FAMILIAL HYPERCHOLESTROLEMIC XANTHAMATOSIS

(Review of literature and report of a case)

By

ROY VARGHESE,* M. I. JOY,** & K. I. JOHN,***

The increasing incidence of ischaemic heart disease has focussed attention on the factors producing atheroma, among these the role of cholesterol has been extensively studied. The cutaneous manifestations of the disturbance of lipid metabolism are commonly known as xanthomas. Xanthomas associated with hypercholestrolemia with a familial background is designated as the Familial Hypercholestrolemic xanthamatosis.

The earliest descriptions of tendinous and tuberous xanthomas appear to be that of Addison and Gull (1857)[1] and Fox (1879)[3]; Fagge in 1873 observed the association of xanthamatosis and cardiovascular disease. Muller in 1938 noted the high incidence of angina among these patients with xanthamatosis. Burns in 1920 demonstrated the defective cholesterol metabolism present in this syndrome. The familial nature was mentioned by Torok (1893) and Gossage (1908)[6].

Familial hypercholestrolemic xanthamatosis come under the general group of disorder of lipid metabolism. According to the type of lipoproteins present they are classified into Five syndromes.[13]

Type I Hyperchylomicronemia or the essential familial hyperlipimia.

Type II Hyperbeta lipoproteinimia or the familial hypercholestrolemic xanthamatosis.

Type III Hyper beta lipoproteinimia and hyper pre beta lipoproteinimia.

Type IV Hyper pre beta lipoproteinima.

Type V Hyperchylomicronemia and hyper beta lipoproteinimia.

Cutaneous xanthamatosis may be classified into three.[14]

1. Hypercholestrolomic.
2. Normocholestrolemic.
3. Hyperlipimic.

Hypercholestrolemic xanthamatosis occur in the following conditions.

1. Familial hypereholestrolemia.
2. Hypercholestrolemia of biliary cirrhosis and precholangitic biliary cirrhosis.
3. Post operative biliary tract obstruction.
4. Haemochromatesis.

Normocholestrolemic xanthamatosis occur in,

1. Hand schular christian syndrome.
2. Diabetes insipidus.

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* Post-graduate student in Medicine.

** Asst. Professor, Dermatology and Venereology.

*** Assistant Professor of Medicine Medical Colloge, Trivandrum.

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Hyperlipimic xanthamatosis occur in,

1. Idiopathic hyperlipimia.
2. Hyperlipimia of untreated diabetes and pancreatitis.
3. Glycogen storage disease.
4. Lipoid nephrosis.

Genetics:

The evidences so far obtained are insufficient to establish a completely acceptable genetic theory. This condition is thought to be due to a single dominent gene, but there may be varying degrees of abnormality in the expression of the disease. Hypercholestrolemia in the absence of any other sign or symptom may be the sole evidence. There is some evidence not conclusive at present that the full clinical picture represents the homozygous state, whereas lesser degree of expression, say, hypercholestrolemia alone denote the hetrozygous state. Theoretically homozygotes with a double dose of dominant gene would be expected to have severe manifestations of the disease. But it cannot be assumed that hetrozygosity assures a minimal expression. It may safely be said that this disorder is brought about by a fully penetrant dominent gene of variable expressibility.[4,9].

Biochemistry:

At present there is inadequate information to guide speculation about biochemical defect in this disease[1,8]. The biochemical abnormality in the familial hypercholestrolemic xanthamatosis lies not in the metabolism of cholesterol alone but in the factors which normally maintains steady concentration gradient for cholesterol between the plasma and the liver. There is 2 to 10 fold increase in serum cholesterol in beta lipoprotein in the serum.

Presentation of the case: (Fig. 1, 2, 3).

A 22 year old businessman was admitted to our hospital for angina of effort and breathlessness on exersion. He was well until eleven years previously when nodular swellings appeared first over the knee joint then on the elbow and then gradually to both upper and lower limbs.

During the past seven years he was experiencing palpitation on exertion and for two years he was having angina of effort and breathlessness on exersion.

Family history of similar incidence in more than one member of his family. He is nonvegetarian, not addicted to alcohol or tobacco.

