CLINICAL AND LIPID PROFILE STUDIES IN XANTHELASMA PALPEBRARUM
(Analysis of 45 Patients)

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Summary

The clinical and lipid abnormalities in 45 cases of xanthelasma are reported. These findings suggest that xanthelasma is seen in some patients as an isolated clinical symptom with normal serum lipid levels, representing a local derangement of cellular lipid metabolism. Nevertheless, it is noted in many patients with moderate elevation of different serum lipid fractions without any other clinical manifestations, occurring probably as a result of benign derangement of systemic lipid metabolism. Less frequently, it is observed with significant elevation of serum lipid levels in association with certain grave abnormalities like hypertension, ischaemic heart disease, familial hypercholesterolemia, familial xanthomatosis, diabetes etc. Thus, it is inferred that the symptom xanthelasma signifies disturbed lipid metabolism of several types and the patient needs thorough investigation.

KEY WORDS : Xanthelasma Palpebrarum, Clinical Abnormalities, Lipid Profiles.

Xanthomas are circumscribed aggregations of lipid containing cells in the skin and subcutaneous tissue, occurring due to cellular dysfunction as well as from abnormal composition or concentration of blood lipids[1,2]. Xanthelasma is considered to be a type of plane xanthoma and is characterised by yellowish-orange, soft, unilateral or bilateral, circumscribed papules located on the eyelids. Although the name 'Xanthelasma' was coined by Erasmus Wilson[3], it was Rayer[4], a French dermatologist, who first documented a picture of Xanthelasma palpebrarum (XP) in 1835 under the cutaneous xanthomas in his atlas on skin disorders. Fredrickson et al[5] in 1967 classified the metabolic abnormalities in xanthomatosis into five lipoprotein profiles (type I - V), based on their results with ultracentrifugation and paper electrophoresis of serum lipoproteins. According to this criterion, XP is included under type II.

Xanthelasma is probably the most commonly seen cutaneous xanthoma in clinical practice[6,7,8]. It is cosmetically a minor skin lesion yet draws great attention because of its controversial relationship with familial hypercholesterolemia and ischaemic heart

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disease. Different opinions have been expressed about its significance and etio-pathogenesis. Montgomery[6] viewed it as a cutaneous marker of familial hypercholesterolemia. Impressed by the convincing lack of family history of hypercholesterolemia in majority of the patients studied by them, Vacca et al[7] considered it as a manifestation of disturbed lipid metabolism. Epstein et al[9] believed that it is of great importance to exclude hypercholesterolemia and ischaemic coronary disease, in patients with XP. Reporting a large series of XP cases from India, Chetri et al[10] described that this condition is most often accompanied by coronary disease and the risk appears to be more if the patient has associated diabetes. In contrast to this Caplan and Curtis[11] observed that often the lesions are not associated with lipid abnormalities and hence, of no serious significance. Interested by these reports we thought it worthwhile to study the clinical and lipid abnormalities in XP.

Material and Methods

This study was based on 45 cases of XP seen during a period of two years among the patients and their relatives who attended the out-patient clinic of Skin and V.D. department. A detailed history was taken in all the cases in relation to the family history of xanthomas, hypertension, ischaemic heart disease, cerebrovascular episodes, diabetes, hepatic and biliary disorders. In the physical examination details about nutritional status, BP and extrapalpebral xanthomas were noted. The duration, extent and nature of XP were recorded. Associated abnormalities, referrable to diabetes mellitus, CVS, CNS and hepatobiliary disorders were investigated for.

A complete lipid profile analysis was carried out in all the cases. The serum cholesterol, phospholipids, free fatty acids, triglycerides and total lipids were estimated by the methods of Zlatkis et al[12], Fiske and Subba Row[13], Traut et al[14], Van Handel Zilversmith[15] and Chabrol and Charoumant[16] respectively. Paper electrophoresis of the serum lipoproteins was carried out according to Lees and Hatch[17]. The results of these studies, except those of paper electrophoresis, were matched to the data obtained in a large series of carefully selected control group.

