A Case of Proteinuria with Analbuminuria

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A 46-year-old black man with diabetes mellitus and hypertension was hospitalized because of myocardial ischemia and chronic renal failure. The electrophoretogram for protein in urine revealed proteins only in the α1, α2, and β regions. These protein fractions were identified as small molecules by sodium dodecyl sulfate/polyacrylamide gel electrophoresis. No albumin was detected in the urine. The molecular mass of albumin, the protein present in highest concentration in serum, is near the glomerular filtration threshold, and this protein is not reabsorbed by renal tubules; therefore, albumin is consistently present in proteinuric specimens. Thus this analbuminuric pattern is highly unusual. Although the mechanism of the analbuminuria in this case is not fully understood, we wished to document this extremely rare electrophoretic pattern to alert clinical chemists and pathologists of its existence.

Additional Keyphrases: electrophoresis, agarose · urine · renal disease

Electrophoresis of urinary proteins is a useful tool for distinguishing between glomerular and tubular proteinuria. Albumin is consistently present in proteinuric specimens, regardless of etiology. Recently we encountered a case of proteinuria with no albuminuria. This unusual pattern has not, to our knowledge, been reported in the English literature (1–5), nor has it been encountered before in the 2321 urine specimens electrophoresed in our protein chemistry laboratory during the past 10 years.

We report here the clinical and laboratory findings of this case and discuss a possible mechanism of this unusual electrophoretic pattern.

Case History

A 46-year-old black man with a 15-year history of diabetes mellitus and a 10-year history of hypertension was hospitalized after a prolonged episode of shortness of breath and an electrocardiographic showing of anterolateral wall ischemia. The patient had noticed increased leg swelling and dyspnea on exertion the previous year, but the symptoms had become exacerbated in the month before admission. A year earlier, he had been told he had mild renal dysfunction, but no functional evaluation had been performed at that time. Because of frequent headaches, the patient had taken larger quantities of acetylsalicylate during the preceding month.

On admission, the patient’s blood pressure was 240/140 mmHg. Severe diabetic retinopathy and mild pitting edema on both lower extremities were noted. Total serum protein concentration was 65 g/L, albumin 36 g/L, glucose 8.3 mmol/L, urea nitrogen 45.3 mmol/L, creatinine 707 μmol/L, and creatine kinase (CK, EC 2.7.3.2) 2208 U/L. No CK-MB fraction was demonstrated by electrophoresis. The creatinine clearance rate was 8 mL/min (normal 85–125 mL/min). His 24-h urine volume declined from 1000 mL to 700 mL per day. Urinalysis showed protein 1+ and glucose 1+, but no blood. Microscopic examination of the urine revealed a few leukocytes and occasional granular casts. Renal scanning demonstrated bilateral stenosis of renal arteries.

After admission, the patient’s blood pressure and diabetes were promptly brought under control, but his renal function deteriorated. An arteriovenous fistula was then placed in the left radial artery for hemodialysis. The patient was discharged two days after the operation.

Materials and Methods

Serum and urine samples were assayed side by side, to compare the protein fractions of each, with the high-resolution agarose electrophoresis system (Worthington Diagnostics, Freehold, NJ) (4). Urine specimens were concentrated 100-fold by ultrafiltration in a Minicon B 15 concentrator (Amicon, Danvers, MA). The relative molecular masses (Mr) of the urinary proteins were determined by sodium dodecyl sulfate/polyacrylamide gel electrophoresis (Ames, Elkhart, IN) in comparison with the low-molecular-mass standard from Bio-Rad Laboratories, Richmond, CA (6).

Results

Electrophoresis of concentrated urine specimens showed six narrow protein bands in the regions of α1, α2, and β globulins (Figure 1). Only β2 microglobulin could be definitely identified, according to Laurell’s method (1). The

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electrophoresis on polyacrylamide gel showed a trace amount of protein in the urine (Figure 2). All of the proteins in the urine from this patient had a molecular mass lower than that of lysozyme ($M_r$ 14 300).

**Discussion**

The genesis of urinary proteins can be traced through their molecular masses (1–5). For example, glomerular proteinuria, which results from increased glomerular permeability, is characterized by large protein molecules ($M_r$ >40 000) in urine. Tubular proteinuria, on the other hand, reflects the failure of renal tubules to reabsorb small proteins ($M_r$ <12 000); therefore, the urinary proteins are mainly those of small relative molecular mass. A simple way to distinguish glomerular and tubular proteinuria is to measure the concentration of a small protein such as $\beta_2$-microglobulin in urine (7). An increase in its concentration or in its ratio to urinary albumin indicates tubular proteinuria. The absence of urinary $\beta_2$-microglobulin, on the other hand, suggests glomerular proteinuria. Because absolute quantification of urinary protein is not necessary for distinguishing between these two types of proteinuria (3), urinary protein electrophoresis is the preferred technique, because many protein fractions can be observed simultaneously.

In selective glomerular proteinuria, the major proteins in urine are albumin, $\alpha_1$-antitrypsin, and transferrin (1–5). In tubular proteinuria, the urinary protein fractions most frequently encountered are albumin, $\alpha_2$-microglobulin, and $\beta_2$-microglobulin (1–5). Thus albumin is consistently present in all kinds of proteinuria; not only is it present in serum in the highest concentration of any protein, but also its molecular size is near the glomerular filtration threshold without its being small enough for reabsorption by the renal tubules.

The rarity of the urine electrophoretic pattern seen in this case is evidenced by the absence of a similar pattern reported in the literature and in our own experience in the past 10 years. The physiological background discussed above explains why this pattern is so rare—but not why it may occur. In the case we encountered, many factors could contribute to the damage of renal function. In particular, both diabetes mellitus and hypertension are important causes of severe glomerular disease (5). Although no renal biopsy was performed to provide morphological evidence of glomerulosclerosis, functional tests certainly indicated that the patient had end-stage kidney disease—as shown by the bilateral stenosis of renal arteries, minimal creatinine clearance, increasing concentrations of serum urea nitrogen and creatinine, and decreased urine output. These data also suggest that the glomerular filtration rate might have so declined that practically no protein was being filtered through the glomeruli. The low-$M_r$ proteins probably leaked from the damaged renal tubules, perhaps secondary to analgesic abuse (5). That these low-$M_r$ protein fractions are not the same as those "glomerular fractions" that normally are filtered through the glomeruli is supported by the non-identity in electrophoretic mobility between the urinary and serum protein fractions (Figure 1). None of the major proteins of glomerular origin—albumin, $\alpha_1$-antitrypsin, and transferrin—was present in the urine specimens from this patient.

Although this electrophoretic pattern for urinary protein is rare, if our postulate of the pathogenesis is correct, and if clinical chemists and pathologists are aware of the clinical significance of this pattern, we expect that further cases will be discovered and the real mechanism of analbuminuria eventually fully elucidated.

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**References**