Physical examination revealed a moderately built man with arcus senilis, nodular swellings of varying size were present throughout the upper and lower extrimities, but the lesions were more confined to the joints and were larger in size. Single nodule, to aggragation of numerous nodules were present. They were firm in consistancy non-pruritic and were not associated with an erythematosis shallow.

Cardiovascular system revealed pulse rate of 76 per mt. regular, volume and tension normal, arterial walls not thickened and all peripheral pulsations normal. B.

P. 110/64 mm/Hg. J. V. P. normal. Apex beat was felt in the 4th left intercostal space in the praecordium. Bruit was felt over both carotid Both heart sounds were heard in all areas normally and an ejection systolic murmur was heard throughout the praecordium with maximum intensity in the aortic area and roos of the neck. The murmur was not varying with respiration.

Respiratory system, alimentary system and Central Nervous system were within normal limits.

Investigations revealed the following :

Urine–NAD

Blood–Total and D. C. white cell counts–normal.

ESR–15 mm in the first hour–serum clear.

Serum cholesterol was 853 mg. on a previous occasion and 483 mg. at present.

Serum proteins and liver function normal.

Oral glucose tolerance test within normal limit and cortisone glucose tolerence test also normal. Serum non-esterified fatty acid within normal limits.

X–ray chest and skull normal.

ECG normal.

Phonocardiogram showed a midsystolic murmer in root of the neck.

Biopsy of the nodule showed the following changes:—

Epidermis appeared normal. There were numerous foam cells or xanthoma cells with reticulated cytoplasm. There was admixture of inflammatory cells, polymorphs, lymphocytes and histiocytes. Fibroblasts were also seen in certain places. Touten giant cells also were seen in the section.

DISCUSSION

A case of familial hypercholestrolemic xanthamatosis is presented. The familial nature of the disease is clearly expressed. Serum cholesterol in all other members of his family could not be studied because of difficulty in getting the cases. One of his brothers were admitted with ischaemic heart disease, arcus senilis, xanthelasma and cutaneous xanthomata and hypercholestrolemia in our hospital in a sister unit on a later date.[11] The variation seen in the serum cholesterol level at different times without any treatment cannot be explained. Arcus senilis is a common accompaniment in this condition. The normal glucose tolerance even with cortisone rules cut possibility of this being a secondary hypercholemia of diabetes.

Normal liver function tests, euthyroid state exclude the possibility of secondary hypercholestrolemia due to chronic liver disease or hypothyroidism. The finding in the cardiovascular system explain the angina of effort, and the obstruction in the great vessels at the root of the neck, probably due to atheromatous plaque.

In a full blown picture vascular abnormality in the nature of atheromatous involvement of arteries and endocardium are very common. Isolated cases of aortic stenosis has been attributed to this disease.[2] Coronary artery involvement is much more common in these cases[9].

SUMMARY

A brief review of literature and a case of familial hypercholesterolemic xanthamatosis is discussed.

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REFERENCES

1. Addison T. Gull, W. : Guy's Hospital Report 7-265-1837.
2. Barr, D. P., Rothbard, S. and Eder M.A., J.A.M.A. 156-943, 1954.
3. Fox T. C., Lancet, 2-688, 1879.
4. Butterworth and Strean: Clinical Genodermatology, 1962 Iod. Williams & Wilkins Co.
5. Gofman, J. W., Rubin L., Megnely, J. P. and Johns H. B. Am. J. Med. 17-514, 1954.
6. Gossage, A. M., Quarterly Med. J. 1-331, 1968.
7. Gould, R. G. : Am. J. Med. 11-209, 1951.
8. Harris-Jones J. N. Lancet 1-857, 1957.
9. Hirschern K. Wilkinson, C. F., Am. J. Med. 36-60, 1959.
10. Leonard J. C., Lancet 2-1239, 1956.
11. Mathew Roy V. C. : Personal communication.
12. Piper J and Orlid L , Am. J. Med. 31. 34, 1936.
13. Stanbery, J. B., Hyngaardin, J. B. and Donald S. Frederickson Metabolic basis of inherited diseases-2nd Edn. 1967, Page 449.
14. Thannhauser S. J. Lipoidosis 2nd Edn. 1950 Page 97.