Polyarteritis or glomerulonephritis?

Clinical History (Dr. J. F. Goodwin)

The patient was a man aged 24 years, a rivet heater by trade. In 1948 he was treated for pneumonia with sulphonamides. In 1949, after discharge from the Army, he developed upper abdominal pain and nausea, unrelated to food, but relieved by alkalies. He remained well until September 1952, when he developed increasing dyspnoea on exertion and a cough, followed in October by repeated small haemoptyses. A chest X-ray at this time was normal, but a further film taken two weeks later showed shadowing in the mid-zones of both lungs (Figs. 1 and 2). He was treated with bed rest and penicillin for two weeks. The haemoptyses ceased but he noticed increasing pallor and dyspnoea and developed urinary frequency and nocturia. On December 14 he was admitted to Hammersmith Hospital.

On Examination. A pale, anxious young man with pyrexia of 99 to 100°.

Cardiovascular System. Heart normal. B.P. 125/60. Jugular venous pressure 1 cm. above the sternal angle.

Optic Fundi. Scattered hard white exudates surrounded by fine red stippling. Small haemorrhages. No papilloedema.

Respiratory System. Crepitations at the base of the right lung.


No skin lesions, petechiae, icterus or lymphadenopathy.

*Held at the Postgraduate Medical School of London (Hammersmith Hospital) on May 27, 1953. The report was assembled by Dr. Bernard Lennox. The sections were prepared under the direction of Mr. J. Griffin and the photomicrographs are by Mr. E. V. Willmott.
Investigations

**Blood:** Hb., 511 g., 35 per cent. R.B.C., 2.1 million. M.C.V., 81 c.μ. M.C.H.C., 30 per cent. Reticulocytes, 5.9 per cent. W.B.C., 7,000; normal differential count; no eosinophilia. E.S.R., 37 mm. in one hour (corrected for anaemia, 1 mm. in one hour). Platelets, 296,000 per c.mm. Bleeding time, 24 min. Clotting time, 4 min. Plasma proteins, 6.5 g./100 ml. A/G ratio, 1.5. Blood urea, 25 mg. per cent. Serum bilirubin, 0.5 mg. per cent. Blood cultures, sterile. Direct Coombe’s test, negative. W.R., negative. Electrolytes, normal. Agglutinations, negative.

**Electrocardiogram** (Fig. 3). Low voltage complexes and flat T waves consistent with severe anaemia.


**Bone marrow biopsy:** Signs of iron deficiency anaemia. No L.E. cells.

**X-ray of chest:** Considerable resolution of shadows previously seen.

Progress

The patient remained febrile and had several epistaxes. Red blood cells became more numerous in the urine and the urinary output began to fall while the blood urea rose (247 mg. per cent. on December 24, 1952). He developed signs of collapse of the lower lobe of the left lung, which was confirmed by X-ray, and was thought to be due to an infarct. Several superficial vein thromboses occurred on the arms, but a biopsy of the skin over one of these did not show any vascular lesion. There were still no neurological signs and no hypertension, and the fundi remained unchanged.

**Treatment**

Repeated blood transfusions were given and the haemoglobin rose to 84 per cent. The patient was given a protein-free diet consisting of 400 g. carbohydrate and 100 g. fat, with vitamins added, through a nasal drip. Parenteral penicillin therapy and oral cortisone, 100 mg. per day for 10 days, followed by 50 mg. per day for 31 days, was administered.

**Further Progress**

He improved on this therapy and the fundal changes regressed slightly. His serum electrolytes remained normal except for reduction in bicarbonate and sodium. On January 24, 1953 they were: Na, 135 mEq./l.; K, 4.8 mEq./l.; Cl, 100 mEq./l.; CO₂, 15 mEq./l. The blood pressure rose transiently to 170/100 but fell to 135/85. The blood urea rose to 412 mg. per cent. and by February 6, 1953, he was anuric and drowsy.
with hissing respirations. The electrocardiogram (Fig. 4) showed augmented T waves characteristic of hyperkalaemia. Electrolytes: Na, 132 mEq./l.; K, 7 mEq./l.; Cl, 81 mEq./l.; CO₂, 17 mEq./l. Blood urea: 536 mg. per cent.

