CASE REPORTS

PYELONEPHRITIS, MALIGNANT HYPERTENSION AND ULCERATION OF SMALL INTESTINE IN A CHILD

BY

J. EDGAR MORISON, M.D., B.Sc.

Department of Pathology, Queen's University, Belfast, Northern Ireland

Cases of arteriosclerosis in childhood have been reported frequently and an excellent review with a discussion of two cases was given by Guild, Kindell and Gibson (1938). Recently the relationship of pyelonephritis to arteriosclerosis at all ages was emphasized by Weiss and Parker (1939), and this association in childhood has been reviewed by Kimmel (1942). Detailed records of single cases are now probably superfluous, but a case of chronic pyelonephritis developing malignant hypertension and arteriolonecrosis, and dying with extensive ulceration of the small intestine secondary to vascular lesions, presented certain interesting features. The relationship of these lesions is not yet widely appreciated by clinicians and pathologists and merits further study and discussion.

Clinical history. Six months before death the patient, a girl then aged twelve years, started to complain of severe headaches. One month later she was admitted to hospital. A trace of albumin and a few red blood cells were found in the urine and the blood urea was 80 mgm. per 100 c.c. One of two specimens of urine gave a growth of enterococci. A skiagram of the chest revealed nothing abnormal and the blood pressure was not recorded. She went home, but lost weight and became paler and was re-admitted three months before death. She still suffered from headaches of increasing severity and frequency. There was now slight oedema, the blood urea was 138 mgm. per 100 c.c. and the urine contained no pus or organisms, but continued until death to show a little albumin and some red blood cells. The blood Wassermann reaction was negative and a lumbar puncture revealed no abnormality. No record was made of the blood pressure. With rest the oedema disappeared and the blood urea fell, to fluctuate between 60 and 70 mgm. per 100 c.c. until death.

Though some complaint of abdominal pain was made four days before death there was no rigidity of the abdominal wall and no blood was noted in the stools. The patient gradually became more toxic and semi-comatose and died.

Post-mortem findings. The following is the anatomical summary of the findings after histological examination of all the organs. Only the more essential features will be described in further detail:

Bilateral chronic pyelonephritis with hyperplastic proliferative renal arterio- and arteriolo-sclerosis:

chronic ureteritis and cystitis. Hypertrophy of left ventricle: arteriosclerosis and early arteriolonecrosis in the adrenals, pancreas, spleen and stomach: arteriosclerosis and marked arteriolonecrosis small intestine with multiple mucosal ulcers and localized fibrino-purulent peritonitis. Slight dwarfism (3 ft. 10 in.: normal 4 ft. 10 in.) without renal rickets or parathyroid dystrophy. Small areas of organized, unresolved pneumonia. Chronic venous congestion of lungs and slight splenic fibrosis. Chronic cholecystitis and cholelithiasis. Calcified primary tuberculous complex right lung.

KIDNEYS AND URINARY BLADDER. Both kidneys were small and the left weighed 15 gm. and the right 30 gm. The capsule was removed with difficulty, especially from the surface, over many deep scars. Everywhere its removal left a coarsely granular surface. The cortex was very narrow and often indistinguishable, and ill-defined and pale yellowish-white areas as well as several larger scars distorting the renal architecture. The pelves were not dilated and their lining epithelium was smooth. The ureters were thick walled and more patent than usual. There was no trabeculation or thickening of the bladder musculature and the lining epithelium showed no abnormality. The ureters opened normally and there was no obstruction in the urethra.

INTESTINAL TRACT. Loops of small intestine, especially the ileum, were loosely adherent to one another by a fibrinous exudate. This reaction was related to areas where the intestinal wall was eroded,

FIG. 1.—The mucosal ulcers in the anti-mesenteric border of the ileum.

but not completely perforated, by small, circular ulcers extending into the muscle from the mucosa (fig. 1). These ulcers lay in the anti-mesenteric segment of the bowel wall and few reached one centimetre in diameter. Seen from the mucosal aspect the ulcers and their surrounding zone of congestion and non-ulcerated areas of brown or gray diphtheritic membrane were sometimes confluent over ten to twenty centimetres of the anti-mesenteric border of the ileum. The mesenteric lymph glands and the lymphoid follicles of the bowel were not enlarged. The large intestine and the stomach showed congestion of the mucosa but no ulceration.

Microscopic examination.

KIDNEYS. In some areas the whole width of the

hyalinization and no fibrin or red blood cells disorganized the vessel walls (fig. 4).

