Urinary erythrocyte morphology in acute glomerulonephritis

Recent reports emphasise the importance of examining the morphological features of erythrocytes in urine as an aid to determining their origin (glomerular or non-glomerular).¹⁻³ Finding pronounced distortion of the majority of the erythrocytes favours a glomerular origin and might be especially helpful for diagnosing glomerulonephritis in patients presenting without erythrocyte casts or proteinuria. In two recent blind controlled studies this test had a diagnostic specificity and sensitivity of over 90%.^{2,3} To our knowledge, however, no serial study of the morphological characteristics of urinary erythrocytes has been carried out in cases of acute glomerulonephritis. We present such a study in one case.

Case report

A 17 year old boy presented with gross haematuria four days after a pharyngeal infection, for which he had been given erythromycin. There was no oliguria, and physical examination showed only arterial hypertension. On admission the serum creatinine concentration was 239 $\mu\text{mol/l}$ (2.7 mg/100 ml), and a 24 hour urine collection yielded 2 g protein. Kidney biopsy (day 13) showed a diffuse exudative endocapillary proliferative glomerulonephritis with a coarse granular peripheral deposition of C3.

The diagnosis of acute infectious (poststreptococcal) glomerulonephritis was supported by a low serum C3 concentration (28 IU/l; 22 mg/100 ml) and an antistreptolysin O titre of 1250 MU/l. Throat and urine cultures were sterile. An intravenous pyelogram was normal. Bladder catheterisation was not performed. On discharge (day 21) the serum creatinine concentration was 177 $\mu\text{mol/l}$ (2.0 mg/100 ml) and one month later 87 $\mu\text{mol/l}$ (0.98 mg/100 ml). Proteinuria and hypertension had disappeared.

During his stay in hospital fresh clean voided morning urine was examined almost daily. Erythrocytes in uncentrifuged urine were counted in a Fuchs-Rosenthal chamber. Erythrocyte morphology was studied on the sediment stained with SediColor and using simple light microscopy, as described.⁴ Rare erythrocyte casts were observed consistently from the first day. The figure shows the changes in the total erythrocyte count and percentage of distorted (glomerular) erythrocytes.

Changes in urinary erythrocyte count (solid line) and percentage of distorted (glomerular) erythrocytes (broken line) in a case of acute glomerulonephritis.

Comment

This patient presented a typical picture of acute glomerulonephritis, with gross haematuria, erythrocyte casts, and proteinuria on admission. Nevertheless, during the first week the urinary erythrocytes showed predominantly conventional morphological appearances and the count decreased. Only from day 10 was there a clear cut change to a predominantly glomerular morphology, which persisted thereafter in more than 90% of the cells.

False negative results occur in a minority of cases of glomerulonephritis proved by biopsy.¹⁻³ In at least one study this was especially true in patients presenting with gross haematuria.⁵ We present the first serial study, showing an almost inverse relation between the severity of haematuria and the degree of morphological change. This observation emphasises the importance of repeated examination of

urinary sediment, which may help to avoid hasty decisions and unnecessary urological investigations in less typical cases.

The observation also argues against the hypothesis ascribing the erythrocyte distortion to physical disruption during passage through the glomerular basement membrane.² More probably the damage occurs in the distal nephron.^{2,3} Osmotic forces may be important, but phagocytosis of the erythrocytes by renal tubular epithelium has also been proposed.³ Such a process may be less efficient if erythrocytes are present in large numbers. This may explain our findings.

Phase contrast microscopy has been proposed as essential to observe the morphological changes of urinary erythrocytes.¹⁻³ We use an easier and cheaper technique which, in our experience, is more reliable than phase contrast examination.⁴

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(Accepted 7 June 1983)

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Meningitis due to beta lactamase producing type b *Haemophilus influenzae* resistant to chloramphenicol

Cases of meningitis due to strains of type b *Haemophilus influenzae* resistant to both ampicillin and chloramphenicol have been reported only in California¹ and Bangkok.² We report the first such case in Great Britain. The patient responded to treatment with co-trimoxazole and latamoxef (Moxalactam).