He died in coma on February 9, 1953.

Clinical diagnosis: Polyarteritis nodosa.

Pathology (Dr. G. A. K. Missen)

The significant macroscopic findings at autopsy, which was performed 21 hours after death, were confined to the lungs and kidneys, but the appearances of the latter were not conclusive. However, the histological appearances were those of polyarteritis nodosa of the microscopic type (Davson, Ball and Platt, 1948; Wainwright and Davson, 1950).

The body was that of a young man, 5 ft. 11 in. tall and weighing 10 st. 3 lb. The serous cavities showed no inflammation or excess fluid. The kidneys (245 g. and 240 g.) were increased in size, their cut faces being tense and bulging and showed no focal lesions. The cortices were swollen and of a dull greyish-pink in colour. The pattern of the cortex and its demarcation from medulla appeared normal, though after fixation the glomeruli were visible to the naked eye as opaque, whitish dots. Medullae appeared normal. Capsules stripped easily to reveal uniform, dull-pink surfaces (Fig. 5). The bladder contained 750 ml. of turbid brown urine.

The lungs (right, 880 g., left, 580 g.) were congested and relatively airless especially in their dependent parts. Five small organizing infarcts

Fig. 4.—Electrocardiogram three days before death showing augmented T waves due to hyperkalaemia (serum potassium 7 mEq./l.).

Fig. 5.—The kidneys.
Fig. 6.—The infarcts in the right lung.

Fig. 7.—Low power view of kidney to show absence of normal glomeruli. H. & E. × 36.

Fig. 8.—A glomerulus. Severe glomerulitis of some standing with slight crescent formation. The afferent arteriole shows moderate fibrinoid necrosis. H. & E. × 160.

Fig. 9.—Acute arteritis in the sinus renalis. H. & E. × 160.
was oedematous and infiltrated with plasma cells and lymphocytes, especially around the glomeruli.

Despite examination of sections at many different levels, the only abnormality of the renal vessels to be found was fibrinoid necrosis of a few glomerular afferent arterioles (Fig. 8). Acute arteritis of three small vessels was found in the sinus renalis (Fig. 9) as well as veins containing organizing thrombus. The larger arteries in this site were normal.

**Lungs.** Sections of the hilar regions showed congestion, haemorrhage, some oedema and many siderophages. Sections of the right middle lobe confirmed the presence of an organizing infarct. Within this area were a number of arteries containing organized thrombus and showing destruction, confined to a sector of their circumference, either of intima and elastica only or else of all coats (Figs. 10 and 11).

**Liver.** Showed periportal and a little centrilobular fatty infiltration.

**Spleen** (130 g.) showed no arterial or other lesions.

No vascular or other relevant lesions were found in any of the following organs or tissues: Heart, voluntary muscles, pituitary, adrenal, thyroid, parathyroid, pancreas, testis, epididymis, spermatic cord, small intestine, vertebral bone marrow and cerebral cortex.

**Summary**

Polyarteritis nodosa of microscopic type leading to pulmonary infarction and diffuse necrotizing glomerulitis with ultimate renal failure.

**Table 1**

<table>
<thead>
<tr>
<th>Frequency of Lesions Occurring in Polyarteritis Nodosa (Modified from Harris, Lynch and O'Hare, 1939)</th>
<th>Per cent</th>
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<tr>
<td>Renal lesion</td>
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<td>Pyrexia</td>
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<td>Leucocytosis*</td>
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<td>Hypertension</td>
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<td>Anaemia</td>
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<tr>
<td>Oedema†</td>
<td>...</td>
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<tr>
<td>Peripheral neuritis</td>
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<td>Fits</td>
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*Eosinophilia, 20 per cent.
†Due to renal or cardiac failure or to myositis.

Skin lesions, cardiac involvement, pulmonary and ocular changes also occur.

