A New Concept of the Mechanism of the so-called Uraemic Lung Syndrome

Z AJEWSKI, A WASIUTYŃSKI and T ORŁOWSKI
Warsaw Medical School, Warsaw, Poland

The aim of this study was to find out whether experimental uraemia without accompanying overhydration, left ventricular failure or arterial hypertension could result in the appearance of the pulmonary changes of the radiological and clinical entity known as 'uraemic lung'.

MATERIALS AND METHODS

Fifteen dogs were studied of which 9 constituted Group I, in which morphological studies were conducted at the peak of uraemia. In 2 dogs (Group II) morphological investigations were carried out after regression of symptoms of uraemia. Group III consisted of 2 dogs subjected to surgical procedure, exactly as in Groups I and II, but without producing uraemia. Group IV comprised 2 healthy dogs, and in these only morphological investigations were carried out. As a model of uraemia the procedure of Yullis, Morrin and Bruce (1965) was chosen. This consists of inducing infarction of 3/4 of the parenchyma of the left kidney, establishing a ureteroduodenal anastomosis on the right side and inserting a Pezzer's catheter into the pelvis of the right kidney through the renal parenchyma and letting out the other end through the abdominal wall (Figure 1). No tests were performed for 14 days following this procedure. Later, control measurements were made of haematocrit, haemoglobin, urea, creatinine, sodium, potassium, chloride, bicarbonate, and arterial pH, Pco₂, and Po₂ (Homolka, 1958; Orłowski, 1961; Tuleczyński, 1962). Next, cardiometric studies were performed under general anaesthesia with the use of Courmand catheters Nos. 8 and 9, inserted through the carotid vein to the right atrium, right ventricle and pulmonary artery, and through the femoral artery to the aorta and the left ventricle of the heart. Blood pressure measurements were made by means of an Elema-Schönander electromanometer. Blood flow was determined by the dye-dilution method using indocyanin green. Recordings of dilution curves were obtained with the use of a photocell, and a recording apparatus (Kipp). Calibration of the system
was carried out before each measurement. The area under the dilution curve was measured with a polar planimeter (Luisada, 1965; Sparling et al, 1960; Zijlstra & Mock, 1962). One day after heart catheterisation, a plug was inserted into the external outlet of the Pezzer’s catheter diverting the urine outflow into the duodenum. On the 7th, 10th and 14th day the entire series of biochemical tests was repeated and in cases where the urea level in the blood was 300 mg/100 ml or more the cardiometric tests were also repeated. On the following day the dogs in Group I were killed. The dogs of Group II were sacrificed after allowing the biochemical parameters to become normal. The dogs belonging to Group III were killed 4 weeks after the surgical procedures. All dogs were sacrificed by a rapid injection of 10g KC1 into the vein of the front limb, thereby causing sudden death.

Tissue samples for morphological examinations were obtained from numerous regions of the lungs (Figure 2) and immediately placed into fixative. Material for electron microscopic examination was fixed in cold glutaraldehyde and stained in 2% solution of osmium tetroxide. It was dehydrated in alcohol and acetone and embedded in Epon. In 6 dogs a Hale reaction test was done directly after fixation in glutaraldehyde for the purpose of visualising
the lining film of the lung alveoli (Groniowski & Biczyskowa, 1964). Histological and histochemical examination was carried out on material fixed in buffered formalin and embedded in paraffin. Granular cells (pneumocyte II) were best seen when stained with Astra Blue at pH 0.25. Granular cells were counted in the field of vision of a light microscope at magnification x 600, avoiding areas of great atelectasis and emphysema. At least 10 fields of vision were counted in each section and at least 10 sections from different regions of the lung were examined. Results were evaluated statistically by determining the arithmetic mean and standard deviation. In an attempt to evaluate the lining film quantitatively, the areas of most intense reaction in a section selected at random were photographed at a magnification of x20,000, and arranged in a scheme from the area showing the most intense to the area showing the weakest reaction.

RESULTS

In all dogs of Groups I and II symptoms of biochemical uraemia were induced, with an elevated blood level. No significant differences were observed regarding the creatinine, sodium, and chloride levels. The potassium level was high but did not exceed 6 mEq/l. The bicarbonate level was low, but never below 15 mEq/l. No significant differences were noted regarding pH or Pco2. Only a slight decrease of Po2 was noted. The results of haemodynamic investigations were analysed mainly with a view to confirming or excluding circulatory insufficiency and in order to examine the blood pressure in the pulmonary and systemic circulation during uraemia as compared with the values before uraemia. The pressure in the right atrium, in particular the mean pressure, did not alter and was normal before uraemia as well as at the peak of uraemia. Diastolic pressure in the right ventricle was normal throughout.
Figure 3. Granular cell at the beginning of uraemia. Lamellar structures are quite well preserved (arrows). x 20,000

Figure 4. Granular cell in advanced uraemia with lamellar structures having the 'empty' appearance or showing diminished osmiophilic properties. x 20,000
Diastolic pressure in the left ventricle, especially in the last phase of diastole, was also normal. These results indicated that the right and left ventricles of the heart continued to function properly during the course of uraemia.

No changes were observed in the weight of the dogs.

On gross examination a region of peripheral emphysema was observed, as well as diminished inflation of parenchyma in the perihilar region of the lung. In the group of dogs with uraemia histopathological sections confirmed the existence of peripheral emphysema and showed the presence of foci of atelectasis in perihilar regions. In the atelectatic tissue there were very few lymphocytes or monocytes. In some alveoli there were single macrophages. However, neither extensive oedema nor hyaline membranes were encountered.

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![Figure 5. Hale reaction.](image)

A. A dog with uraemia. Intense reaction is evident only in the first micrographs in form of black lining on the epithelial surface. In other micrographs there is complete lack of the reaction.

B. Control dog. In all micrographs there is a uniform, thick layer of Hale positive substance in form of black lining on the epithelial surface. x 20,000
The number of granular cells was more or less the same in topographically different regions of the lung. A diminished number of granular cells in the microscopic field was observed in the dogs with uraemia as compared with the control group. Examination of electron microscopic sections prepared by the osmium method detected changes in the granular cells consisting mainly of a decrease of osmiophilic lamellar structures or even of their complete disappearance (Figures 3 and 4).

In electron microscopic sections prepared according to the Hale method a decrease was noted in the amount of Hale positive substance on the lamellar structure of granular cells and on the surface of the alveolar epithelium of the lung compared with the control group (Figures 5 and 6).

The electron microscope investigation outlined above was mainly concerned with structures that are thought to participate in the regulation of the surface tension of lung alveoli. In the control groups (III and IV) of 4 dogs operated according to the method of Yulis et al (1965) none of the abnormalities discussed above were encountered.
CONCLUSION

The cellular apparatus responsible for the production of the substance controlling the surface tension of lung alveoli seems to have a significant influence on the pathological mechanism of pulmonary changes in the course of experimental uraemia.

REFERENCES

Yulis, G. P., Morrin, P. A. and Bruce, A. W. (1965) Journal of Urology, 93, 37