Lack of correlation of P blood group phenotype and renal scarring

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Lack of correlation of P blood group phenotype and renal scarring. Renal scarring is in most instances caused by infection in the young child. The most commonly occurring etiological agent in urinary tract infections is Escherichia coli. An important virulence factor for these nephropathogenic E. coli is the ability to adhere to urinary tract epithelium. This adhesion is often mediated by P-fimbriae, which recognize and specifically bind to the receptor structure (α-D-Galp-(1-4)β-D-Galp) present on the cell membranes of human urinary tract epithelium. This carbohydrate structure occurs as an entity of the glycosphingolipids that correspond to the antigens of the human P blood group system. It has been proposed recently that children with recurrent acute pyelonephritis have a higher frequency of the P1 blood group phenotype than the expected 75%. We have studied 56 adult female patients with a history of febrile urinary tract infection and signs of renal scarring on urogram. The P blood group phenotype was determined in all patients. There was no increase of the P1 blood group phenotype in the patients with verified renal scarring. In conclusion, our results do not support a role of the P1 blood group phenotype in the pathogenesis of renal scarring due to previous febrile urinary tract infection.

Absence de corrélation entre le groupe sanguin de phénotype P et la scérose rénale. La scérose rénale est souvent dûe à une infection chez le jeune enfant. L’agent étiologique le plus souvent retrouvé dans les infections du tractus urinaire est Escherichia coli. Un facteur de virulence important de ces E. coli néphrogènes est la capacité d’adhérer à l’épithélium du tractus urinaire. Cette adhérence est souvent mediée par P-fimbria, qui reconnaît et se lie spécifiquement à la structure du récepteur (α-D-Galp-(1-4)β-D-Galp) présent sur les membranes cellulaires de l’épithélium du tractus urinaire humain. Cette structure glucidique fait partie des glycosphingolipides, qui correspondent aux antigènes du système de groupe sanguin P humain. Il a été récemment proposé que les enfants ayant des pyélonéphrites aigües récidivantes avaient une fréquence plus élevée du phénotype P1 du groupe sanguin, que les 75% attendus. Nous avons étudié 56 malades adultes ayant une histoire d’infection fébrile du tractus urinaire et des signes de scérose rénale à l’urographie. Le phénotype P du groupe sanguin a été déterminé chez toutes les malades. Il n’y avait pas d’augmentation du phénotype P1 du groupe sanguin chez les malades ayant une scérose rénale vérifiée. Nos résultats ne sont donc pas en faveur d’un rôle du phénotype P1 du groupe sanguin dans la physiopathologie de la scérose rénale dûe à des infections fébriles du tractus urinaire préalables.

The general consensus now holds that focal renal scarring in earlier healthy kidneys is in most instances caused by renal infections, in particular, in the young child. The most common organism is Escherichia coli. Many features such as O- and K-antigens, hemolysin production and resistance to bacterial activity of serum have been implicated as important in bacterial virulence. However, more recent results indicate that yet another bacterial property, namely, the ability of the bacteria to adhere to the target epithelium, is of major importance for the virulence of nephropathogenic E. coli strains [1]. In particular, the ability of E. coli strains to specifically adhere to urinary tract epithelial cells by means of P-fimbriae mediated binding appears to be essential in severe urinary tract infections in both the child [2] and in the adult [2, 3]. P-fimbriae enable the bacteria to firmly attach to human uroepithelial cells by recognition of a specific carbohydrate structure (α-D-Galp-(1-4)β-D-Galp), which is confined within all the glycosphingolipids/glycoprotein(s) related to the human P-blood group antigens [4]. The P blood group antigens P, P1, and Pk are found on erythrocytes of individuals of P1 blood group phenotype, and the P and Pk antigen are found on erythrocytes of individuals of P2 blood group phenotype.

Children who have experienced one attack of acute pyelonephritis are at higher risk of recurrent urinary tract infections, and each new infection predisposes to a higher recurrence rate [5]. Uroepithelial cells from infection-prone adults [6] and children [7] bind uropathogenic E. coli more abundantly than uroepithelial cells from healthy controls. We suggested and later showed that this difference, in part, might be explained by a difference in the number of accessible P-fimbriae specific receptors on the uroepithelial cells in infection-prone vs. non-infection-prone children [4, 8]. Lomberg et al. [9] reported that among girls with recurrent acute pyelonephritis there was a significantly higher proportion of individuals of the P1 blood group phenotype than expected from the random frequency (75%) of this phenotype. It was proposed that differences in amount of glycosphingolipids and thus in receptor density on uroepithelial cells in between individuals of P1 and P2 phenotype accounted for this finding. We herein present the results of a study of adult female patients with verified renal scarring and a history of febrile urinary tract infection in relation to their P blood group phenotype.
Methods

Patients

The urograms of all patients who had undergone urography at the Karolinska Hospital from January, 1973, to April, 1981, were reviewed, and the patients with signs of renal scarring were selected for study. Renal scarring was defined as calyceal deformity with corresponding parenchymal reduction. The charts of these patients were studied and those born after 1911 and who had a history of febrile urinary tract infection were selected in the study. Patients with obstruction of the urinary tract, papillary necrosis, and compromising diseases, for example, diabetes mellitus, were excluded. Fifty-six female patients who were 19 to 72, mean age 43.8 yrs, were included in this study. All patients were interviewed and all available hospital charts were examined for history or finding of previous urinary tract infection. Glomerular filtration rate was determined in a total of 48 of 56 patients (86%). Glomerular filtration rate data from four patients were not used because the patients had undergone renal surgery or nephrectomy. Four patients refused to participate in the kidney function test.