Case report

A previously healthy 2½ year old boy presented in January 1983 with a three day history of anorexia, drowsiness, vomiting, and fever. On the day before admission his family doctor had prescribed amoxycillin syrup. He had been admitted to this hospital twice before with fever and symptoms of upper respiratory tract infection. On examination he was found to be listless and dehydrated with a rectal temperature of 39°C. Neck rigidity and Kernig's sign were noted. Lumbar puncture confirmed the clinical diagnosis of meningitis, and treatment with intravenous chloramphenicol 300 mg every six hours (100 mg/kg/24 h) and ampicillin 500 mg every six hours was started.

His condition remained virtually unchanged until day 3, when, in view of reported resistance to the two antibiotics being used, treatment was changed to intravenous co-trimoxazole 6 mg/kg/24 h and latamoxef 600 mg every six hours. Thereafter his condition improved rapidly. From day 5 co-trimoxazole was given by mouth. On day 7 an urticarial rash and some blistering at the site of the infusion appeared and the intravenous latamoxef was stopped. Thereafter he made an uneventful recovery. Co-trimoxazole was continued for a total of 12 days. Follow up at six weeks did not show any sequelae.

MICROBIOLOGY

The initial sample of cerebrospinal fluid was turbid and contained 1.5 × 10⁹ white blood cells/l (94% polymorphonuclear leucocytes). Cerebrospinal

fluid protein and glucose concentrations were 0.7 g/l and 0.3 mmol/l (5.4 mg/100 ml) respectively (serum glucose concentration was 5.2 mmol/l (94 mg/100 ml), and Gram staining showed numerous Gram negative coccobacilli. Culture yielded a profuse growth of *H influenzae* type b, and this was sensitive to sulphamethoxazole, trimethoprim, and latamoxef and resistant to ampicillin and chloramphenicol by the comparative method of disc diffusion. Resistance to ampicillin was confirmed by demonstrating production of β lactamase (Intralactam Strip, Mast Laboratories). Resistance to chloramphenicol was reported the following day after it had been rechecked. A further sample of cerebrospinal fluid obtained on day 3 showed no change from the initial sample, but a sample obtained on day 4 (after treatment had been changed) contained only 0.435×10^9 white blood cells/l, and culture yielded no growth.

Minimum inhibitory concentrations of the drugs were ampicillin 128 mg/l, chloramphenicol 12 mg/l, and latamoxef 0.06 mg/l. An inoculum of 10^5 colony forming units was used, and the medium was Levinthal's. Chloramphenicol acetyltransferase production was shown by the method of Slack *et al.*³

Throat swabs were taken from family contacts but failed to yield a growth of *H influenzae*.

Comment

Although resistance of capsulate strains of *H influenzae* to ampicillin is now fairly common, resistance to chloramphenicol is rare. Only one case of haemophilus meningitis due to a chloramphenicol resistant strain has been reported in this country, and this strain was sensitive to ampicillin.⁴ As it is common practice to treat cases of haemophilus meningitis, at least initially, with a combination of ampicillin and chloramphenicol the isolation of a strain resistant to both of these agents has grave implications for future treatment. Prompt recognition of such resistance is important, and we believe that the method of Slack *et al* for the rapid demonstration of chloramphenicol acetyltransferase production should now be routinely applied to strains of *H influenzae* isolated from patients with meningitis.

We thank Dr D C Turk of the public health laboratory, Sheffield, for confirming the identity of the isolate, and Dr M P E Slack of the bacteriology department, University of Oxford, for determining the minimum inhibitory concentrations.

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(Accepted 15 June 1983)

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A fishy tale: trout borne *Aeromonas hydrophila* septicaemia

We report a case of septicaemia in a man receiving haemodialysis, from whom *Aeromonas hydrophila* was isolated from blood and a skeletal muscle abscess; the organism was also isolated from trout that had been prepared for him by his wife before helping him insert dialysis needles.

