of coronary anatomy.

In the present report, besides striking similarity in atherosclerotic stenosis, localization and character of left anterior descending artery, the similarity in coronary anatomy was not observed in RCA and Cx arteries. While in Twin I right coronary artery system was dominant, twin II showed balanced coronary distribution, and a different branching pattern in the circumflex artery. (Table II) (Figure 1-2).

In our case, twin II (SÖ) had no symptoms, although he had coronary lesions at the time when twin I (BÖ) was admitted to our clinic with complaints of chest pain and received a diagnosis of unstable angina pectoris.

Risk factors are considered to have an impact on timing of symptomatic onset and severity of coronary lesions. In line with the present report, in the previous reports as well, the presence of additional risk factors had caused an early appearance of the coronary lesions. This may explain the level of responsibility of environmental factors superimposed on genetic predisposition. Twin I, who had more severe coronary lesions than twin II, had higher LDL and LP(a) levels. Twin I was a heavy cigarette smoker, as well.

The early onset of coronary artery disease observed in 12 of the reported twin cases, suggests a susceptibility to premature CAD in identical twins. In our twin pair (32 years old) CAD was shown angiographically. Besides, the elder brother of the twin pair (35 years old) had no clinical or angiographical evidence of arterial pathology. This fact points to the importance of investigation of CAD in the other sibling if CAD is present in one of the twins, despite the early age.

The polymorphic property and the genotypical variations in Apo E gene is considered to be one of the most important genetic determinants. Apo E genotype of both twin I and twin II was 3/3.

CONCLUSION

These observations, in line with the described similarities in twins with CAD support the idea that there is an important relation between

genes, coronary anatomy and development of atherosclerosis. In clinical practice, these findings also emphasize the importance of alertness for occult CAD in an asymptomatic twin with a symptomatic sibling having a documented disease.

In addition to genetic predisposition, the presence of environmental risk factors (smoking, hyperlipidemia, hypertension, obesity, etc.) should be considered and tried to be controlled to prevent or delay the atherosclerotic changes.

REFERENCES

1. Herrington DM, Pearson TA: Clinical and angiographic similarities in twins with coronary artery disease. Am J Cardiol 1987; 59: 366-367.
2. Holmes DR, Kennel AJ, Smith HC: Coronary artery disease in twins. Br Heart J 1981; 45: 193-197.
3. Kreulen TH, Cohn PF, Gorlin R: Premature coronary artery disease in identical male twins studied by selective coronary angiography. Cathet Cardiovascular Diagn 1975; 1: 91-96.
4. Schilling RJ, Norell MS: Coronary artery disease in identical twins. Eur Heart J 1995;16: 134-135.