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Familial Hypercholesterolemia Type-II B-A Case Report

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Summary :

A young male of 25 years presented with multiple xanthoma at the outpatient department of Sher-e Bangla Medical College Hospital, Barisal. He was diagnosed as a case of familial hypercholesterolemia type-II B on the basis of clinical features, family history, serum lipid profile and histopathologic findings. The patient had all the features typical of the condition with some unusual unexplained features. He had all varieties of xanthomas including plane xanthoma, eruptive xanthoma, tuberous xanthoma; his mother and one brother had multiple keloids developed from tiny scars of boils. This prompted us to present this case.

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Introduction :

Elevated concentration of lipids (hyperlipidemia) occur as a result of inborn error of metabolism or secondary to variety of disease states. Two life threatening complications—premature atherosclerosis and recurrent pancreatitis bring its importance in clinical medicine. Familial hypercholesterolemia is a genetically determined disorder rarely encountered in clinical practice. Biochemically, on the basis of serum lipid profile two types are recognized. They are type II A and Type II B. The latter constitutes about 10% of the familial hypercholesterolemias. Its proper diagnosis is important because proper management may prevent disability and delay death of the patients as well as other unaware members of the family.

Case Report :

A 25 years old young male attended the outpatient department of Sher-e Bangla Medical College Hospital, Barisal for gradual development of painless nodular erruption throughout the body for the last two years and retrosternal chest discomfort for last one year.

He is an unmarried shopkeeper, a sedentary worker, nonsmoker, nonalcoholic and comes from poor socio-economic background. He has a normal apetite with a diet average for our community i.e. dominated by carbohydrates. He has no diabetes, hypertension or obesity. He did not complain of any cold intolerance, constipation or hoarseness of the voice. He has no abdominal pain or urinary problem or features of claudication or transient ischaemic attack.

His complexion is fair with a yellowish hue in the skin. Pulse and blood pressure are normal. Arterial wall is palpable over all the major arteries. Apex beat is found in normal position. Auscultation reveals ejection systolic murmur over the aortic areas suggesting aortic stenosis. Bruit is felt over the left carotid artery. Xanthelesma is present over the both eyelids and xanthoma striata palmaris over both palm creases. Xanthoma tendinosum is found along all long tendons including Achillis tendon (Fig-1). Tuberous xanthomas are found over the extensor surfaces of both elbows (Fig-2). Tuberoeruptive xanthomas of pea to lemon size are present over the buttocks and back of the thighs. Arcus juvenilis is absent.

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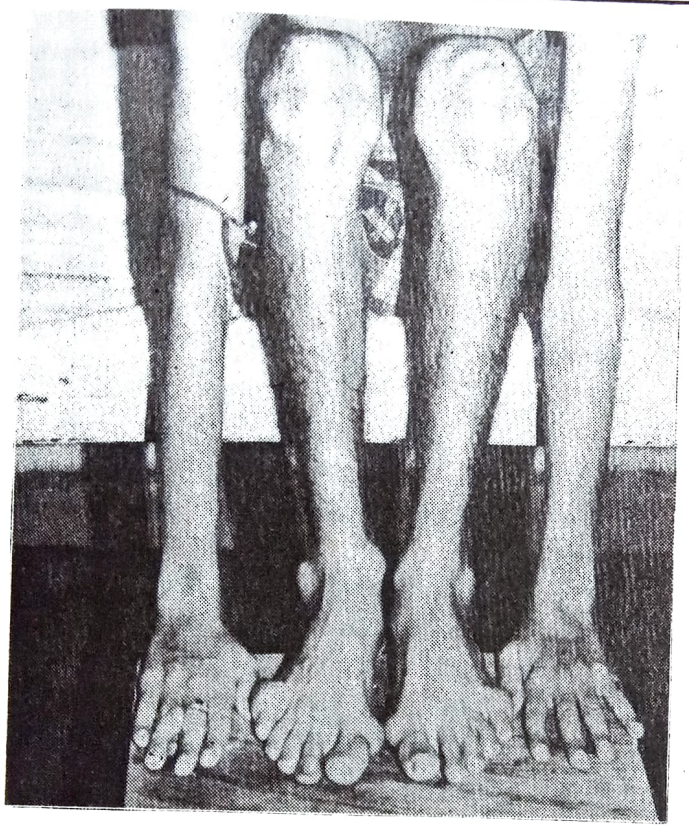