The P blood group phenotype was determined in all 56 patients and in a control group of 39 healthy women (mean age 40.5 yrs, range 19 to 63 yrs) without a history of symptomatic urinary tract infection. The controls were selected from a routine health control.

Determination of P blood group phenotype

Citrate blood was drawn and the P blood group phenotype was determined by agglutinability of erythrocytes by undiluted sheep anti-human P1 specific serum (Bundes Republic Deutschland, Behnngwerke AG, Marburg, West Germany). Patients whose erythrocytes agglutinated were judged to be of P1 phenotype and the others as of P2 phenotype.

Determination of glomerular filtration rate (GFR)

Glomerular filtration rate was measured in 46 patients by plasma clearance of $^{51}$Cr EDTA using a single injection technique [10]. In one patient, GFR was measured using the plasma clearance of $^{51}$Cr DTPA, and in one patient using the renal clearance of inulin [11]. The values were corrected for body surface area, which was estimated according to du Bois’ nomogram [12].

Statistical analysis

Results are given as mean ± one standard deviation. Student’s $t$ test and chi$^2$ test were used.

Results

The distribution of P blood group phenotype in the 39 healthy women were 79% of P1 and 21% of P2 blood group phenotype (Table 1). This corresponds to the expected incidence in a normal population [13]. In the 56 studied patients, 71% were of P1 and 29% were of P2 blood group phenotype (Table 1), which does not significantly differ from the healthy women. Twenty-nine patients had a history of recurrent febrile urinary tract infections, defined as five episodes or more. Sixty-nine percent of these patients were of P1 and 31% were of P2 blood group phenotype (Table 1). The patients who had a history of recurrent urinary tract infections and their first clinical episode before fifteen years of age were in 65% of P1 and 35% of P2 blood group phenotype.

Twenty-seven patients had earlier been examined with voiding cystourethrography. Reflux grade II [14] or higher was found in 18 cases, of which 67% were of P1 and 33% were of P2 blood group phenotype. Twenty-one patients had their first known clinical episode of febrile urinary tract infection in early childhood before the age of five. In this group of patients, 67% were of P1 and 33% of P2 blood group phenotype (Table 1). In the same group of patients, 18 children had a history of recurrent urinary tract infection (> 5 episodes). The P phenotype distribution in this group was 61% of P1 and 39% of P2 blood group phenotype, respectively (Table 1).

This distribution of P1 and P2 phenotype in the subgroups of the patients did not differ from the distribution in either all the 56 patients or the 39 healthy women.

The mean GFR in the 48 patients (mean age 43 ± 15 yrs) was 75 ml/min × 1.73 m$^2$. The normal GFR in this age group is 100 ± 25 ml/min × 1.73 m$^2$ [10]. Thirty-three (69%) of the patients (mean age 44 ± 15 yrs) were of P1 and 33% of P2 blood group phenotype and fifteen patients (31%) (mean age 41 ± 15 yrs) were of P2 blood group phenotype. Neither age nor P blood group distribution differed significantly between the patients who underwent kidney function test and all the 56 patients. The mean GFR in the patients who were of P1 blood group phenotype did not differ from the patients who were of P2 blood group phenotype (Fig. 1).

Discussion

The ultimate goal of treating patients with urinary tract infections (UTI) is to prevent renal damage. Host factors that have been demonstrated as important for development of renal scarring in connection with UTI are gross abnormalities of the urinary tract, vesicoureteral reflux, the clinical course of the infection, sex and age of the patient.

It has been proposed that children with recurrent acute pyelonephritis have an increase in F-fimbriae receptors [9]. This assumption was based on a finding of a higher than expected frequency of the P1 phenotype.

In the present study we have investigated adult patients with renal scarring to study the relevance of the P blood group phenotype for the outcome of the renal disease. We found no correlation between renal damage and P blood group pheno-
types. The distribution of the P1 and P2 blood group phenotypes was normal. One possible explanation for the low incidence of individuals of P1 phenotype found in our material could be that individuals of P1 phenotype had died in their renal disease. However, since the mean glomerular filtration rate is equal in the groups of P1 and P2 individuals, it is unlikely that the kidney damage of the P1 individuals progresses more rapidly.

A possible explanation for the discrepancy between the results obtained by Lomberg et al [9] and those obtained by us is that our patient populations differed. The goal of our study was to examine a group of adult patients with more or less pronounced renal scarring and loss of renal function. To determine whether the P1 phenotype was important in any group of our patients, we studied the material in different ways. Lomberg et al found a correlation with the P1 phenotype in children with recurrent UTI [9], and on extending their material, in children with recurrent febrile UTI. Among our patients, a history of more than five infections did not increase the frequency of the P1 phenotype in children with recurrent UTI [9], and on extending their material, also reported that the increase in P1 phenotype was confined to the group of patients without marked vesicoureteral reflux [15]. In our retrospective study, information on the presence or absence of reflux was available in less than half of the patients. It, therefore, cannot be concluded whether more than the observed 18 of 27 investigated patients had some degree of vesicoureteral reflux at the time of infection. Thus, the patients studied by us may not necessarily represent an adult extension of the group studied by Lomberg et al, that is, patients who had had recurrent febrile UTI without reflux. The issue whether the P blood group is important for development of renal scarring will not be known until a cohort of adults who were studied for reflux as children is studied for P blood grouping.

Our findings do not support a role of the P1 phenotype in the pathogenesis of renal damage due to previous febrile UTI. Although it is possible that the P1 phenotype plays a role for the increased risk of recurrent UTI in children, such infections may, however, only rarely cause renal scarring in the absence of other predisposing factors, such as gross reflux.

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![Fig. 1. Glomerular filtration rate and P blood group phenotype in 48 patients with renal scarring and a history of febrile UTI.](image-url)

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