Nephritis and Common Skin Diseases


Br. med. J., 1964, 2, 1369–1371

Glomerulonephritis may accompany some common dermatoses, especially those in which haemolytic streptococci play a part. In anaphylactoid purpura renal involvement is well documented, but in erythema multiforme, erythema nodosum, acute guttate psoriasis, and those pyodermae which harbour streptococci the occurrence of glomerulonephritis is less well appreciated.

The following case histories show how glomerulonephritis may accompany apparently benign skin diseases.

Case Histories

Case 1. Acute Nephritis; Insect Bites; Erythema Multiforme

A woman aged 51 had had an itchy eruption on the shins, thighs, buttocks, and forearms, with malaise and pains in the elbows, knees, and ankles for two weeks. There was no history of recent sore throat, herpes simplex infections, or drug ingestion. She was a chronic alcoholic. In 1957 she had been treated for syphilis and gonorrhoea, and in 1962 for body lice; in early 1963 she had had an urticarial reaction after eating crab, and at the end of 1963 she had eaten fish roes a few days before the symptoms which led to her admission to hospital. The skin on the ankles, calves, and buttocks had a number of erythematous papules 0.5–1 cm. in diameter with central hemorrhagic puncta. Some were arranged in lines and were bed-bug bites. She also had lesions of erythema multiforme on the legs and forearms; some were bullous (1–2 cm. diameter) and others target-like. Pubic lice were present. The joints of the ankles, knees, and elbows were painful and at times swollen. The liver was palpable, the blood-pressure 120/70, and the urinalysis normal.

Investigations.—Four days after admission the blood-pressure had risen to 175/115, reaching a maximum on daily testing of 180/120, and the ankle swelling increased further. The skin eruption was intense, and the urine contained red cells and white cells. There was an increase in serum creatinine, and the blood glucose was normal. The blood sugar showed a curve with a peak at 8 a.m.

Summary

In the present study the urinary excretion of Figlu has been estimated in 102 pregnant women and correlated with the haematological state, including the bone-marrow appearance in every case and the serum folic-acid activity and serum vitamin-B12 levels where available. Estimation of Figlu excretion was of little value in the diagnosis of the type of anaemia and was no substitute for bone-marrow biopsy; the serum folic-acid activity was found to be a better guide to the type of erythropoiesis. A number of patients were found to have low serum vitamin-B12 levels in association with normal Figlu excretion and a significant proportion of these had megaloblastic or transitional erythropoiesis.

We are grateful to Professor L. J. Witts for helpful criticism and advice and for allowing us to use the facilities in his department for the folic-acid assays, which were carried out under the direction of Dr. G. H. Spray; to Professor Chassar Moir and Mr. Mostyn Embrey, who kindly allowed us to study patients under their care; and to Dr. R. Wright for all his help. This study has been financed by a grant from the Nuffield Committee for Advancement in Medicine.

References

and remaining at about this level for over three weeks. There was oliguria; the urine contained protein (4+), with granular casts, red blood cells (3+), and white blood cells; culture was sterile. The daily urinary output of protein was between 2.7 and 14 g. per 24 hours. The blood urea rose from 36 to 60 mg./100 ml. Other investigations were normal: blood count, E.S.R., serum proteins, W.R., antistreptolysin (ASO) titres, throat swab, serum bilirubin, lupus erythematosus cells, antinuclear factors, occult blood in the stools, radiographs of the chest, and renal areas.

The blood-pressure, urinary output, and blood urea returned to normal and the skin healed after four weeks, but some proteinuria and casts remained.

Case 2. Nephrotic Syndrome and Infected Sebhoroeic Eczema

A storekeeper aged 61, with no past history of skin or kidney disease, developed a rapidly spreading seborrhoeic dermatitis. After two weeks he was admitted to hospital with extensive impetiginized areas, particularly around his ears and axillae. Two weeks later he was oedematous, his weight had increased by 31 lb. (14 kg.), and his urine contained protein, granular and hyaline casts, and "numerous" red and white blood cells. His blood-pressure, which was 140/80, never rose above 150/90. The urine, tested daily, contained between 2 and 4 g. of protein per litre (Esbach) and the highest of four blood-urea estimations was 45 mg. There was no evidence of diabetes mellitus or connective tissue disorder.

Eighteen months later, after systemic corticosteroids and diuretics had been considerably reduced, he returned to work. He had slight proteinuria and minimal eczema; his weight was normal.

Case 3. Focal Nephritis, Acute Guttate Psoriasis, and Erythema Nodosum

A machinist aged 33 developed generalized guttate psoriasis and erythema nodosum of the shins 10 days after an acute tonsillitis which had been treated with oral penicillin. He had had acute rheumatism at the age of 12, and recurrent tonsillitis which was treated by tonsillectomy at 23. He gave no family history of psoriasis.