**Discussion**

**DR. GOODWIN:** Whether we accept this case as one of periarteritis nodosa or not it may be helpful to review the disease very briefly in terms of the clinical picture produced by the various patho-
logical lesions. Periarteritis nodosa is, I think, somewhat of a misnomer, because the lesion, as I understand it, is initially a pan-arteritis with fibrinoid necrosis which involves the inner coats first and then spreads outwards, the periarteritis being a secondary phenomenon. The lesion produces thrombosis in the vessel, and by weakening of the wall produces nodular aneurysms. The lesions may be scattered along the course of arterioles and arteries anywhere in the body, so that a pleomorphic clinical picture can occur. Kussmaul and Maier defined periarteritis nodosa as a clinical and pathological entity in 1866, and in 1878 Meyer added the diagnostic triad of chlorotic marasmus, polymyositis and polyneuritis, and gastro-intestinal symptoms. This triad did not include a renal element, although a type of Bright's disease with febrile features had been described. Christeler in 1926 added nephritis to the triad. Harris, Lynch and O'Hare (1939) analyzed the symptoms and signs in order of frequency in 101 published cases with 87 autopsies (Table 1). It will be seen that this patient suffered from five of the nine listed complaints: Severe anaemia, pyrexia, abdominal pain, renal insufficiency and slight oedema; but it is interesting to note that hypertension was not a feature. In addition, he presented with fleeting pulmonary infiltrations similar to those described by Elkeles and Glynn (1944) who considered them to be due to areas of infarction or atelectasis. The present case also had fundal changes consisting of small, hard, white exudates adjacent to arteries, and small haemorrhages. Sampson and Herson (1949) described retinal detachment, haemorrhages and exudates, occlusion of the central retinal artery and hypertensive retinopathy. Lesions of the outer eye (conjunctivitis and iridocyclitis) may also occur. Skin lesions are sometimes a feature of the disease and consist of purpuric eruptions, variants of erythema nodosum or subcutaneous nodules. Coronary occlusion, pericarditis and even endocarditis may occur (Miller and Daley, 1946), but clinical evidence of cardiac disease was equivocal in this patient.

Davson, Ball and Platt (1948) classified the renal lesions and pointed out that in addition to producing an acute arteritis with infarcts the disease could occur in a microscopic form, the appearances being those of malignant nephrosclerosis or glomerulo-nephritis.

A clinical diagnosis of periarteritis nodosa is usually possible if the condition is kept in mind in patients with obscure fever and vascular and renal lesions. In an excellent paper Miller and Daley (1946) suggested that the disease could be roughly divided into various types: (1) Pyrexia of unknown origin; (2) Atypical abdominal symptoms with or without hypertension; (3) A primary renal disease with atypical features, and (4) A disease showing polyneuritic or polymyositic features.

As regards prognosis, Grant (1939) found that about 50 per cent. of cases recovered, and it seems that if the lesions do not involve important viscera, recovery may well be possible and, in fact probably often occurs. The cause of periarteritis is supposed to be some sort of anaphylactic hypersensitivity; I do not know of any better suggestions having been made. The responsible antigen is usually bacterial in origin (Miller and Daley, 1946), but drugs such as sulphonamides, thiouracil, iodine and deoxy corticosterone acetate have been suspected. This patient had no drugs other than sulphonamides and alkalis, the former many years ago.

Finally, treatment. Schick and his associates (1950) treated six cases with cortisone or ACTH of whom four recovered and two died of renal failure.* When the kidneys are involved particularly severely the prognosis is extremely bad, which is, in fact, what Dr. Milne said when he kindly saw the case in consultation.

Prof. Dible: I am not at all happy, you know, about the diagnosis of polyarteritis nodosa in this case. If the name means anything, it is difficult to see any polyarteritis. The one outstanding lesion was the glomerular lesion and that was a capillaritis, not an arteritis. That might be a quibble but the fact remains that every glomerulus in that kidney showed the most extensive changes and it was only by extremely thorough searching that any lesions could be found in any other parts of the body which might be interpreted as being examples of polyarteritis. Whether polyarteritis and glomerulo-nephritis are distinct diseases or not, on the basis of what we have seen and heard this morning I am beginning to wonder. But if we are to regard them as distinct diseases I feel that the evidence here is that the lesion is nephritic and not an arterial or arteriolar condition.

