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A Case of Pseudoxanthoma Elasticum Complicated by Angioid Streaks and Hypertension*)

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ABSTRACT

Pseudoxanthoma elasticum complicated by angioid streaks and various other vascular problems was described. The patient was a 69-year-old female and was found to be hypertensive with the left ventricular hypertrophy. Skin biopsies from bilateral sides of the neck disclosed a typical lesion indicating pseudoxanthoma elasticum. Subsequently, several complications were sorted out and hypertension has been well under control. Apart from angioid streaks and hypertension, the possibility of vascular lnvolvement, such as in the gastrointestinal tract, four extremities, lung and heart was cautioned. And, attention to this disorder, especially among internists, was aroused.

INTRODUCTION

Rigal[11)] in 1881 described first a dermal lesion designated as "diffuse xanthelasmique" which was considered compatible with pseudoxanthoma elasticum of our present knowledge. Following this, Balzer[2)] in 1884 mentioned the skin lesion to be due to elastic fiber disorder based on the first necropsied case. The term "pseudoxanthoma elasticum" (PXE) was coined by Darier[4)] in 1896. In 1929, Grönblad[6)] and Strandberg[12)] pointed out association of angioid streaks in the optic fundus with PXE. We report a 69-year-old woman with PXE complicated by angioid streaks and several other vascular problems including hypertension.

CASE PRESENTATION

A female, born in 1913, visited the Department of Medicine, Nanyo Hospital in late September 1980. She had complained of tinnitus and general malaise. In addition, for two months prior to the consultation, she occasionally manifested a sudden onset of weakness of the left fingers, especially of the thumb; this made her difficult to grasp objects properly. Blood pressure then measured 188–98 indicating hypertension and electrocardiogram disclosed the left ventricular hypertrophy. Another outstanding feature of this patient was numerous light yellow, flat, tiny papules, some of which tended to be confluent, over the regions of dermal stress, including the inner canthus of eyelids, neck, axilla, cubitus and groin, bilaterally. As to family history, the patient has two each of elder and younger brothers; one of the younger brothers seems to have similar skin lesion to the patient, although we have had no opportunity of its confirmation.

Nine days later, *i, e.*, early October, she was admitted to the Hospital. During the first admission, skin from the left side of neck was biopsied; the diagnosis of PXE was tentatively made. Optic fundus showed arteriosclerotic retinopathy of the Keith-Wagener II and several ill-defined blackish pigmented spots and round white patches near the posterior pole. Laboratory data was not contributory except for slightly decreased Fishberg's concentration test

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and creatinine clearance (Table 1); serum calcium and cholesterol were normal.

By taking a reserpine preparation, blood pressure went down to 140-70, and she was discharged about two weeks later. Because of, however, gradually elevating blood pressure, precordial distress, anorexia and insomnia, she was admitted for the second time in the middle of February 1981. The second skin biopsy obtained from, this time, right side of neck confirmed PXE, and also ophthalmologic examination revealed the angioid streaks around the optic disc which appeared reddish brown and spread towards the periphery. After one week of thorough examination, she was discharged, and currently blood pressure is well under control, ranging from 130-150 in a maximum and 70-80 in a minimum, although she is suffering from psychohogical instability such as an attack of irritability or depression. Throughout the clinical course, she has never developed any other symptoms such as gastrointestinal hemorrhage or intermittent claudication.

Pathological findings. The epidermis was intakt and the upper thirds of dermis sppeared almost normal. In contrast, the middle and lower thirds of the dermis was occupied by a rather sharply defined belt-like lesion (Fig. 1). The lesion was stained deeply basophilic by hematoxylin-eosin (Fig. 2), dark-brown to black by von Kossa for calcium, deep-scarlet by