Results

45 patients were studied. These included 33 males and 12 females. The subjects were in the age group of 25 – 60 years. The peak incidence in both the sexes was in the age group of 31 – 40 years. Family history of hypertension, coronary disease and diabetes was present in 3 (6.7%) patients each, xanthelasma and other xanthomas in 4 cases (8.9%), and cerebro-vascular episode in 2 cases (4.4%). The mean serum cholesterol levels were found to be considerably raised in these cases.

The duration of XP varied from the first detection in the clinic to more than 15 years and it was 1 – 3 years in majority of the cases. Clinically, the lesions were seen as circumscribed, yellowish–orange, soft to firm, 3 mm to 1 cm sized, asymptomatic papules on the eyelids near the canthal margins (Fig. 1). In two cases the lesions were seen as confluent plaques forming circumocular rings. In most of the cases, lesions were bilateral involving the four eyelids, although the upper eyelids were affected more commonly than the lower. Other associated findings were obesity in 5 cases (11.1%), diabetes in 4 (8.9%), extrapalpebral xanthomas (tuberous) in 2 (4.4%) and coronary disease with hypertension in one (2.2%). The mean serum cholesterol levels were considerably elevated in these patients.

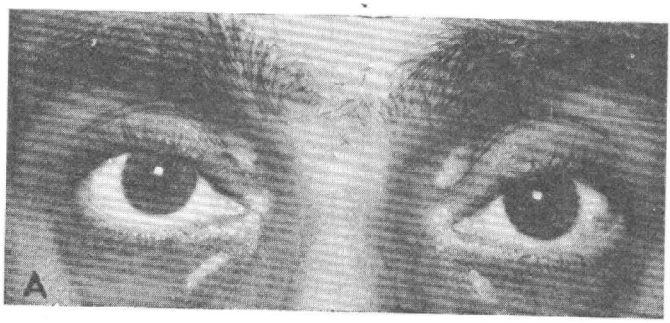

Fig. 1
Characteristic lesions of XP.

The lipid profile analysis is summarized in Table 1. All fractions of serum lipids were raised in majority of the XP cases. However, in comparison to the profile in the control group the difference was significant statistically in terms of cholesterol, phospholipids and free fatty acids. The levels were found to be raised for cholesterol in 80%, phospholipids in 88.9%, free fatty acids in 64.4%, triglycerides in 46.7% and total lipids in 57.8% of the patients (Table 2) Nevertheless, degree of elevation was not very high. The serum cholesterol levels were found to be more than 350 mg% in 7 (15.6%), phospholipids more than 350 mg% in 4 (8.8%), triglycerides more than 250 mg% in 3 (6.7%) and total lipids more than 1000 mg% in 6 (13.3%) cases. The results obtained in serum lipoprotein electrophoresis revealed no specific abnormalities other than a prominent beta band (Fig. 2) and no attempt was made to quantify

TABLE 2
Serum Lipid Levels in 45 patients with Xanthelasma

Serum Lipids	Number of Patients			
	Normal	%	Elevated	%
Cholesterol	9	20.0	36	80.0
Phospholipids	5	11.1	40	88.9
Free Fatty Acids	16	35.6	29	64.4
Triglycerides	24	53.3	21	46.7
Total Lipids	19	42.2	26	57.8

TABLE 1
Serum Lipids in Control Group and Xanthelasma Patients

Serum Lipids	Control Group	Xanthelasma patients		
Cholesterol (mg%)				
Mean ± S.D.	216.6 ± 52.3	282.11 ± 77.5	t = 5.16	P < 0.001
Range	150 — 300	155 — 560		
Phospholipids (mg%)				
Mean ± S.D.	205.7 ± 50.8	290.7 ± 81.1		
Range	104.1 — 307.5	120 — 460	t = 5.34	P < 0.001
Free Fatty Acids (m/Eq %)				
Mean ± S.D.	1.3 ± 1.1	1.78 ± 0.46		
Range	0.5 — 1.5	1 — 4.5	t = 2.89	P < 0.01
Triglycerides (mg%)				
Mean ± S.D.	108.6 ± 40.6	115.1 ± 74.99		
Range	50 — 175	15 — 319	t = 0.52	P > 0.05
Total Lipids (mg %)				
Mean ± S.D.	719.4 ± 198.6	778.7 ± 230.6		
Range	400 — 1200	330 — 1330	t = 1.43	P > 0.1