Prof. McMichael: That is a challenge to the pathologists, surely.

Dr. Doniach: Can we call Dr. Milne a pathologist for this purpose?

Dr. Milne: I am not going into the morass of pathological argument, but from the clinical point of view this disease could never have been glomerulo-nephritis. First of all there is absolutely no history of any phase typical of acute Type I nephritis. He was an intelligent man and we went into that history very carefully. There was no

*Since the Conference took place Simpson, Hall and Morgan (Brit. med. j., ii, 659, 1953) have reported recovery of a patient with polyarteritis nodosa following treatment with ACTH.
history of an oedematous state typical of Type II nephritis. That is negative evidence. The positive evidence was, first, the presence of transient pulmonary infiltrations which are very typical of the pulmonary infiltrations of polyarteritis nodosa. Second, the severe anaemia and the fever which resisted antibiotic treatment. Third, and even more typical, are the retinal lesions. I do not know whether these are specific retinal lesions of polyarteritis nodosa (and I do not very much care), but I do know that they are not secondary to the usual causes of retinal lesions in glomerulonephritis. Retinal lesions in glomerulonephritis are secondary either to severe hypertension which may cause exudate, haemorrhage and papilloedema, or to capillary damage due to severe uraemia which does seem to lead to a haemorrhagic tendency. Now this man had neither of those when he had severe retinal lesions, he had no hypertension, he had no evidence of past hypertension and he had no uraemia at that time; the blood urea was low. I have seen the same phenomenon in cases of phaeochromocytoma, but in them, of course, there is a paroxysmal hypertension to account for it. Another thing in favour of polyarteritis nodosa is the extreme rapidity of progress of the renal lesion to severe fatal uraemia despite the fact that there was not the vicious circle of Bright's disease so well described by Clifford Wilson. He states that in the development of uraemia in Bright's disease the rapidity of progress is dependent on the diastolic pressure. Cases with a high diastolic pressure progress rapidly to severe uraemia and death. This man progressed terribly quickly despite a normal or only very slightly raised diastolic blood pressure. That was very suggestive of a primary arterial lesion and I think the pathologists have demonstrated this—or, to be strict, a panarteriolitis or pancapillaritis in the kidneys. That to me is typical of the microscopic variety of polyarteritis nodosa.

PROF. MCMICHAEL: Well, that is very emphatic and I must say I support it. I think that there are are some obviously queer border lands between severe arterial damage and glomerulitis. Experimentally many years ago Wilson and Byron showed that in experimental malignant hypertension there was an associated glomerulitis. I very well remember a case of a boy who presented with a picture which we took clinically to be an acute nephritis which turned out to be a kind of juxta-glomerular arteritis at post-mortem. So I think we are here on a border-land between nephritis—or capillaritis, if it is to be called that—and arteritis. I wonder if we ought not to drop the term 'nodosa' because there were, in fact, no nodules either macroscopically or microscopically. It might help if we merely called them arteritis rather than periarteritis nodosa. There was very little periarteritis here.

DR. LENNOX: May I just interject something which I think is relevant to everything that has been said so far? I think the views of Pearl ZeeK on the matter of polyarteritis have been neglected rather more than they deserve. She maintains that there are two different diseases mixed up in polyarteritis. One is the typical textbook 'polyarteritis nodosa' with hypertension in which the lesions are confined to the arteries and in which the 'nodosa' is often justifiable because you see macroscopically visible aneurysms. That is a disease which may be simply a variant of malignant hypertension. The other is a sensitivity disease in which the lesions are never macroscopic and in which not only the arteries are involved but also the lungs and sometimes the veins. Now this would fit in perfectly. It is not a 'nodosa' type, i.e., there are no lesions of larger arteries. Admittedly we have no evidence of the sensitivity phenomenon, but that is a difficulty in any attempt to explain the glomerulitis in this case and it may be that there is some sensitization we have missed. We have got venous lesions and lung lesions and there was no hypertension. It is in these atypical cases of polyarteritis without hypertension and with venous and pulmonary lesions that we get just such a confusing border-line picture as the present case. Perhaps all these so-called microscopic arteritides, non-nodose polyarteritides, fall into this second group.