Table 1. Laboratory data on admissions

	First Admission (Oct. 9, '80)	Second Admission (Feb. 18, '81)
Blood picture		
RBC (μ/l)	505×10^4	501×10^4
Hb (g/dl)	14.8	16.0
Ht (%)	44	51
Reticulo. (‰)	16	24
Thrombo. (μ/l)	17.2×10^4	23.0×10^4
WBC (μ/l)	7200	7300
Diff. (%)		
St.	0	1
Seg.	70	76
Eo.	2	2
Ba.	0	0
Ly.	27	20
Mo.	1	1
Liver function		
Bilirubin		
Total (mg/dl)	0.46	0.29
Direct (mg/dl)	0.20	0.10
AlP (K. A. u)	6.0	6.0
Gamma-GTP (mu/ml)	5	12
LAP (u)	151	140
LDH (u)	350	365
GOT (u)	5	7
GPT (u)	5	5
ChE (ΔpH)	0.66	0.76
ZTT (u)	5.0	7.0
TTT (u)	1.1	1.9
CCF	(—)	(—)
Electrolytes (mEq/l)		
Na	137	131
K	4.0	4.3
Ca	4.3	4.8
Cl	97	90
Uric acid (mg/dl)	5.5	6.6
Lipids (mg/dl)		
Cholesterol	182	184
Triglycerid	111	73
Beta-lipoprotein	413	338

Table 1. Cont'd

	First Admission (Oct. 9, '80)		Second Admission (Feb. 18, '81)	
Renal function				
Urea-N (mg/dl)	13.9		14.9	
Creatinine (mg/dl)	1.1		1.0	
Fishberg I	90(ml)	1.011		
II	25	1.018		
III	15	1.024		
PSP 15'	30(ml)	45(%)	15' 60(ml)	30(%)
30'	10	66	30 2	30.5
1°	20	92	1° 25	54.5
2°	40	114	2° 25	70.5
Creatinine clearance (ml/min)	68.9			
Plasma renin activity (ng/ml/hr)	6.6			
Serum protein				
Total (g/dl)			7.40	
Fractions (%)				
Alb.			62.7	
Glob.				
Alpha-1			4.0	
Alpha-2			8.9	
Beta			9.3	
Gamma			14.9	
A/G			1.68	
FBS (mg/dl)			114	
WaR	(—)		(—)	
HbAg			(—)	

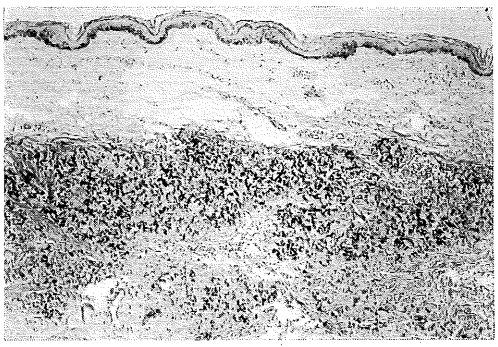

Fig. 1. Skin biopsy from the lateral neck, showing a rather sharply defined belt-like lesion in the middle and lower thirds of the dermis. von Kossa, ×40.

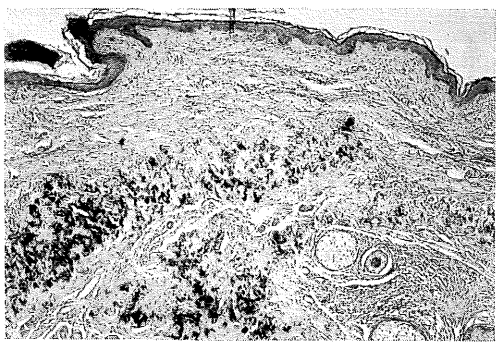

Fig. 2. A skin lesion in the dermis stained deeply basophilic by hematoxylin-eosin. ×40.

Masson's trichrome, and adove all, purplish black by elastica van Gieson for elastic fibrils. With the elastic fiber staining, a few normal-appearing fibers ran parallel to and adjacent to the belt-like lesion. The amount of collagen fibers in the lesion was found to be reduced by silver impregnation. Area surrounding the altered elastic fibers was strongly stained blue with alcian blue, indicating an accumulation of acid mucopolysaccharide[7]. There was no tissue reaction against altered elastic fibers, such as the presence of inflammatory, foam or giant cells. In higher magnification (Fig. 3), the altered elastic fibrils appeared fragmented, considerably curled and, in some areas, clumped together showing coarsely granular fiber conglomerations.

