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ACUTE NEPHRITIS ASSOCIATED WITH CONGENITAL SYPHILIS

BY

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[WITH SPECIAL PLATE]

Two clinical forms of renal disease have been described in association with congenital syphilis and early acquired syphilis; these are the nephrotic syndrome and a rare form of acute nephritis, but the latter has been poorly documented. Only two cases of acute glomerulonephritis associated with congenital syphilis are recorded in the English literature (Mitchell, 1951; Yampolsky and Mullins, 1945). In view of the rarity of the condition we describe two further cases of acute nephritis in association with congenital syphilis seen in the paediatric wards of the Baragwanath Hospital.

Case 1

A well-nourished 6-weeks-old male African infant was admitted with a two-day history of blood-stained urine. Before the onset of haematuria the baby was perfectly well, and there was no history of snuffles or skin rashes. On examination he was found to be pale and extremely irritable, with marked generalized oedema. There was an icteric tinge to the conjunctivae. The heart and chest were normal, and the systolic blood-pressure was 100 mm. Hg. by the flush method. The liver and spleen were each enlarged to 2 cm. below the costal margin in the mid-clavicular line, and bilateral regular kidney masses were palpated. Examination of the urine disclosed albuminuria ++++ and innumerable red blood cells and granular casts; an excess of bilirubin and urobilin was also present.

An intravenous pyelogram showed that the pelves of the kidneys failed to fill. Radiography of the femora revealed marked periostitis Haemoglobin level 10.7 g. per 100 ml.; white cell count 52,000 per c.mm. (neutrophils 53%, lymphocytes 23%, monocytes 24%); prothrombin index 45%. Serum bilirubin 5.7 mg. per 100 ml., of which 4.1 mg. direct; blood urea 95 mg. per 100 ml., serum cholesterol 260 mg. per 100 ml. V.D.R.L. tests (Harris *et al.*, 1948) on both mother and child positive.

Treatment was begun with 250,000 units of crystalline penicillin six-hourly. During the next six days massive haematuria and albuminuria continued (results with Esbach's reagent varied between 1 g. and 5 g.), but the blood urea level fell to 54 mg. per 100 ml. On the sixth day the urinary abnormalities began to resolve; the liver had decreased in size and the spleen was no longer palpable. However, the patient became stuporous on the following day, and lumbar puncture revealed a purulent cerebrospinal fluid from which *Escherichia coli* was isolated. Despite vigorous antibiotic treatment he deteriorated steadily and died on the tenth day.

Post-mortem Findings

The body was oedematous, the oedema being most marked over the lower extremities. There was generalized pallor of the skin, and the hair was sparse and lighter in colour than normal. The heart showed moderate generalized enlargement and weighed 45 g. The kidneys were both markedly enlarged (right kidney 50 g.; left kidney 60 g.). The capsules stripped easily, leaving smooth but rather pale surfaces which had some retention of foetal lobulation. The cut surfaces of both kidneys showed marked pallor of cortex and medulla. Histological examination of the brain (520 g.) showed the presence of an acute suppurative leptomeningitis. Microscopical examination of the kidneys revealed marked changes in the glomeruli. These were swollen and showed endothelial and epithelial proliferation and infiltration by occasional neutrophils. Many glomeruli completely filled the glomerular space, and in some there were adhesions between tuft and Bowman's capsule. In addition there was slight focal thickening of the basement membrane. An occasional glomerulus showed focal eosinophilic necrosis (Special Plate, Figs. 1–3). Many tubules contained hyaline and granular casts and there were fine fat droplets in their lining cells. The blood-vessels were normal. The interstitial tissue showed an occasional focus of lymphocytic infiltration and extramedullary haemopoiesis. The histological features were those of an acute proliferative glomerulonephritis. Section of the femur failed to reveal any evidence of periostitis or epiphysitis. Spirochaetes were not isolated from any of the organs.

Case 2

An African female aged 2 months was admitted to the hospital with a history of swelling of the face and feet for one week. There was no history of haematuria, breathlessness, or cough. The mother's pregnancy had been uneventful, and delivery was at full term and normal. There had been no neonatal jaundice or cyanosis; the baby, who weighed 10¼ lb. (4.65 kg.), was breast-fed.

Examination showed moderate oedema of the legs and puffiness about the eyes. Mucous membranes were moderately pale and there was no clinical jaundice. Mouth and pharynx were healthy and the heart and lungs normal. The abdomen was slightly distended, but no free fluid was present. The liver edge was palpable 2 cm. below the costal margin in the mid-clavicular line, and the spleen 1 cm. below the costal margin.