Case report

A 62 year old rector had been receiving haemodialysis for seven years for chronic renal failure. Three days after his last home haemodialysis he was admitted with severe loin pain, fever, rigors, diarrhoea, and vomiting. His history included polyarthropathy with subsequent analgesic nephropathy and multiple urothelial malignancies that had required extensive

surgery. Since starting haemodialysis he had had four episodes of fistula associated *Staphylococcus aureus* (phage type 29/79) septicaemia.

On examination he was confused with a uraemic flap, temperature was 39.5°C, and tender masses were palpable in the left loin, left quadriceps muscle, and above the fistula in his left forearm. White cell count was 20×10^9 /l. A clinical diagnosis of septicaemia with abscess formation was made and empirical treatment begun with intravenous ampicillin and flucloxacillin. The three soft tissue masses continued to enlarge and his condition worsened. After two days an oxidase positive, Gram negative rod was isolated from two blood cultures. It was resistant to ampicillin, carbenicillin, and azlocillin, sensitive to the aminoglycosides and trimethoprim, and was at first thought to be a pseudomonad; later it was identified as *A hydrophila*. Antibiotics were changed to intravenous gentamicin with rapid clinical improvement, and later to oral trimethoprim. One week later the masses in the leg and loin had resolved, but the mass in his left forearm had become fluctuant and required surgical drainage. *A hydrophila* with the same sensitivity pattern as the isolates from the blood was grown in pure culture from the 20 ml of pus obtained. Four days later he developed a vasculitic, purpuric rash that settled spontaneously over the next two weeks and his subsequent recovery was uneventful.

The patient recalled that his wife had prepared trout, obtained fresh from a fish farm, before helping him insert dialysis needles shortly before he became unwell. A second trout was obtained from the family freezer, one gram of its flesh homogenised in broth, and duplicate serial 10-fold dilutions of this subcultured to blood and MacConkey agars. The total aerobic bacterial count was 3×10^9 colony forming units/g, of which 1.5×10^9 were *A hydrophila*. Strains from the patient were identified as subspecies *hydrophila* but that from the trout as subspecies *anaerogenes*.

Comment

Septicaemia is the second most common cause of death in patients receiving haemodialysis¹ and is usually due to *Staph aureus* associated with fistula or shunt infections. *A hydrophila* is widely distributed in fresh and stagnant waters and is a well recognised pathogen of cold blooded animals. It has been reported as a rare cause of four syndromes in man: cellulitis or wound infection associated with exposure to water or soil, acute diarrhoea of short duration, septicaemia in immunocompromised patients, and various local conditions including surgical wound and urinary tract infections, meningitis, otitis media, peritonitis, and endocarditis.² In several reports *A hydrophila* septicaemia has been followed by metastatic abscess formation, particularly in skeletal muscle, and by the development of a vasculitic rash similar to the ecthyma gangrenosum of *Pseudomonas aeruginosa* septicaemia.

The oxidase positive *A hydrophila* is frequently mistaken for *Ps aeruginosa* on initial isolation, but it is usually resistant to the anti-pseudomonal penicillins such as carbenicillin and azlocillin by virtue of a β -lactamase.³ Two other reports of *A hydrophila* sepsis in home dialysis patients suggested contamination of the dialysis equipment or contact of recently used vascular access sites with flood water as sources of infection, but results of environmental cultures in these cases were negative.^{4,5} In our patient organisms were almost certainly transferred from the fish to the patient's fistula when his wife was inserting the dialysis needles. It seems unlikely that *A hydrophila* survived grilling, although the history of diarrhoea makes the enteric route of infection a possible alternative.

We thank Dr A L Furniss, of the Public Health Laboratory, Maidstone, for biotyping the organisms and Dr A J Wing for permission to report this case.

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(Accepted 10 June 1983)

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