Histological findings above described were so impressive that one was able to exclude a conventional calcinosis cutis with ease.

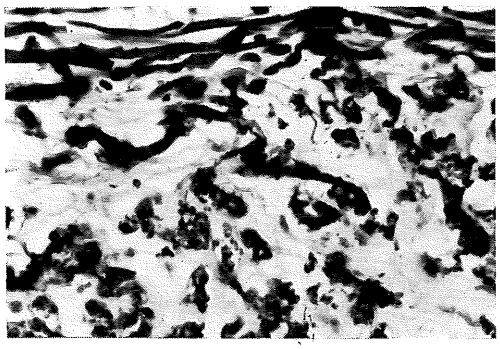

Fig. 3. The altered elastic fibrils appearing fragmented and clumped together (below), in contrast to normal-appearing fibers running parallel to the lesion (above). Elastica van Gieson, ×400.

DISCUSSION

The pseudoxanthoma elasticum (PXE) is regarded as a disease, *i. e.*, a deranged metabolism of elastic fibrils; this gives rise to an increse of abnormal elastic fibers which will be replaced by premature calcification and fragmentation[7]. Therefore, PXE is a generalized disease not only affecting the skin but other various organs. For instance, once this occurs in the Bruch's membrane (glassy membrane), which situates between the choriocapillary layer and the pigment epithelium of retina and is rich in plexus of elastic fibers, we see so-called angioid streaks in the optic fundus. This sometimes causes decreased visual acuity subsequent to hemorrhage. Another major problem is involvement of elastic fibers in the cardiovascular system; in our patient hypertension was the basic problem. Other complaints of the patient included angina-like precordial discomfort, transient cerebral ischemic attacks which manifested as a sudden onset of finger weakness, and a series of unstable complaints such as tinnitus, insomnia and depression which may be attributed to premature and severe atherosclerosis due to PXE in the central nervous system[5].

Once blood vessels of the gastrointestinal tracts are involved, though we have not experienced in our patient, intractable bleeding will ensue[3]. Involvement of peripheral arteries of the extremities will naturally cause narrowing or occulsion which leads to intermittent claudication. Recently described extensive calcification of the lung[8] due to PXE, though not reported previously, may also cause pulmonary dysfunction such as exertional dyspnea and cough. Lastly, and most important of all, when the coronary artery is affected, the patient may succumb to myocardial infarction or congestive cardiac failure[10].

Since skin lesion mimicks xanthoma, we may overlook the lesion so easily as a conventional xanthoma. When, however, we pay attention to rather symmetrical occurrence of the lesion not only in canthus but in other regions of dermal stress and normal calcemia and lipidemia, we are able to think of PXE as the most crucial one for differential diagnoses. Subsequently, one can explain other various clinical manifestation as described, which are based on abnormal metabolism of elastic fibers, to be under PXE as a symptom complex.

Like in our case, the patients often seek medical advice to the medical department; it might be worthwhile to be aware of PXE, in particular, among internists. Therefore, whenever we see rather obscure skin lesions, local biopsy is strongly recommended. In this way, we may expect PXE more frequently than previously reported figures of one in 70,000 individuals[1]. Although the skin lesion of PXE *per se* has often no any harm apart from cosmetic, we would like to draw attention to several complications such as gastrointestinal or cardiovascular, which will be sometimes fatal.

PXE is known to be a disease of autosomal recessive or dominant inheritance[1,3], whereas polyposis coli to be of autosomal dominant. The polyposis coli is one of phenotypes seen in Gardner's syndrome, which represents a disease of mesenchymal disorder. Recent report[9] of a case carrying both PXE and polyposis coli is worthy of note; a comprehensive chromosomal study on the patients with PXE may offer some clues for clarification of the disease.

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