Hereditary Retinal–Renal Dysplasia

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Hereditary nephropathies constitute an important cause of chronic renal failure in childhood(1,3). The usual eye lesions that have been described in association with these nephropathies are those involving the lens-cataracts, spherophakia and anterior lenticoconus(4,5). Retinitis pigmentosa is an uncommon but characteristic ocular anomaly associated with various hereditary nephropathies which include oxalosis, cystinosis and Alport's syndrome(5,6). Renal-retinal dysplasia is a distinct syndrome characterized by an autosomal recessive inheritance, insidiously occuring renal failure in the first or second decade of life and retinitis pigmentosa. It is a rare anomaly and only a few reports are available in literature(4-6). Described below is a brief report of the first patient with this entity reported from this part of the sub-continent.

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Case Report

A 10-year-old Hindu boy from Punjab presented with a short history of rapid breathing, anorexia and oliguria for 10 days. He was detected to be hypertensive by a general practitioner, started on anti-hypertensive therapy and referred to our institute for further management.

There was no history forthcoming of episodes of urinary tract infection, hematuria, polydipsia, polyuria in the past. There was history of night blindness since early childhood but no history of hearing deficit. He was born of non-consanguinous marriage, and his two other siblings both girls, aged 8 and 12 years, were reportedly normal. There was no history of eye or kidney disease in the family.

On examination he was markedly pale with a sallow complexion, stunted with a weight of 22 kg and height of 110 cm, both below the third percentile for his age. There was frontal bossing and widening of wrists. The blood pressure on anti-hypertensive therapy was 130/90 mm Hg. The eyes showed a normal pupillary reaction with visual acuity of 6/9. Fundoscopy revealed waxy pallor of the discs, attenuation of arterioles, suggestive of retinitis pigmentosa.

Investigations showed a hemoglobin of 9.0 g/dl, a reticulocyte count of 0.2%, platelet count of 1,50,000/mm^3 and a total leucocyte count of 7400/mm^3. The blood urea was 135 mg/dl, creatinine 2.5 mg/dl, serum sodium 135 mEq/L and serum potassium 3.5 mEq/L. Blood gases revealed a metabolic acidosis with respiratory compensation (pH 7.32, PaO_2 of 120 mm Hg and $PaCO_2$ of 15 mm Hg and HCO_3 of 15 mEq/L). Urine examination showed specific gravity of 1.010, pH of 5.5, albumin of 1+ but no sediment or casts

and skeletal survey revealed features of renal osteodystrophy. The micturating cystourethrogram did not show any evidence of vesico-ureteral reflux.

The child was started on conservative medical management antihypertensive therapy, vitamin supplements, aluminium hydroxide with dietary protein and phosphate restriction. The urine output ranged between 700 ml-1000 ml/day. On the 10th day of hospitalization his blood pressure increased to 160/100 mm Hg and he developed frank signs of fluid overload. Renal functions showed a concomitant rise of blood urea to 150 mg/dl and creatinine to 6 mg/dl. Urgent peritoneal dialysis was instituted but the child died during the procedure.

Autopsy revealed that kidneys were small, contracted, equal in size and granular in appearance. The combined weight of kidneys was 80 mg (less than 50% of normal). Ureters, renal arteries and urinary bladder were normal. Pelvicalyceal system was normal. No gross cysts were seen on the surface. Microscopically varying degree of sclerosis was seen in about 80% of the glomeruli (*Fig. 1*). Mild periglomerular fibrosis was seen in otherwise normal looking glomeruli (*Fig. 2*). Tubules showed patchy areas of atrophy and dilatation. There was marked lymphomononuclear cell infiltration in areas of tubular atrophy. Immunofluoroscence of the kidney was negative for IgM and IgG. Electron microscopy showed normal glomerular basement membrane thereby excluding Alport's disease (*Fig. 3*). The eye was not examined. The family of the child has not yet reported for follow up.

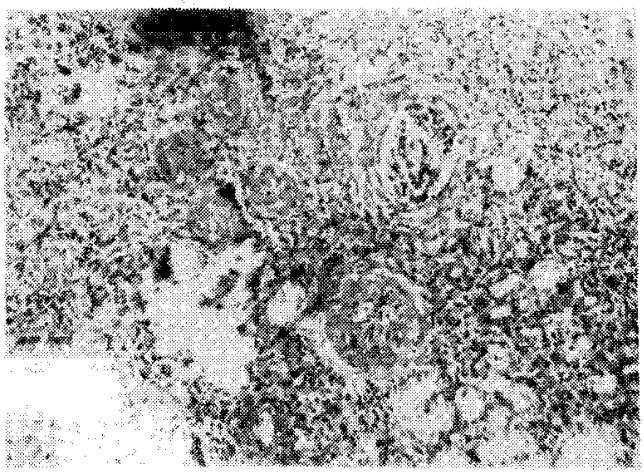

Fig. 1. Photomicrography of kidney showing large number of hyalinized glomeruli; interstitium shows chronic inflammatory cells (H & E ×120).

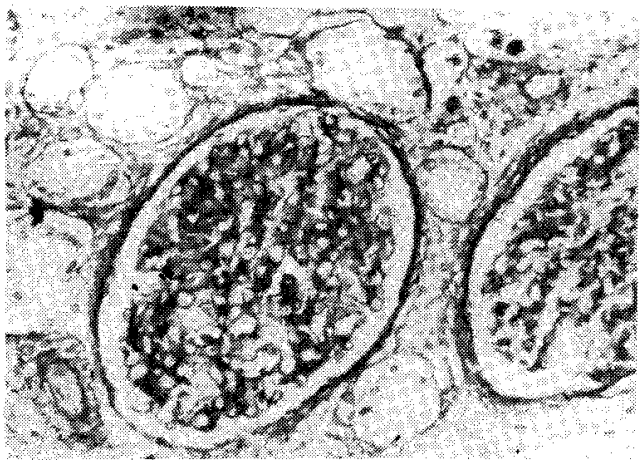

Fig. 2. Mild periglomerular fibrosis around a normal glomerulus (PAS ×480).