ILEUM. Sections through the ulcers showed that these only rarely extended into the circular muscle coat. Necrotic fibrin, red blood cells and disintegrating polymorphonuclear leucocytes formed their floor. The submucosal tissue round an ulcer and usually all the muscle layers deep to it were oedematous and infiltrated by acute inflammatory cells and fibrino-purulent exudate lay on the adjacent serosa. Round the margin of the ulcers and forming the areas of diphtheritic membrane there were fibrin, red blood cells, polymorphonuclear leucocytes and the remains of the mucosal epithelium. The underlying submucosa was grossly congested and

FIG. 2.—The capsule is adherent to a pyelonephritic scar and surviving renal elements are grossly distorted and fibrous tissue increased.

kidney was atrophic and consisted only of tubules filled with colloid, lined by flattened epithelium and separated by fibrous tissue infiltrated by lymphocytes and a few plasma cells. Glomeruli were present only as hyalinized masses. In other areas (fig. 2) some renal tubules were larger and more dilated than normal, but many were atrophic and there were no entirely normal tubules. Here glomeruli were sometimes normal, but they often showed changes ranging from fibrosis around Bowman's capsule to complete hyalinization of the tuft and capsular tissues. They showed no epithelial proliferation and no adhesion of the tuft to the capsule. Even in these areas fibrous tissue was prominent, especially in the medulla between the larger collecting tubules. Inflammatory cells in the interstitial tissue were almost entirely mononuclear leucocytes. Similar cells were present in the sub-epithelial tissue of the renal pelvis and ureter and here fibrous tissue elements were replacing muscle fibres. Throughout the kidneys arcuate and interlobular arteries showed extreme proliferation of well formed and concentric elastic laminae (fig. 3). In the arterioles there was often considerable cellular proliferation and thickening of the wall, but there was little

FIG. 3.—A collection of arteries showing proliferation of internal elastic laminae. Elastin stain.

oedematous. Arterioles showed marked hyaline thickening of their wall and narrowing of their lumen, while fibrin and even red blood cells were often found in their wall. These arteriolonecrotic changes were not confined to the areas of reaction

FIG. 4.—Arterioles narrowed by concentric cellular proliferation.

around the ulcers, but were also present, though to a lesser extent, in areas free from ulceration or mucosal inflammation.

THE INTIMATE VASCULATURE OF OTHER ORGANS. The walls of the arterioles of the pancreas, spleen, stomach, large intestine and adrenals were grossly thickened, sometimes by concentric cellular proliferation, but more often there was extensive hyalinization and sometimes fibrin was present in the wall. In the arteries there was no proliferation of the intima and no fibrosis of the media.

Discussion

In the past many cases of pyelonephritis have been misinterpreted both by clinician and pathologist. In chronic pyelonephritis the passage of organisms and pus cells may be slight and intermittent, and inadequate histological examination of small blocks of tissue taken at autopsy has often attributed the scarred and contracted kidneys to chronic glomerulonephritis or to benign or malignant hypertension. Even histological differentiation may be extremely difficult, but the coarse and more focal scarring of the kidney, the invasion of cortex, medulla, pelvis and even capsule by fibroblasts, lymphocytes, plasma cells and polymorphs are features favouring a pyelonephritis. It is doubtful if Weiss and Parker are correct in regarding colloid casts in the tubules as pathognomonic of pyelonephritis. In pyelonephritis, as in arteriosclerosis, all the glomeruli lying in large focal aggregates arranged at right angles to the capsule tend to be involved to much the same extent. The diffuse and varying involvement of glomeruli scattered throughout the kidney as seen in chronic nephritis is absent and adhesions of the tuft to the capsule are exceptional. Acute necrotic lesions in arterioles are not seen. In chronic pyelonephritis the arteries show gross proliferation of internal elastic laminae, and in the arterioles cellular hyperplasia without hyaline change narrows the lumen. Weiss and Parker maintain that these changes are the result of inflammatory changes in the tissues around the vessels and that they are to be distinguished from those secondary to parenchymatous atrophy. They believe that pyelonephritis often produces generalized hypertension, and they found in a large series of cases that the extent to which hyperplastic changes in the renal vessels were developed could be correlated with the development of clinical hypertension. They emphasize that in cases with hypertension the vascular changes are diffuse throughout the kidney and not confined, as in uncomplicated pyelonephritis, to areas of gross post-inflammatory scarring, and that vascular lesions in the kidney are in excess of those elsewhere in the body.