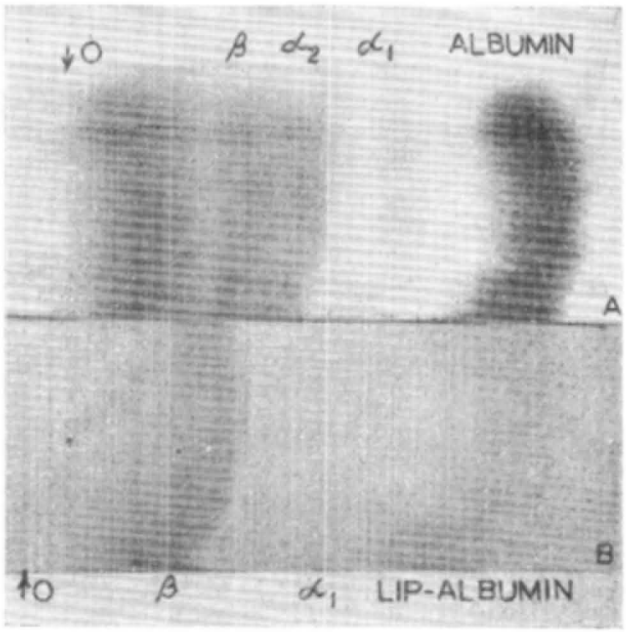

Fig. 2

Serum lipoprotein electrophoresis in XP. Serum proteins stained with bromophenol blue are shown in the upper strip (A) and the serum lipoproteins stained with oil-red 0 are shown in the lower strip (B). Note the dense beta band (β).

these results because of our limited experience with the technique.

Discussion

The present study substantiates the fact that XP is the most commonly seen cutaneous xanthoma in practice, since we observed 45 cases of XP in a span of two years and in only 2 cases, extra-palpebral xanthomas were associated. This is in accordance with previous observations[6,7,8]. XP has been considered as a manifestation of familial hypercholesterolemia[6]. The studies of Vacca et al[7] and Chetri et al[10] revealed a conspicuous lack of positive family history of xanthomas and prominent ischaemic heart disease in majority of the XP cases. Similarly, in our series even after careful interrogation, positive family history of xanthelasma were present only in 8.9%, ischaemic heart disease in 6.7% and hypertension in 6.7% of the cases. However, it is important to note the high levels of serum cholesterol observed in these patients with positive family history. Thus, it appears logical to consider that though the mere presence of XP is not necessarily indicative of familial hypercholesterolemia, careful evaluation of the patient and the family is needed.

Certain abnormalities have been observed in relation with XP. Montgomery[6] reported increased blood lipid levels in 40% and CVS disease in 25% of XP cases. In a study of 35 patients, Epstein et al[9] noted an incidence of 35% coronary disease and hypercholesterolemia of more than 300 mg% in 47% of the cases. Curtis and Berger[18] detected higher values of serum cholesterol in 58% and total lipids in 66% of the cases. Similar findings were reported by others[7,8,10]. No doubt, the blood lipid levels were found to be high in large majority of the patients in our series. Inspite of this, it is curious to note that XP was the only detectable clinical finding in many cases, except in a few where it was observed in association with obesity (11.1%), extrapalpebral xanthomas (4.4%) and ischaemic heart disease with hypertension (2.2%). The incidence of heart disease is much lower

in our series than that reported by earlier workers[6,8,10]. This anomaly is most probably due to the variation in the subjects studied. The patients investigated in the previous studies were basically from general medical out-patient department and it is natural that the patients report to this clinic only if there is some associated systemic involvement like heart disease, diabetes, hypertension, etc. In contrast the subjects studied in the present series were mainly the patients who came for the cosmetic disability on account of the skin lesions as well as their family members. In some patients the skin lesions were incidentally detected for the first time in the skin clinic. The serum lipoprotein electrophoresis pattern appears to be non-specific in XP. The only abnormality detected in our study was the prominent beta band. Similarly, Epstein et al[9] failed to observe any significant abnormalities other than increased beta lipoprotein levels in XP patients with cardiac complications.

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