CASE REPORTS

Familial Hypercholesterolaemia IIA with Bicuspid Aortic Valve


Abstract
A young male presented with multiple xanthomas and xanthelesmas, progressive breathlessness and angina on exertion. Investigations confirmed diagnosis of familial hypercholesterolaemia, bicuspid aortic valve with severe aortic stenosis and significant obstructive coronary artery disease.

Introduction
Familial hypercholesterolaemia (FH, Fredrickson IIa) predisposes to premature atherosclerotic coronary artery disease as well as aortic root involvement. Aortic root and valve involvement are rare in heterozygotes and occur only with severe, prolonged hypercholesterolaemia, possibly accelerating age related degenerative effects or concomitant structural valvular disease.

Case Report
Young male with familial hypercholesterolaemia, bicuspid aortic valve, accelerated atherosclerotic aortic stenosis and coronary artery disease.

18 year male, non addict, resident of Mumbai, presented to hospital with complaints of multiple nodular swellings on both lower limbs and buttocks since 8 years. These nodular, painless, swellings increased gradually over years. He also gave history of progressively increasing breathlessness and chest pain on exertion since 2 years. He had no history of similar complaints in past, no similar complaints in family members. Examination revealed multiple tuberous xanthomas over lower limbs, left elbow and buttocks, xanthelesmas and arcus juvenilis (Figures 1 and 2). Cardiovascular examination revealed slow rising pulse and grade III ejection systolic murmur over aortic area radiating to carotids. Other system examination was normal. Electrocardiogram (Figure 3) revealed LVH with strain pattern and dynamic ST-T segment changes. (ST segment depression on minimal exertion or fever.) 2D echocardiography and colour Doppler examination showed bicuspid aortic valve, severe aortic stenosis and mild AR.

Laboratory examination revealed anaemia, alarmingly high total cholesterol (621 mg/dl) VLDL-C (69 mg/dl), LDL-C

Fig. 1: Overall tuberous xanthomas over lower limb and buttock
(567 mg/dl) levels; normal triglycerides and HDL levels. Apoprotein B levels were high 3.39 (0.56-1.62), with normal Apoprotein A levels.

Screening of family members (his mother and sibling) revealed very high cholesterol levels with normal HDL and triglyceride levels.

A diagnosis of Familial hypercholesterolaemia Type II A (Fredrickson), congenital bicuspid aortic valve and accelerated atherosclerotic AS was made. Bicuspid aortic valve provided a substrate for accelerated atherosclerosis.

Coronary angiogram revealed ostial left main stenosis with triple vessel disease. (LAD 50% ostial stenosis, 60% ostial stenosis in LCx, and 90% RCA stenosis) (Figures 4 and 5).

This patient was started on high dose of statins and was planned for revascularisation with BAV/AVR.

**Discussion**

In most populations studied, heterozygous FH occurs in about 1:500 people, but not all develop symptoms. Homozygous FH occurs in about 1:1,000,000. The relative risk of death of FH patients not treated with statins is between three and fourfold but treatment is effective, and delays or prevents the onset of coronary heart disease (CHD). Untreated heterozygous FH carries a high mortality. The increase in death rate relative to the general population is almost exclusively due to CHD occurring before the age of 60 years. Atherosclerosis involves aortic root first followed by aortic valve and then coronary ostia. Sudden cardiac death is common. Homozygotes with very high cholesterol levels show early involvement of aortic root and valve. LDL may undergo spontaneous aggregation when subjected to turbulent blood flow during systole. In contrast, in heterozygotes; aortic valve and root involvement are rare and occur only with severe and prolonged hypercholesterolaemia, (cholesterol year score > 900 mmol/years).

Bicuspid aortic valve predisposes to development of early aortic stenosis (i.e. in fourth and fifth decade of life); however prolonged levels of very high cholesterol in our patient contributed to early development of aortic stenosis. Presence of severe ostial coronary lesions also implicate accelerated atherosclerotic plaque deposition in milieu of high
cholesterol level and increased blood turbulence due to stenotic bicuspid valve.

Reduced/defective LDL receptor, ApoB B protein mutations account for most of the cases. Most common genetic defects in FH are LDLR mutations (prevalence 1 in 500, depending on the population), ApoB mutations (prevalence 1 in 1000), PCSK9 mutations (less than 1 in 2500) and LDLRAP1.3

Since the advent of statin therapy, the life expectancy in treated FH has dramatically increased. Our patient was started on high dose of rosuvastatin with subsequent improvement in lipid levels.

References