Occurrence of Hereditary Nephritis, Pretibial Epidermolysis bullosa and Beta-Thalassemia minor in Two Siblings with End-Stage Renal Disease

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Dear Sir,

Several cases of renal and urinary tract disorders have been reported in patients with epidermolysis bullosa. These include primary amyloidosis [1–4], secondary amyloidosis [5–11], IgA nephropathy [12], upper and lower urinary tract obstruction [13–16], and papillary transitional cell carcinoma of the bladder [17].

A variety of kidney abnormalities associated with β -thalassemia have also been reported, e.g. painless hematuria [18, 19], failure of urine concentration ability [20], acute uric acid nephropathy [21], porphyrinuria [22], acute post-streptococcal glomerulonephritis [23], renal phosphaturia [24], aminoaciduria [25], and acute renal failure due to rhabdomyolysis [26]. We would like to present a unique association of hereditary nephritis, epidermolysis bullosa, and β -thalassemia minor, which, to our knowledge, has not been previously reported.

Case Report

A 19 year-old boy and a 17 year-old girl (siblings of an Oriental Jewish family) with features of three hereditary diseases in each of them, i.e. hereditary nephritis (HN), pretibial epidermolysis bullosa (PEB) and β -thalassemia minor (β -TM) were treated because of chronic renal failure by hemodialysis (5 years) and continuous ambulatory peritoneal dialysis (1 year), respectively. The clinical findings in both included: multiple recurrent infected skin blisters of the lower extremities followed by atrophy, nail dystrophy, bilateral lacrimal duct stenosis, sensorineural deafness, nephrotic range proteinuria and anemia due to β -TM. In addition, a single right kidney and defective teeth were noted in the brother, while agenesis of the distal vagina and bilateral cervical ribs were found in the sister. A skin-biopsy evaluated by light microscopy and

immunofluorescence demonstrated complete separation between the epidermis and dermis with focal epidermal edema and mild perivascular mononuclear infiltrates and negative immunofluorescence confirming the clinical diagnosis of PEB [27]. The histological features

Fig. 1. The family pedigree, showing results of HLA typing.

on kidney biopsy supported the diagnosis of HN: on light microscopy except for focal enlargement of basement membrane in occasional glomeruli no other abnormalities were seen, while immunofluorescence failed to detect fibrinogen, immunoglobulin or complement deposition. Electron microscopy revealed splitting of the basement membrane of glomeruli and tubules and thickening of the basement membrane of glomeruli in affected areas with inclusion of electron-dense particles. Clusters of foam cells in the interstitium were apparent. A diagnosis of β-TM was proved by hemoglobin electrophoresis. Eight and 6 years after the appearance of skin lesions in the brother and sister, respectively, renal death occurred necessitating dialysis, which brought about prompt resolution of the bullous skin lesions in the brother (treated by hemodialysis), but not in the sister (treated by continuous ambulatory peritoneal dialysis). The family pedigree and HLA typing (fig. 1) demonstrate that this syndrome appears to be inherited as an autosomal-recessive trait.

Basement membrane composition and collagen metabolism seem to be altered in both hereditary nephritis [28, 29] and epidermolysis bullosa [30, 31]. It is noteworthy that epidermal basement membranes of kindreds with Alport-type familial nephritis exhibited a multilaminated appearance and antigenic abnormalities of type IV collagen, similar to those found in their renal basement membranes [32]. We therefore postulate that our commu-

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nication – which presents a combination of hereditary nephritis, neurosensory deafness and pretibial epidermolysis bullosa – possibly depicts an entity characterized by a common genetic

defect in the metabolism of basement membrane collagen, as previously suggested by Spear [33].

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