KYRLE'S DISEASE : A CUTANEOUS MARKER OF RENAL DISORDER

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Twenty one cases of Kyrle's disease were subjected to a thorough clinical examination and various investigations in order to find out the association of Kyrle's disease with other systemic disorders and to elucidate the association between specific biochemical abnormalities and Kyrle's disease. It was found that all the cases of Kyrle's disease were associated with systemic disorders and that the major systemic disorder was nephropathy. The significant biochemical abnormality detected was a raised phosphorus level. So it is probable that the elevated phosphorus may be triggering the occurrence of Kyrle's disease.

Key Words : Kyrle's disease, Systemic disorder, Nephropathy, Serum phosphorus

Introduction

Kyrle in 1916 described a dermatosis which he named "hyperkeratosis follicularis et parafollicularis in cutem penetrans".[1] Carter and Constantine in 1968 reported 5 such cases and also analysed the literature and put forward strict clinical and histological criteria for its diagnosis.[2,3] Several authors have reported the association of Kyrle's disease with diabetes mellitus, renal disease, liver disease, congestive cardiac failure, hyperlipidemia, an infective process and an abnormal vitamin A metabolism. Aram et al also postulated a hereditary transmission of the disease.[4-6] Prompted by these reports a study was undertaken with the following aims:

(1) To find out the association of Kyrle's disease with systemic disorders, and

(2) to detect the presence of any specific biochemical abnormality in Kyrle's disease.

Materials and Methods

Twenty-one patients of Kyrle's disease who attended the outpatient departments of Dermatology and Venereology, Medicine, Nephrology and Gastroenterology at Medical College Hospital, Trivandrum, during the period 1991-92, and who fulfilled the clinical and/or histological criteria laid down by Carter and Constantine[2,3] were taken up for this study.

A detailed history was taken in all the cases followed by a thorough clinical examination. Routine blood and urine examination and biochemical investigations which included blood sugar levels, renal function tests, liver function tests, calcium, phosphorus, cholesterol and uric acid were done. The corrected ionic calcium value was calculated using the formula :

Corrected ionic calcium = 0.8 x deficient albumin + calcium.

Skin biopsy and histopathological examination were carried out using H&E stain and special stains like Masson's trichrome and Verhoeff - Van Gieson's stain. Special investigations like renal biopsy and ultrasound abdomen were done in a case of suspected renal tumour.

Patients without any cutaneous disease but with various systemic diseases such as diabetes mellitus, liver disease, nephropathy and congestive cardiac failure were randomly chosen as controls, with each group having

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20 patients. Comparison of the means was done using the student's 't' test.

Results

The age and sex distribution of the patients are given in Table I. There was no

Table I. Patients

Age group (years)	Number of patients			
	Male	Female	Total	%
10-19	1	0	1	4.8
20-29	1	4	5	23.8
30-39	4	3	7	33.3
40-49	5	1	6	28.5
50-59	0	1	1	4.8
60-69	0	1	1	4.8
Total	11	10	21	100.00

family history of a similar illness in any of the patients. Duration of the disease varied from 2 weeks to 8 years and majority of the patients (85.8%) had a duration below 5 years. There was exacerbation and remission of the lesions in all the cases.

Diabetes mellitus was the most frequently encountered systemic disease among the 21 patients in this study. Fourteen patients (66.6%) had diabetes mellitus with a mean duration of 7-10 years. Of the diabetics, 12 (85.7%) had some form of renal involvement (nephropathy) (Table II). Six of

Table II. Renal involvment in Kyrle's disease - causes

Diabetic nephropathy	:	12
Chronic glomerulonephritis	:	4
Renal calculi	:	1
Renal tumour	:	1
Benign nephrosclerosis	:	1
Total	:	19

these patients (50%) had overt renal failure also. Other co-existent conditions were congestive cardiac failure in 2 patients and genitourinary tuberculosis in 1 case.

Of the remaining 7 patients without diabetes, 6 had renal failure due to the following conditions: chronic glomerulonephritis (4), urolithiasis and obstructive uropathy (1) and hypertensive nephrosclerosis (1). One patient had an onchocytoma of the left kidney and had no metabolic derangement.

The common co-morbid conditions co-existing with Kyrle's disease were anaemia, hypoproteinemia, oedema and hypertension. One of them had jaundice and hepatomegaly and was HBsAg positive.

Of the 12 patients with renal failure, 7 underwent repeated dialysis and most of them gave a history of partial clearing of the lesions following dialysis.