There was macroscopic haematuria and the urine contained a marked excess of albumin. Microscopical examination of the urine showed numerous erythrocytes and hyaline and granular casts. The haemoglobin level was 8.6 g. per 100 ml., and the white cell count 10,100 per c.mm. with a normal differential count. The mother gave a positive reaction to the V.D.R.L. test, but the baby's reaction was negative. Radiography of the baby's knees showed a typical syphilitic metaphysitis and periostitis. Further investigations showed: blood urea 26 mg. and serum cholesterol 245 mg. per 100 ml.; total serum proteins 5.5 g. per 100 ml., with albumin 1.3 g., α1-globulin 0.39 g., α2-globulin 0.85 g., β-globulin 0.92 g., and γ-globulin 2.04 g.; serum bilirubin 0.12 g. per 100 ml.; alkaline phosphatase 29.2 units per 100 ml.; thymol turbidity 10 units; zinc sulphate turbidity 3.2 units; thymol flocculation 2 units; zinc sulphate flocculation negative.

The patient received 5 million units of penicillin over a period of 12 days, after which the spleen and liver were much smaller but the urine still showed numerous erythrocytes and mild albuminuria. The blood urea level was then 18 mg. per 100 ml. A further 1½ million units of penicillin was given over five days, by which time the urine was free of erythrocytes, casts, and albumin and the spleen and liver were no longer palpable.

Radiography of the knees repeated 25 days after starting treatment showed no metaphysitis but still a well-marked periostitis.

Discussion

Many authors mention the association of glomerulonephritis with neonatal syphilis, but there are remarkably few fully documented reports. Standard textbooks of paediatrics make very brief mention of this association. Ruben (1959), writing on the nephrotic syndrome in children, states that " the aetiology is unknown except for relatively rare instances associated with specific diseases such as syphilis." He does not indicate with which phase of syphilis it is associated, and does not mention at all an association between syphilis and acute nephritis. Ellis (1956) makes no mention of renal involvement in neonatal congenital syphilis. He states that in juvenile congenital syphilis renal damage manifests itself by an albuminuria and occasionally by a more acute syphilitic nephritis. Sheldon (1951) holds the view that the kidneys may be involved in infantile congenital syphilis and that this " is indicated by the occasional presence of albumin, casts, and blood cells in the urine and sometimes a generalized oedema." He also considers that the kidneys may be involved in late congenital syphilis, manifesting with albuminuria, passage of casts, and occasional attacks of haematuria. Paterson and Moncrieff (1947) state that acute nephritis is rare in infancy, " but that, when it does occur, syphilis is a prominent aetiological factor because syphilitic infants are readily affected by streptococcal infections of the nasopharynx and skin." This is also the view of Rich (1932), who regards congenital syphilitic nephritis as ordinary glomerulonephritis occurring in infants who are rendered susceptible to streptococcal invasion by the congenital syphilis. Baker (1939) supports this and claims that the improvement that sometimes results from antisyphilitic treatment in these cases is due to healing of nasopharyngeal ulceration and the clearing of secondary streptococcal infection. Unfortunately antistreptolysin titres were not determined in either of our cases.

Renal disease has been shown to be not uncommon in early syphilis in adults, and Thomas and Schur (1946), reviewing 112 cases of early acquired syphilis, found 12 with evidence of renal disease, two of which had acute haemorrhagic nephritis and the remaining 10 manifested with a nephrotic syndrome. In their review Furman *et al.* (1951) confirm this pattern of the incidence of nephropathy in early acquired syphilis.

The two cases here reported showed features of both acute nephritis and nephrosis. Case 1 had features of acute nephritis, including hypertension, haematuria, and azotaemia. However, the severe albuminuria with low serum albumin and raised serum cholesterol levels in this case are usually associated with nephrosis. Case 2 had more of the features of nephrosis, but macroscopic haematuria again indicated a mixed picture. The raised γ-globulin level in this case is not seen in the usual nephrotic syndrome except when it is associated with an autoimmune disease such as systemic lupus erythematosus. This patient responded very well to antisyphilitic therapy in terms of the renal, skeletal, and reticulo-endothelial lesions. There was no evidence of nasal or pharyngeal ulceration or secondary infection in any site in either case.