In the present case there is unequivocal histological evidence of chronic pyelonephritis. Though no blood pressure readings are available the hypertrophy of the left ventricle in the absence of valvular lesions, and the widespread arteriolosclerosis are satisfactory evidence of hypertension. The escape of fibrin and red blood cells into the walls of

arterioles, especially those of the intestinal tract, suggests that there was a malignant termination to this hypertension. The proliferative lesions narrowing the lumen of the renal arteries and arterioles are diffuse throughout the kidneys and in excess of those elsewhere in the body. Weiss and Parker would regard the renal vascular changes as secondary to pyelonephritis, probably exaggerated somewhat by the resultant hypertension. It may be possible, as they claim, to predict the occurrence of hypertension from the extent of the narrowing of the renal vessels alone. It is an attractive speculation to consider that the reduction of the lumen of these vessels by the proliferative reaction, secondary to the inflammation of pyelonephritis, proceeds in advance of the loss of renal parenchymatous tissue. The resultant ischaemia of renal tissue might then lead to a hypertension comparable to that following narrowing of the renal artery by a clamp as in the classical experiments of Goldblatt. In growing children the fibrosed kidney with its damaged vascular system cannot develop with the growth of the child. This is paralleled by the experiments of Drury (1938). He encircled, but did not constrict, the left renal artery of young rabbits with a ligature. With the growth of the animals hypertension developed, and this was exaggerated by the renal insufficiency which followed removal of the right kidney. The development of hypertension in a patient will depend on the amount of functioning renal tissue surviving as well as on the establishment and maintenance of a delicate balance between ischaemia and death in the kidney tissue supplied by the narrowed vessels. Pyelonephritis may be accepted as responsible for a high percentage of the few cases of hypertension in childhood and must always be excluded in such cases. In adults it is more difficult to decide how far a co-existing pyelonephritis is responsible for the initiation of hypertension and not merely an incidental association.

In this case a feature of considerable interest is the ulceration of the small intestine in the absence of uraemia.

Fishberg (1939) describes ulceration and necrosis as a complication of uraemia and does not consider it apart from uraemia as a complication of hypertension. Several case reports of hypertension without uraemia in childhood describe, but do not discuss, intestinal lesions similar to those of the present case (case 11 of Weiss and Parker and case 1 of Guild et al.). Jaffe and Laing (1934) found ulceration in 27 of 136 cases with blood urea varying from 50 to 250 mgm. per 100 c.c. They quote Siegmund, who was inclined to associate uraemic intestinal necrosis and ulceration with lesions of the arterioles. They found, however, that vascular necroses were always in close proximity to the necrosis of the mucosa and regarded them as secondary and as comparable to the arteriolar necroses of dysenteric ulceration. They regard the uraemic necrosis and ulceration as secondary to haemorrhages from small blood vessels the permeability of which is altered by some substance in the blood associated with the uraemia. In the

present case submucosal haemorrhages very probably preceded the ulceration, but they were secondary to arteriolar lesions like those studied by Goldblatt (1938) in the intestine of dogs with experimental malignant hypertension.

The case provides no direct evidence as to whether a toxic factor retained by damaged kidneys is necessary for the development of arteriolonecrosis as well as a high intra-lumen bursting tension. It is interesting to note that the arterioles in the kidney itself have been protected from necrosis by the proliferative changes narrowing the arteries, and this may be compared to the similar protection of the renal arterioles by the clamp narrowing the renal artery in Goldblatt's hypertensive dogs.

The patient was 12 inches under the normal height for her age. Ellis and Evans (1933) describe rickets, dwarfism and infantilism as secondary to renal insufficiency in childhood. All of these were not necessarily present in any one case. Histologically there was no irregularity of the epiphyseal junctions in the present case and she was too young to show genital infantilism. Most of the cases of Ellis and Evans were due to bilateral hydronephrosis with or without infection. Usually no organic lesion was demonstrable in the urethra, the bladder was dilated and a sphincteric imbalance was postulated. In the present case the cause of the pyelonephritis is obscure and there was no bladder outlet obstruction.

Between her first and second admission there was some cardiac decompensation as shown by the slight oedema and the high blood urea of 138 mgm. per 100 c.c. This improved with rest, but slight chronic venous congestion of the lungs and fibrosis of the spleen persisted. The small areas of unresolved pneumonia probably date from about the time this decompensation was most apparent, and some such infection may have contributed to its development.

Summary

Malignant hypertension in a child of twelve years followed chronic pyelonephritis. Ulcers in the ileum secondary to hypertensive lesions in the arterioles produced a terminal peritonitis.

REFERENCES

- Drury, D. R. (1938). *J. exp. Med.*, **68**, 693.
 Ellis, A., and Evans, H. (1933). *Quart. J. Med.*, **2**, 231.
 Fishberg, H. (1939). Hypertension and nephritis, London.
 Goldblatt, H. (1938). *J. exp. Med.*, **67**, 809.
 Guild, H. G., Kindell, F. B., and Gibson, T. A. (1938). *Johns Hopk. Hosp. Bull.*, **62**, 159.
 Jaffe, R. H., and Laing, D. R. (1934). *Arch. intern. Med.*, **53**, 851.
 Kimmel, G. C. (1942). *Amer. J. Dis. Child.*, **63**, 60.
 Weiss, S., and Parker, F. (Jr.) (1939). *Medicine Baltimore*, **18**, 221.