Fig-1. *Showing tendon xanthomas along the long tendons of the extremities.*

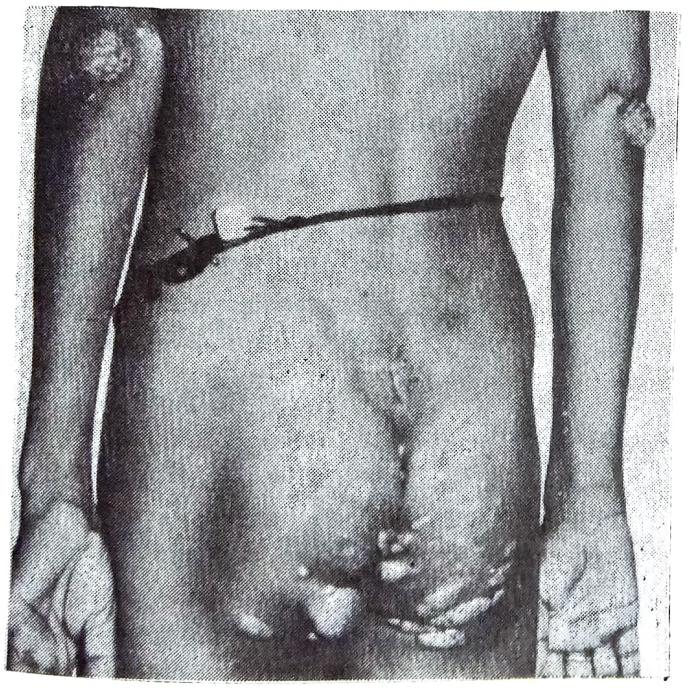

Fig-2. *Showing the tuberous xanthomas at the elbows and eruptive xanthomas at the buttocks and back of the thighs.*

Family History :

The patient's father died six months ago from sudden severe chest pain and one and half year back his younger brother died of similar type of chest pain. That brother also had yellowish nodular swellings like those of the patient. There was no consanguity in his family. His mother aged about 50 years and one brother (20 yrs) have multiple keloids over various sites of the body. These are distributed over the sternum, front of the chest, scapular region, lumber regions and the thighs. As the history suggests these developed from the tiny scars of boils. The other brothers and sisters of the patient are free from these types of abnormalities.

The pedigree chart is given in the fig-3.

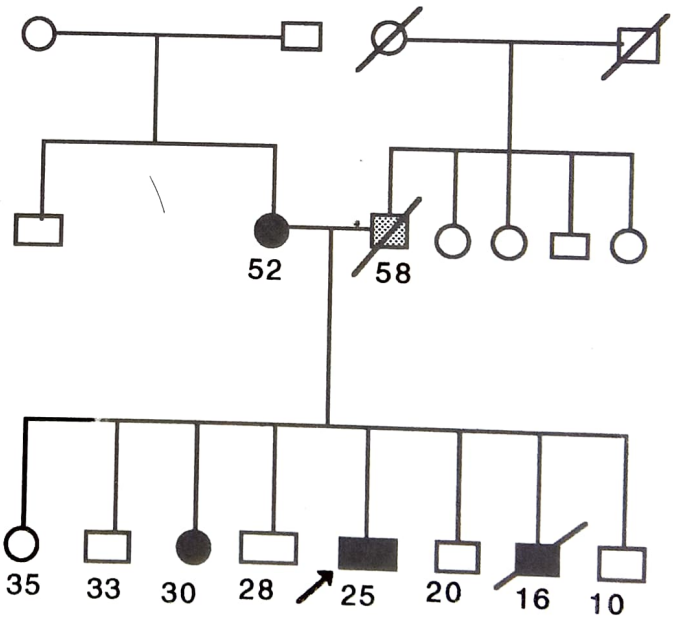

Fig-3 : *showing the pedigree chart of the patient's family.*

Investigations :

Routine blood count, ESR, Hb%, routine urine & Stool analysis and Fasting blood sugar shows no abnormalities.