Investigations.—Blood-pressure 130/80 and urinary output normal. Urine contained protein (+), R.B.C.s, W.B.C.s, and hyaline casts (+); culture was sterile. Blood urea 26 mg./100 ml. Throat swab (after penicillin treatment) was sterile, but ASO titre was 250 units/ml. Hb 13.6 g./100 ml, W.B.C.s 9,850/c.mm., with normal differential. Serum proteins normal. No L.E. cells.

The renal exudate persisted for three weeks, the erythema nodosum for two weeks, and the guttate psoriasis had gone after eight weeks.

Case 4. Recurrent Focal Nephritis and Acute Guttate Psoriasis

A housewife aged 46 had had three attacks of generalized guttate psoriasis during the past two years. Each followed two to four weeks after beta-haemolytic streptococcal tonsillitis. During the last two attacks her urine had contained protein (+), R.B.C.s (+), and W.B.C.s (+); culture was sterile. Her blood-pressure and blood urea were normal throughout each attack.

The renal exudate cleared after three weeks.

Case 5. Focal Nephritis and Generalized Exfoliative Psoriasis

A schoolteacher aged 32 developed acute guttate psoriasis three weeks after acute tonsillitis which was treated with penicillin. He was subject to recurrent tonsillitis. The urine contained albumin (+), R.B.C.s (-), and W.B.C.s (+); culture was sterile. Blood-pressure 120/80. Blood urea 20 mg./100 ml. ASO titre was 50, 90, and later 100 units/ml. The skin lesions progressed to a generalized exfoliative psoriasis.

The renal exudate cleared in four weeks.

Case 6. Focal Nephritis and Anaphylactoid Purpura

A printer aged 54 had had a purpuric eruption with macular and urticarial lesions 0.5–1 cm. in diameter on his legs and buttocks for six weeks. This had followed four weeks after a sore throat treated with aspirin. He had no joint, gut, or kidney symptoms. In adolescence he had had rheumatic fever.

Investigations.—Blood-pressure 160/90 (fat arm). Urine contained protein (2+), R.B.C.s (+), W.B.C.s (+); hyaline and granular casts (+); culture was sterile. ASO titre 250 units/ml. Blood urea 39 mg./100 ml.

Physical examination normal. Capillary fragility (Hess's test) negative. Hb 15.2 g./100 ml. W.B.C.s 7,300/c.mm. with normal differential. Platelets normal. E.S.R. (Westergren) 12 mm. in one hour, serum proteins normal, W.R. negative, no L.E. cells, antinuclear factors negative. Radiograph of chest normal.

The eruption cleared after three weeks. The urinary deposit persisted for five weeks, but the albuminuria remained.

Discussion

Glomerulonephritis is a term which implies a delayed hypersensitivity reaction affecting the glomerular vasculature. It is a syndrome initiated by different stimuli, involving many complementary immunological mechanisms, though commonly beta-haemolytic streptococci are responsible (Peters, 1963). In susceptible individuals initial attacks result from only a few serological types of group A beta-haemolytic streptococci, but exacerbations may be caused by any type (Rammelkamp, 1962). Marked biological variance of immune response to antigens in normal and diseased persons explains the range of effects from benign subclinical to fulminating (Peters, 1963).

Four groups of diffuse glomerulonephritis are well defined: post-streptococcal acute glomerulonephritis, nephrotic syndrome, and subacute and chronic glomerulonephritis. Now a fifth group, focal nephritis, is accepted as a definite entity on clinical and histological grounds (Wilson, 1962; Hepinstall and Jockes, 1963). The classical manifestations of diffuse nephritis—oedema, hypertension, renal failure—are absent in focal nephritis, where the sole sign may be a minimal and transient renal exudate. The implication, now proved histologically, is that only a few glomeruli are pathologically affected.

In anaphylactoid purpura the incidence and outcome of the renal lesions are very variable (Hepinstall and Jockes, 1963). The renal pathology is similar to acute glomerulonephritis, but the lesions are commonly focal and not generalized (Milne, 1962).

Erythema multiforme is a clinically distinct syndrome of multiple aetiology affecting the skin and mucous membranes, and rarely the kidneys (Comanish and Kerr, 1961), producing lesions with some histological similarities to acute nephritis, although the normal blood-pressure, transient arthralgia, and occult blood in the stools may suggest anaphylactoid purpuric syndrome. Drugs, sera, streptococci, viruses, mycoplasma pneumoniae (Ludlam et al., 1964), and chemical substances (Yaffe and Stargarder, 1963) have been blamed—as they have in all the necrotizing "allergic" angitides (Winkelmann and Ditto, 1964). It is possible to link nephritis and erythema multiforme in Case 1, imputing as an antigen the foreign material from the insect bites or the fish. The course of the patient's disease was similar to that of experimental foreign protein nephritis, where there is a generalized polyanteritis with manifestations of serum sickness (Peters, 1963).

