Discussion

Termination of pregnancy with abortifacient paste appears at first to be a satisfactory method. The points in its favour are ease of insertion, usually without a general anaesthetic, and the possibility of evacuating the uterus up to 20 weeks of gestation without opening the abdomen. Lachelin and Burgess (1968) claimed that there is no need for routine curettage, but this was done in the present series. The pain during abortion, in my opinion, is much greater than the pain of a spontaneous abortion. However, the complications which might occur are not rare and often are severe and even fatal. In our experience this method has proved so unsatisfactory that it has been abandoned.

I wish to thank all the consultants in the department of obstetrics and gynaecology for permission to report on cases under their care.

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MEDICAL MEMORANDA

Heparin-treated Haemolytic-Uraemic Syndrome Simulating Fabry's Disease

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Giromini and Laperrouza (1969) reported a case of the haemolytic-uraemic syndrome with intractable malignant hypertension requiring bilateral nephrectomy. We here report a similar case where prednisone and heparin produced only temporary improvement and may have been responsible for unusual histological changes. Renal transplantation was carried out a year later.

Case Report

In July 1969 a boy aged 12 developed a swelling of the face, vomiting, abdominal pain, and a purpuric rash and passed dark scanty urine. Examination at Torbay Hospital showed anaemia (Hb 10·0 g falling to 6·0 g/100 ml), thrombocytopenia (23,000/mm^3), and uraemia (400 mg/100 ml). A presumptive diagnosis of haemolytic-uraemic syndrome was made, and on the patient's transfer to us the diagnosis was supported by a finding of 8 nucleated red cells per 100 white cells and numerous schistocytes in the blood film and the presence of methaemalbumin in the serum. Heparin (Piel and Phibbs, 1966) 20,000 units daily by continuous intravenous injection was started immediately. After six weeks this was increased to 24,000 units for a further four weeks. Renal biopsy could not therefore be performed at this stage. The uraemia was controlled by a high-calorie, low-salt, low-protein diet, with one peritoneal dialysis and subsequent haemodialyses (twin coil) through a Scribner arteriovenous shunt (Fig. 1). Prednisone (60 mg/day reducing to 30 mg/day after three weeks) was given by mouth from the third day. After six days and three dialyses the urinary output began to rise, and after two weeks was 2 litres/day. At the beginning of this phase the serum cholesterol was 700 mg/100 ml.

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One month after admission the urine output decreased and uraemia and hypertension (175/135) returned, with epileptic fits, papilloedema, and retinal exudates and haemorrhages. Dialysis failed to control the hypertension, retinopathy, and fits. The platelet count remained below 150,000/mm^3 and the haemoglobin fell to 7·5 g/100 ml. Bilateral nephrectomy was performed on 1 October 1969 and thrice-weekly dialysis instituted. In October 1970 a kidney from the patient's father was transplanted into the patient by Professor R. Y. Calne at Cambridge. After the nephrectomy the blood pressure was easily controlled, the serum cholesterol levels ranged between 282 and 344 mg/100 ml, and platelet counts exceeded 300,000/mm^3. No evidence of lipidosis was observed by slit-lamp examination of the cornea or on bone marrow examination.