Serum lipid profile (fasting) of the patient shows-

Serum cholesterol	320 mg/dl (8.32 mmol/L)
Serum triglyceride	240 mg/dl (2.71 mg/dl)
Serum B lipoprotein	740 mg/dl
Serum total lipids	1252 mg/dl
Serum HDL cholesterol	50.4 mg/dl (1.3 mmol/L)
Serum LDL cholesterol	222 mg/dl (5.77 mmol/L)
Serum cholesterol (patient's mother)	353 mg/dl
Serum cholesterol (patient's sister)-	292 mg/dl 7.4 mmol/L)

In X-ray chest, heart is enlarged in transeverse diameter and in X-ray hands and feet, no bony abnormality is seen.

ECG At rest shows features of left ventricular hypertrophy without strain and after Exertion (rapid walking three flight of upstairs), chest discomfort and T inversion in lead II, III and aVF. We are unable to do a coronary angiogram but most likely he has coronary atherosclerosis.

Histopathology of skin nodules revealed accumulation of plenty of lipid laden macrophages and occasional Tuton's giant cell in the dermis. The histologic diagnosis is xanthoma.

Discussion :

Primary hyperlipidemias are caused by genetic defects. Familial hypercholesterolemia is the commonest primary hyperlipidemia resulting from single gene mutation. The condition is transmitted as an autosomal domionant trait, Recent advance in molecular genetics revealed that familial hupercholesterolemia results from mutations affecting the gene specifying the receptors for LDL. The phenotypic effect of this mutation may be either absence of functional receptors or defective receptors or defective internalization following receptor binding[1].

Clinically familial hypercholesterolemia is characterized by accelerated and premature atherosclerosis and their complications such as myocardial infarction. Other features of the condition include xanthomas, xanthelesma, aortic stenosis and arcus corneas[2].

Two categories of serum lipid pattern type II-A and type II-B are recognized in familial hypercholesterolemia. Of these type II-B constitute only 10% of all familial hypercholesterolemias. In both the types serum LDL is increased, serum HDL is lowered and a prominent band is seen in electrophoresis. In type II-A serum cholesterol-triglyceride ratio is more than 1.5 and the pre B band is of normal intensity. In type II-B there is concomitant increase in serum triglyceride and VLDL[3].

The present case shows all the features typical of familial hypercholesterolemia type II-B. Thus the patient has family history strongly suggestive of autosomal dominant inheritance, tendon and other xanthomas, aortic stenosis and ischemic changes in ECG on exertion. The fasting serum is slightly turbid with raised cholesterol, triglyceride and LDL levels and a lowered HDL level. The cholesterol triglyceride ratio is less than1.5.

However, some unusual features of this case make it more interesting. This patient has got all varieties of xanthomas namely tendon xanthoma, eruptive xanthoma, tuberous xanthoma, plane xanthoma (xanthoma striata palmaris) and xanthelesma. Although tuberous xanthomas occur only very rarely in type II-B hyperlipidemias plane xanthomas occur only in type III hyperlipidemias, these are present in our patient.

Another very peculiar feature of this case is the presence of multiple keloids in the mother and one of the brothers of the patient. The history suggests these keloids developed from the tiny scars of boils. Familial tendency of keloids has been documented by some authors but whether these keloids are mere coincidence or bear relationship to familial hypercholesterolemia yet remains unexplained[4].

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