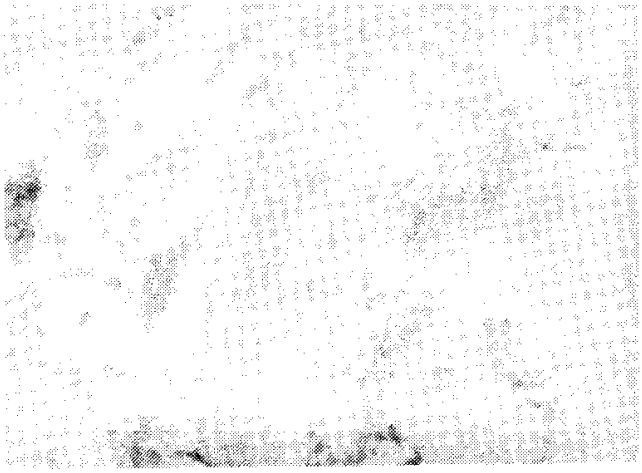

Fig. 3. Electron photomicrographs showing normal glomerular basement membrane (×3000).

Discussion

The term renal-retinal dysplasia has been given to this clinical entity in which

retinitis pigmentosa is associated with insidiously occurring renal failure within the first two decades of life(4-6). The similarity of the renal component of this disorder to juvenile familial nephronopthisis and adult medullary cystic disease is striking. All of these are characterized by polyuria, polydipsia, progressive azotemia and a paucity of abnormal elements in the urine(4,8). However, this disease differs from the other two entities in the uniformly recessive mode of inheritance, characteristic eye manifestations and absence of cysts on renal histology(5,6).

The renal component consists of insidious onset with polyuria, polydipsia, severe anemia and renal failure within the first two decades of life. Hypertension occurs only in advanced disease. The urine is dilute but there is an initial absence of cells and formed elements. Terminally, the kidneys are contracted and histology shows evidence of glomerular sclerosis, periglomerular fibrosis, without any crescents and adhesions. The tubules are atrophic and dilated with marked interstitial infiltration(4-6).

The visual handicap varies from only mild decrease of visual acuity to complete blindness. The degree of visual impairment does not correlate with the appearance of the fundus. Electroretinogram abnormalities are always present(5,6). Pigmentation tends to appear between 3 and 8 years of age but may be absent even in presence of visual impairment. The abnormal disc pallor and attenuation of vessels may be mistakenly attributed to uremia. Pathologically there is degeneration of rods followed by degeneration of the entire neuroepithelium and choriocapillaris of the retina(5,6).

Although we did not yet have a family screening in this case, this combination of chronic renal failure with this histopathological features in association with retinitis pigmentosa is *sine qua non* of this entity.

In all the cases reported so far, the pattern of inheritance has been autosomal recessive. The involvement of two distinct organs, kidneys and eye, is believed to be by inheritance of a single pleiotropic gene.

This entity, though rarely reported, may occur much more commonly than it is diagnosed. A fundus examination and possibly ERG in all cases of CRF of obscure etiology may help in establishing a diagnosis in more cases. Also, screening the renal functions in all cases of retinitis pigmentosa may pick up cases with early renal involvement(5).

It is important to search for asymptomatic disease in family members especially if renal transplant from one of them is being contemplated. A parent to child transplant would be reasonably safe keeping in mind the recessive inheritance(6). The importance of genetic counselling in this disease must also be emphasized.

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Cerebellar Syndrome in Malaria

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Cerebellar syndrome, an unusual manifestation of malaria, is already reported by different authors(1-3). The diagnostic triad of such cerebellar syndrome is characterized by cerebellar signs with fever, presence of malarial parasite in blood and response to antimalarial therapy(1). Recently, we came across five cases of malaria with cerebellar signs which presented in different manner in contrast to previous reports. So, we would like to present the case reports to highlight our point.

Case Reports

An alarming rise in incidence of cerebral malaria is noted in Surat and surrounding areas of South Gujarat in last few years. Cerebral malaria constitutes 2-5% of admissions in Pediatric Ward of Government Medical College, Surat (Unpublished data). We encountered all five cases in last three months from July 1991 to September 1991.

The age group of patients varied from 3-10 years. None received prior treatment before admission. Only one patient admitted with isolated cerebellar signs with behavioral changes and presentation of remaining patients fulfilled the criteria of working definition of cerebral malaria. Bilateral cerebellar signs with unsteady gait were present on admission in two cases and appeared after third day onwards in remaining cases. The average duration of cerebellar signs was one week except in one case. The peripheral smear for malarial parasite was positive in four patients. All patients were treated with quinine (10 mg/kg/d × 10 days) considering the high incidence of chloroquine resistant malaria in our area (Unpublished data). The clinical recovery was complete in all cases (*Table*).

Discussion

The classical malarial syndrome now occurs in only 50-70% cases of malaria, the rest being atypical presentation like abdominal symptoms, bleeding disorders and combination of neurological defects(4,5). The cerebellar involvement in malaria was reported by Deaderic in 1909 and later on, Ringdon *et al.* in their pathological study demonstrated a definite involvement of cerebellum in patients who died of cerebral malaria as well as in experimental animals(6).

The pathogenesis of cerebellar signs is similar like cerebral malaria which results from obstruction of micro-circulation due to sludging of parasitized RBCs and direct

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