Erythema nodosum is a well-known sequel of streptococcal infection, although other causes are more usual at the age of our patient in Case 3 (James, 1961). Likewise acute guttate psoriasis, both in initial and subsequent attacks, has been shown to follow streptococcal throat infections, although the mechanism is poorly understood (Norlind, 1950; Norholm-Pedersen, 1952). One possible explanation is that a streptococcal "toxin" damages the capillaries of the dermis, which are...
abnormal in individuals with an inborn tendency to psoriasis, thus after an interval of 10 to 15 days producing the lesions of psoriasis (Whyte and Baughman, 1964). An antigen-antibody reaction centred on the dermal capillaries, similar to that which occurs in the glomerular capillaries in acute nephritis, seems unlikely, as fluorescent antibody studies carried out on psoriatic skin have been negative (Raskin, 1964).

Pyoderma in patients with seborrhoeic eczema is a very common complication; it is much rarer in atopic eczema, yet 4 out of 492 patients suffering from atopic eczema were found to have glomerulonephritis on presentation (Roth and Kierland, 1964). Impetigo has been reported as a common precursor of glomerulonephritis in the U.S.A. (Blumberg and Feldman, 1962). This could be true in this country: over the past two years in our department half the cultures from 24 patients with impetigo grew beta-haemolytic streptococci.

It is interesting that two of our patients (Cases 3 and 6) had acute rheumatism in adolescence—a further manifestation of their streptococcal hypersensitivity.

Summary

Nephritis may occur with common skin diseases. Examples of various types of nephritis associated with anaphylactoid purpura, erythema multiforme, erythema nodosum, acute guttate psoriasis, and infected eczema are given.

We are grateful for the help of Drs. H. J. Wallace, G. C. Wells, and E. W. Froser Thomas.

REFERENCES


**Variations in Small-intestinal Villous Shape and Mucosal Dynamics**

B. CREAMER,* M.D., M.R.C.P.

*Consultant Physician, St. Thomas's Hospital, London.

The small-intestinal mucosa maintains a constant appearance while being in a continuous state of proliferation and loss. The crypts of Lieberkühn contain immature cells showing frequent division, and from them epithelial cells stream up the villi in a regular fashion to be lost at the tips (Leblond and Stevens, 1948; Creamer et al., 1961). The whole small-intestinal epithelium is replaced in this way about every two days. The rates recorded by observers using many animal species have been remarkably constant, and in man Bertalanffy and Nagy (1961) have estimated the duodenal turnover time to be two days. If the production of new cells is abruptly stopped by either antifolic drugs or x-irradiation the normal villous structure collapses (Phillips and Thiersch, 1949; Wiernik et al., 1962). Within two to three days sheets of epithelial cells are shed and stunted broad villi or a flattened surface is left. This suggests that the structure of the small-intestinal mucosa is plastic and that variations in epithelial-cell turnover may well determine the shape and size of the villi.

The so-called normal appearance of the small-intestinal villi as viewed under the dissecting microscope is finger-shaped, but many healthy people show some leaf-shaped villi. In pathological conditions a whole range of appearances is seen, from normal finger villi to leaves, to convolutions, and in some cases to a completely flat mucosa (Holmes et al., 1961). The purpose of the present study was to see if the change in villous shape from fingers to convolutions could have an explanation in the dynamics of the intestinal epithelial cells. The problem of idiopathic steatorrhoea and the production

of a flat mucosa has been considered previously (Creamer, 1962).

**Materials and Methods**

Twenty small-intestinal biopsies were examined. They were selected solely because they showed a variety of changes from finger villi to convolutions. None of the patients had idiopathic steatorrhoea, but some had gastrectomies, Crohn's disease, or other intestinal disease. Seventeen were obtained perorally and three were surgical specimens, of which two came from the jejunum at a gastrectomy and a gastro-enterostomy stoma under revision.

The sections were all well orientated, so that the crypts were cut longitudinally. On each section a count was made of at least 2,000 epithelial cells, recording separately crypt cells, adult cells, and metaphase mitotic figures. From this the ratio of adult cells to crypt cells was calculated. The mitotic rate was expressed as metaphases per hundred crypt cells.

Where leaf-shaped villi are present the section may be cut through the long axis of the leaf A-A or across the short axis B-B (Fig. 1). If a cell count is made through a long axis A-A fewer adult cells are recorded than if a number of leaves are cut through the short axis B-B. In one case this was done, and the proportion of adult cells to crypt cells was exactly half when a leaf villus was cut down the long axis compared with a similar area where the leaves were sectioned through the short axis. Because of this, an area was always chosen where leaf-like villi were sectioned through the short axis.

The crypt length was estimated by counting the number of cells down one side of a crypt, the average of several crypts