The important laboratory parameters of patients with Kyrle's disease are given in Table III.

On comparing the laboratory variables of patients with Kyrle's disease and those with systemic diseases without any cutaneous disorder, we found that the only biochemical abnormality which was statistically different in the cases was the higher serum phosphorus level (Table IV).

Discussion

The occurrence of systemic disease in all the 21 patients indicates that an underlying systemic disorder may be responsible for the causation of Kyrle's disease. The presence of a renal disorder in 19 out of 21cases, suggests that the underlying systemic disease is most often a renal disorder. The presence of diabetes mellitus in 12 of these patients suggests that diabetes mellitus with nephropathy is a major cause of Kyrle's disease. The occurrence of Kyrle's disease in nondiabetic renal disorders such as chronic glomerulonephritis, renal calculus disease,

Table III. Mean values of biochemical parameters

Mean biochemical parameters	Kyrle's disease	Controls with nephropathy	Controls with DM	Controls with CCF	Controls with liver disease
Haemoglobin	9.2	8.7	11.0	9.1	10.2
PPBS	246.3	196.3	210.7	174.5	163.9
Blood urea	113.3	117.2	26.0	56.6	32.8
S Creatinine	6.1	7.9	1.1	1.3	1.6
S Albumin	3.0	3.0	4.2	3.1	2.6
S Cholesterol	195.6	213.9	196.6	217.1	186.2
S Uric acid	6.4	7.1	3.8	6.3	5.1
S Calcium	7.9	5.2	8.0	10.1	9.8
S Phosphorus	7.8	5.6	4.9	4.6	4.4

Table IV. Comparison of Kyrle's disease versus control groups

Biochemical parameters	t	P-value
PPBS	0.62	> 0.05
Blood Urea	0.173	> 0.05
S Creatinine	1.10	> 0.05
S Albumin	0.20	> 0.05
S Cholesterol	0.76	> 0.05
S Uric acid	0.92	> 0.05
S Calcium	0.64	> 0.05
S Phosphorus	2.61	< 0.05

renal tumour and hypertensive nephrosclerosis denotes that diabetes mellitus alone may not be the only cause of Kyrle's disease. This is further substantiated by the fact that the blood sugar values in cases and controls did not show a statistically significant difference ($P > 0.05$). Except for the patient with renal tumour, all others with non-diabetic renal disease had overt renal failure, substantiating the fact that the metabolic derangement may be the cause of the skin lesions. The 2 patients with diabetes who had no overt renal involvement, had a long duration of diabetes mellitus and a covert nephropathy cannot be ruled out.

It could thus be hypothesised that metabolic derangement associated with nephropathy, possibly some uremic toxins, may be one of the causative factors for Kyrle's disease. The partial clearing of the lesions following dialysis also suggests that a correctible metabolic abnormality is the causative factor for Kyrle's disease. The increased occurrence of Kyrle's disease following dialysis in earlier series, may be due to the inadequeate and inefficient dialysis given in the past.

The more frequent occurrence of Kyrle's disease among patients with diabetic nephropathy possibly suggests an independent role of diabetes mellitus also. The only consistent and significant abnormality seen among these 21 cases was hyperphosphatemia and though slightly premature, one could postulate that this abnormality may play a central role in the pathogenesis of Kyrle's disease. Moreover, other uremic skin manifestations such as pruritus have been implicated to be due to hyperphosphatemia, hypocalcemia and elevated parathyroid hormone.[7]

Mehregan postulated 3 mechanisms by which the dermis deals with foreign materials.[8-11] (1) If inert the material will be gradually carried off to a local lymph node. (2) If very irritating, necrosis or granuloma formation will occur and the material will be walled off or discharged through a necrotic

epidermis, and (3) if moderately reactive, the material will penetrate the follicular opening of the epidermis forming perforating canals and causing a minimal disruption of the epithelium as is seen in the classical perforating diseases. It may be possible that the development of lesions of Kyrle's disease is by such a mechanism whereby a chemical substance like phosphorus which may get deposited in excessive amounts in the dermis is eliminated through the epidermis.

It may be concluded that Kyrle's disease is always associated with a systemic disorder and that the systemic disorder is a chronic renal parenchymal disease in majority of the cases. Thus Kyrle's disease may be considered as a cutaneous marker of renal disorder. Diabetic nephropathy seems to be the commonest renal disorder associated with Kyrle's disease. A significant biochemical abnormality detected in these patients was an elevated serum phosphorus level which may have a pathogenic role. Further studies are required in this direction to arrive at a definite conclusion.

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