There are few records of the pathological changes of congenital syphilis in the kidney. Yampolsky and Mullins (1945) describe a case of congenital syphilis showing the histological picture of acute proliferative glomerulonephritis. The appearances observed in our first case resemble their description. Potter (1952) states that a mild increase in connective tissue in the kidney is the only characteristic change of congenital syphilis, though hyalinization of glomeruli and degeneration of tubules may occur. According to Allen (1952) the kidney of congenital syphilis is characterized by interstitial inflammation in association with great numbers of treponemata in the interstitium, in the tubular lumina, and among the tubular epithelial cells.

Summary

The rare association of congenital syphilis and renal disease, particularly acute nephritis, is discussed. Two cases of infants affected with syphilitic acute nephritis are described.

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Important technical advances have been made in recent years in the fight against rats and mice, and the latest addition to the Ministry of Agriculture, Fisheries and Food's Bulletin series, *Control of Rats and Mice,* by R. A. DAVIS, M.Sc., D.I.C., of the Ministry's Infestation Control Division, has been written in the light of recent research. In this bulletin the author describes some of the dangers, both to health and to property, of infestation by these rodents, and various methods of planning and carrying out control operations. Some of the methods of control described are poisoning—both acute and chronic—trapping, and fumigating and gassing in holes. Detailed descriptions are given of baits, bait containers, and depositors. There are also some suggestions for proofing buildings and maintaining hygienic conditions as methods of control. (H.M.S.O., Bulletin No. 181, price 4s.; by post 4s. 4d.)

D. ABRAHAMS AND W. BRIGDEN: MITRAL INCOMPETENCE AND PULMONARY HYPERTENSION

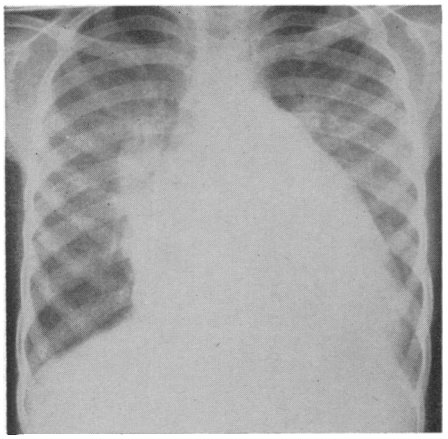

FIG. 1.—Chest radiograph of a girl aged 16 with mitral incompetence and pulmonary hypertension. The aorta is inconspicuous; main pulmonary arteries and outflow tract of right ventricle enlarged.

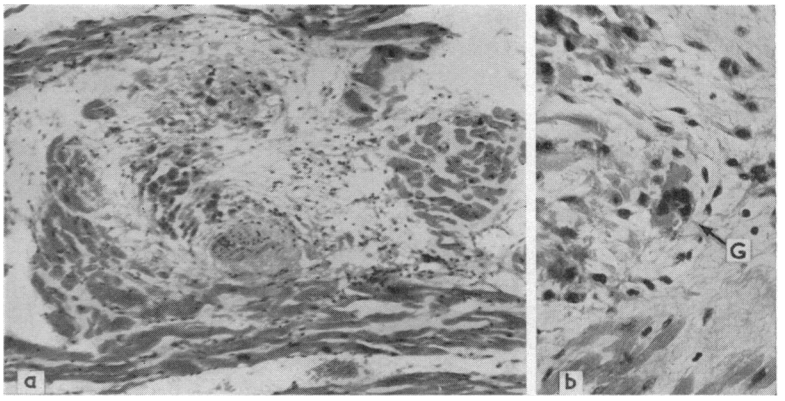

FIG. 3.—(*a*) Aschoff nodule showing collagen debris. (×76.) (*b*) Aschoff nodule showing one of the rare giant cells (G). (×236.)

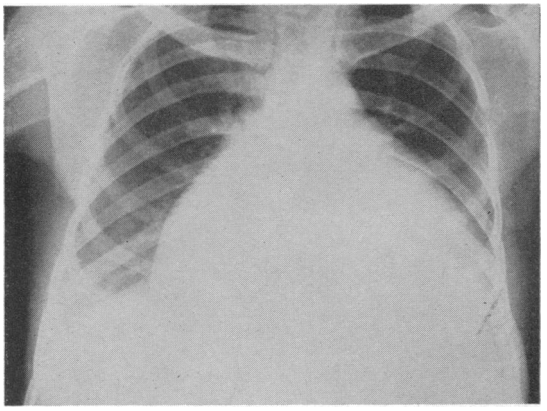

FIG. 2.—Radiograph showing a late stage of mitral incompetence and pulmonary hypertension when tricuspid incompetence has supervened. Right auricle is large; peripheral vascular markings are diminished.