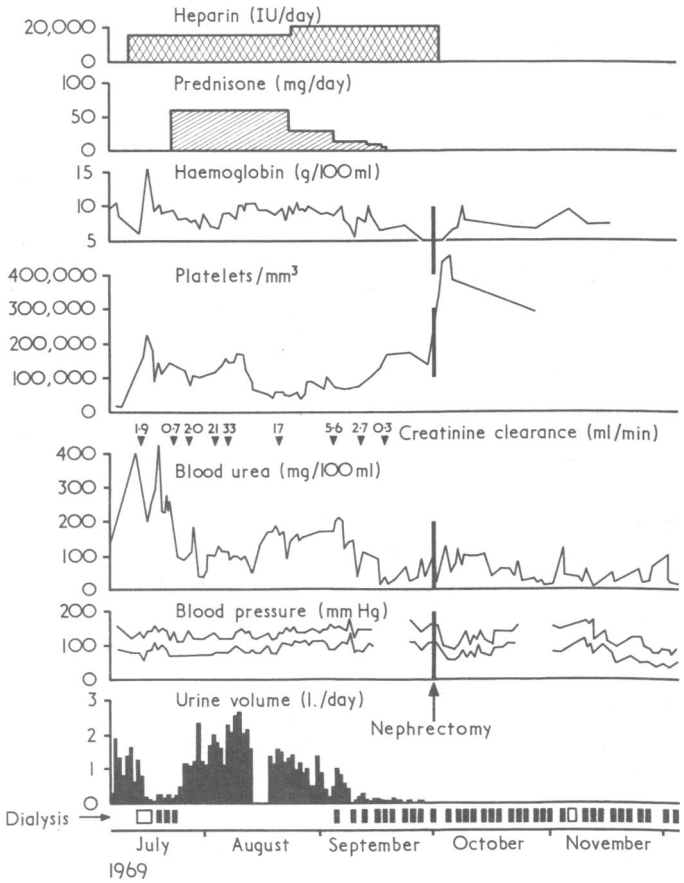

FIG. 1—Clinicopathological course. □ = Peritoneal dialysis. ■ = Haemodialysis through arteriovenous shunt.

PATHOLOGICAL FINDINGS

The left kidney measured 9 by 5·5 by 3·5 cm and the right 9·5 by 5 by 4 cm. The capsules stripped easily, leaving a smooth surface. The cortices were orange-yellow, in sharp contrast to the grey, semi-translucent appearance of the pyramids. The renal pelves were slightly small and contracted. The principal histological changes were found in the glomeruli and interlobular arteries. Many glomeruli showed only general ischaemic fibrillar thickening of mesangial tissues. In a considerable number, however, there were large cells showing conspicuous foamy vacuolation (Fig. 2), and

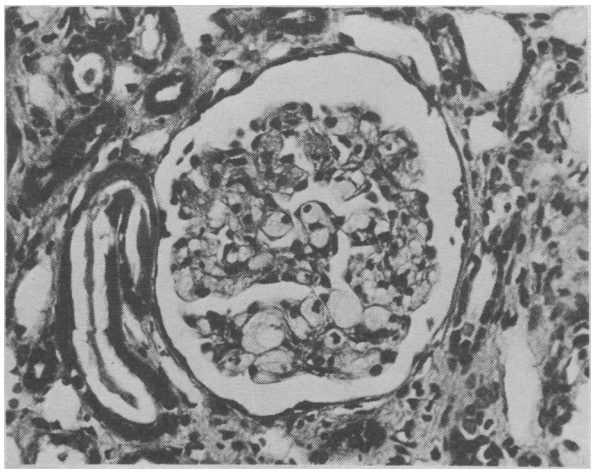

FIG. 2—High-power view of glomerulus stained with haematoxylin and eosin. The tuft shows a "honeycomb appearance" due to intracellular cytoplasmic lipid accumulation.

a few had capsular adhesions. There was alternating atrophy and hypertrophy of the convoluted tubules, many of which contained protein material. Foamy cells were present in a few proximal tubules and a few showed lipofuscin granules. The larger blood vessels were normal, but the intima of the interlobular arteries were greatly thickened by an accumulation of large foamy macrophages and free fat globules, which were also present to a less extent in the media (Fig. 3). The smaller and afferent arterioles,

