ULTRASTRUCTURAL APPEARANCES OF NEPHRON DAMAGE IN ACUTE POISONING WITH ETHYLENE GLYCOL

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Summary

Renal biopsy material from five patients with acute ethylene glycol poisoning was taken five, 10, 16 and 22 days following poisoning and examined by electron microscopy. We found extensive crystal deposits in glomerular interloop spaces. In some of the tubules crystal accumulation seemed independent of time following poisoning. No morphological markers of reabsorption were found in the tubules tightly filled with crystals, while tubules with empty lumen had signs of enhanced reabsorption. In the early period of poisoning there were signs of epithelial damage while in the late periods, signs of epithelial regeneration prevailed. The results provide new information on the pathogenesis of anuria in acute poisoning with ethylene glycol.

Introduction

Recent investigations on renal structural changes induced by ethylene glycol poisoning have revealed renal tubular injuries appearing mainly as hydropic and vacuolar degeneration in the convoluted tubules [1–6]. Large numbers of calcium oxalate crystals were also found within the tubule lumen, leading to partial or total obstruction [1–6]. Renal glomeruli were either unchanged [1,2,4] or insignificantly so [3,5], although Siew [6] described substantial changes. Observations on the renal interstitium were equivocal, some investigators found no changes [1,2,4], while others observed oedema [3] and inflammatory foci [5,6]. Most investigations of the kidney in acute poisoning by ethylene glycol (APEG) have been primarily concerned with its histology [1–5] and only few reports on renal ultrastructure have appeared.

We evaluated ultrastructural changes in the kidney in patients who survived APEG. Renal biopsy was performed at various times following the poisoning, enabling us to assess changes in early periods as well as late.
Material and methods

Renal biopsy specimens were taken once from each of five patients at five, 10, 16 and 22 days following APEG. Biopsy material was fixed in 0.2M cacodylate buffer with 2.5 per cent glutaraldehyde and two per cent paraformaldehyde (pH 7.4) for three hours then, postfixed in two per cent osmium tetroxide for two hours. After dehydration the tissue specimens were embedded in Araldite, cut into ultra-thin sections and examined with a Philips EM 300 transmission electron microscope.

Results

Renal glomeruli

Electron microscopy revealed clearly encapsulated flocculent deposits of amorphous material of low electron density within the mesangium. The podocyte cytoplasm was thinned with a substance of similar consistency. The glomerular basement membrane was formed into layers filled with the same homogenous flocculent material. The parietal lamina of the Bowman’s capsule was thickened in most cases (Figure 1).

Figure 1. The encapsulated flocculent deposits (d) of amorphous material within the mesangium, x 6300 (reduced for publication)
Renal tubules

The lumina of the proximal and distal tubules were tightly filled with deposits; they were observed at all times, five to 22 days (Figure 2). On day five cytoplasmic vacuolisation was noted on the luminal side of the tubular cells. The cytoplasm formed thick spike-shaped protrusions devoid of microvilli, which subsequently became detached into the lumen. The tubular lumen was filled, sometimes tightly, with desquamated cell fragments or whole cells (Figure 3).

As in the glomeruli, deposits of amorphous material, consisting of several separate encapsulated units, were also noted within the proximal and distal tubular lumina.

In the interstitial tissue the deposits were found in the intercellular exudate and were not encapsulated. Sometimes they were located within the tubular basement membrane, rendering it thickened and formed into many layers. Similar amorphous deposits were also found within vascular lumina.

Varying degrees of distension of intervillous and intercellular spaces, as well as in spaces between parabasal invaginations, occurred. In tubules with the lumen or intercellular spaces closed by crystals, the spaces were reduced to a minimum. On the other hand, in the unchanged areas they were markedly distended and

Figure 2. The lumina of the proximal tubules are tightly filled with crystals (c). The basement membrane is formed into layers filled with the same flocculent material, x 5000 (Reduced for publication)
vacuolisation was increased, particularly in the proximal tubules. The renal glomeruli as well as the interstitial tissue between the renal tubules contained blood cells and plasma cells.

In the distal and proximal tubular cells and to a lesser extent, in the podocytes, lysosomal activity was increased as manifest by increased vacuolisation of the Golgi apparatus and formation of primary lysosomes. Also numbers of secondary lysosomes, phagolysosomes and multivesicular and residual bodies were increased. The tubular epithelial cells were injured to varying degrees.

In biopsy material taken later in the course of APEG numbers of patent renal tubules, cleared from deposits, were increased. They were accompanied by epithelial cell desquamation and replacement by regenerated cells.

Amorphous deposits were removed from the interstitial tissue earlier than from the tubular lumen. In the intercellular spaces of the connective tissue electron-lucent exudate with flocculent suspension appeared at the beginning and increased in the course of time, replacing encapsulated homogenous deposits. The lysosomal activity started increasing from day 10 and continued to the end of the observation.

**Discussion**

Renal biopsy material taken from five to 22 days following APEG enabled evaluation of acute as well as late ultrastructural changes accompanying acute
renal failure. Amorphous deposits observed on electron microscopy corresponded with reported calcium oxalate and carbonate crystals [6]. Also the location of calcium oxalate deposits was similar to those reported with other techniques [6]. Calcium oxalate crystals exerted mechanical and toxic effects on the surrounding tissue. Extensive glomerular interloop oxalate deposits compressed the podocytes and reduced their intervillous spaces. Of importance is the fact that the crystals persisted until 22 days following APEG. In the tubules tightly filled with crystals, no morphological evidence of reabsorption was found, while the distension of parabasal and intercellular spaces in the uninjured areas suggested a compensatory increase in tubular reabsorption.

In the early period of APEB, there predominated compression of tubular cell microvilli by crystals, and their toxic effects on tubular cells, leading to pathologic protrusions, desquamation and necrosis of the epithelial cells. In the later period, regeneration of the tubular epithelium and disappearance of interstitial exudates prevailed.

These electron microscopic observations throw new light on the pathogenesis of anuria in APEG while the presence of crystal deposits in renal tissue as late as after 22 days must have therapeutic implications.

References

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