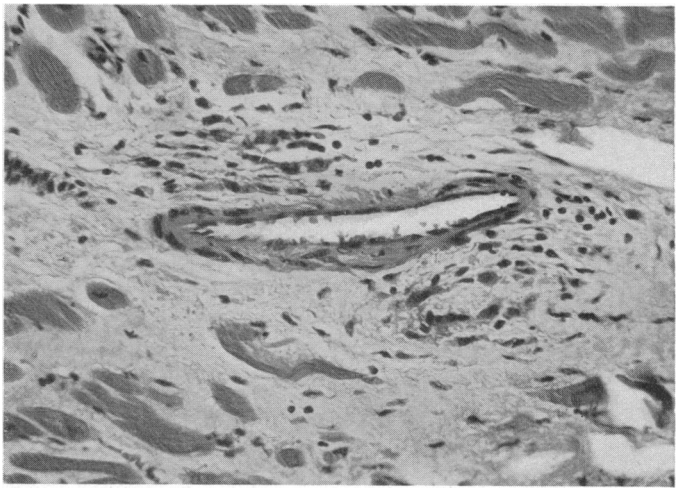

FIG. 4.—Aschoff nodules adjacent to a small vessel. (×228.)

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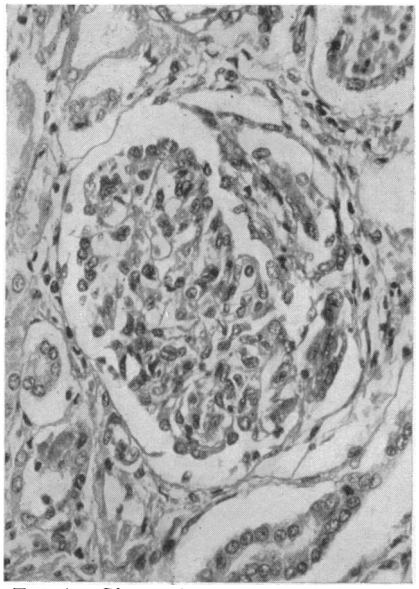

FIG. 1.—Glomerulus from kidney of Case 1, showing hypercellularity and adhesion between tuft and Bowman's capsule. (H. and E. ×260.)

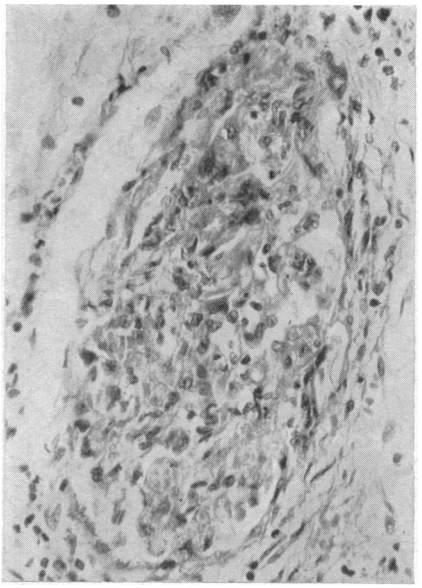

FIG. 2.—Markedly swollen glomerulus. (H. and E. ×260.)

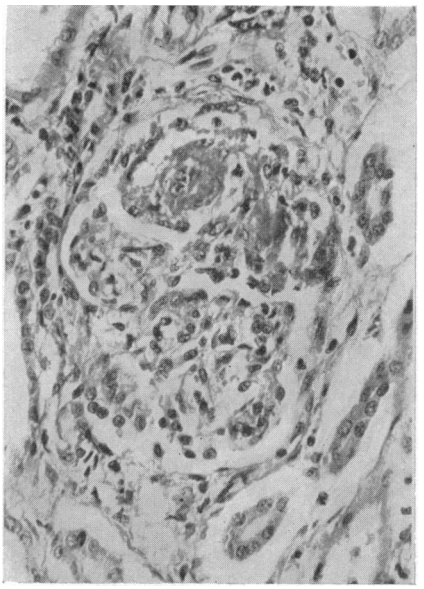

FIG. 3.—Eosinophilic necrosis of glomerular tuft. (H. and E. ×260.)