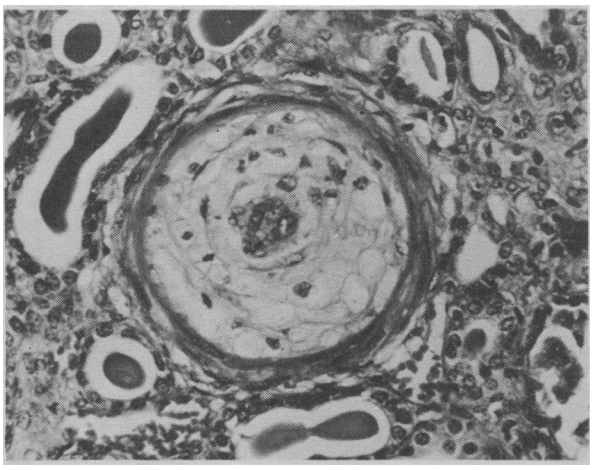

FIG. 3—High-power view of an interlobular artery stained with haematoxylin and eosin. The lumen is very severely narrowed by the presence of lipid-laden macrophages within the intimal and medial coats.

though damaged, were much less affected, and many appeared almost normal. No extension into tuft capillaries was seen.

Histochemical tests were performed on the glomeruli, tubules, and blood vessels. In all three areas the droplets stained positively with Sudan black, developed liquid crystalline anisotropism in polarized light, were orthochromatic with cresyl violet, and reacted moderately positively with the modified periodic-acid Schiff method (negative in the chloroform-methanol extraction). Fibrin stains were negative in the glomerular tufts and mainly negative in the intimal thickenings. There was no evidence of elastic reduplication in the small arteries. These features were strongly suggestive of Fabry's disease. Comparative figures for the biochemical composition and results of thin-layer chromatography are given in the Table.

Thin-layer chromatography showed additionally normal ceramide hexoside pattern, no increase in ceramide dihexoside or trihexoside, and normal ganglioside pattern (usual GM_3 band only). The normal ceramide dihexoside and trihexoside findings made a diagnosis of Fabry's disease untenable, and after histochemical tests it was reported that glomerular lipid accumulations showed a positive reaction for cholesterol (PAN), and patchily for cholesterol esters (OTAN black) and phospholipids (OTAN red). This brought the histochemical analysis into conformity with the finding on biochemical analysis of a large increase of cholesterol esters in the renal tissue. No excess of either ceramide dihexoside or trihexoside was found in 24-hour specimens of urine of the mother, father, or two brothers.

Comment

We believe the heparin treatment may have caused the unusual histological findings identical with those seen in Fabry's disease (glycolipid lipidosis, angiokeratoma corporis diffusum) by light microscopy. The boy developed hypercholesterolaemia, possibly as a result of dialysis (Tsaltas and Friedman, 1968) and corticosteroids. Heparin activates the lipoproteinlipase system, releasing free fatty acids into the plasma, and in the presence of vascular damage this free fatty acid may have been incorporated into the vessel walls in excessive amounts. The previously expressed fear that renal transplantation would be unsuccessful in the haemolytic-uraemic syndrome (Clarkson *et al.*, 1970) was not borne out in this case.

We would like to thank Dr. L. Haas, Torbay Hospital, Devon, for referring the patient; Professor J. N. Cummings for the biochemical analysis of kidney tissue; Professor C. W. M. Adams for the lipid histochemical studies; and the staffs of the artificial kidney unit, Whipton Hospital, Area Department of Pathology, Exeter, and the pathology department of Torbay hospital for their invaluable help. The photomicrographs were enlarged by Mr. C. Dyson.

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Comparative Figures for Biochemical Composition and Results of Thin-layer Chromatography

	Unfixed Normal Kidney	Fixed Fabry Kidney	Fixed Kidney of Patient
Total hexose (g/100g of dry tissue)	1·53	17·36	1·47 (as galactose)
Total cholesterol (g/100g of dry tissue)	1·50	2·07	1·92
Ester cholesterol (g/100g of dry tissue)	0·07	0·18	0·64
Ceramide dihexoside (%)	11·3	26·3	10·98
Ceramide trihexoside (%)	44·9	69·1	38·66 (as sphingosine)
Ceramide Tetra hexoside (%)	43·7	4·4	49·36