DR. HARRISON: I do not think we should take ZeeK's sub-division too literally. When she published that paper I dug out all our polyarteritis cases and tried to divide them according to ZeeK, and they just will not divide. I am sorry, but the data spoils this beautiful theory. However, I do agree with Dr. Lennox, there is an enormous variability in polyarteritis and it probably does embrace a lot more than one standard case. I think Dr. Missen has made out a very good case on the strength of these lung arteries. I think we have to take the polyarteritis very seriously in any artery that has got half its wall bitten clean away.

PROF. DIBLE: Yes, but it is so usual to find these in the spleen. Would not you agree that that is the organ where you find them most frequently? I was a little surprised to find there were not any splenic lesions.

DR. HARRISON: I agree that it is unusual, but can we exclude the diagnosis on that alone?

PROFESSOR MCMICHAEL: There are some questions I would like to ask. First, what is the cause of the anaemia? Clearly it was not related to severe uraemia. The blood urea was only 25 mg. when his Hb. was only 5 g. Second, was the
necrosis of half of the glomerulus similar to the lesion seen in subacute endocarditis? And third, what do you really think was the pathology of these transient lung lesions? You did say some haemorrhage was found in the lungs but no fibrinous oedema. I wonder what they really are. Is there any information on that?

Dr. Goodwin: We were very puzzled by the anaemia clinically and we could not really explain it at all, but we did wonder how much blood he had actually lost. We did not see how the amount he had lost from his alleged haemoptyses would be sufficient to produce that degree of anaemia and we did wonder whether he was losing it via his gastro-intestinal tract. We never got any positive occult blood in the stools and we did not for obvious reasons do barium meals or enema or anything of that sort.

Dr. Doniach: I do not think we can say positively what the central lung lesions were a few months before he died. In a negative way the fact that we found no evidence of fibrosis in the hilar sections would suggest some transient congestion or oedema.

Dr. Bayliss: It could not have been haemorrhage with aspiration of blood? He had quite frequent haemoptyses, had he not? And if he had aspirated blood back down a segment he could have got changes which would have looked like that.

Dr. Doniach: It could have resolved completely—yes, that cannot be ruled out.

Prof. McMichael: I think the radiologist might have something to say.

Dr. Steiner: The interesting feature here was that the patient came to the Chest Clinic with haemoptysis. He was watched there for three weeks with these fleeting shadows and that is what we quite often see. Such shadows are not necessarily either tuberculous lesions or the results of haemorrhage into the lung. We have seen a few shadows due to atypical pneumonias which look like this, and the physicians at that time thought, after they had excluded tubercle, that they were due to atypical pneumonia. I was not aware at the time of these fleeting shadows in polyarteritis nodosa, but at the same time Dr. Sherlock had a patient in her ward who presented with a very similar picture with haemoptyses and with multiple fleeting shadows in the lung which cleared within a week completely. I think at the time the haemoptyses were thought to be due to oozing from a retropharyngeal vein.

Dr. Doniach: We sent a copy of the kidney section to Dr. Davson to get his opinion on it. At the time we sent it we had not the other evidence of arteritis—the lung lesions and the pelvic lesions had not been seen. He wrote back and said that the kidney would do for a microscopic type of polyarteritis, but in the absence of finding any other vessels affected he could not make a definite statement. He said that the nephropathologist in this sort of case gets more help from the clinical story than from looking at sections.

Dr. Fraser: I would like to ask Dr. Milne whether in the earliest phase in such a case as this you would expect to see albuminuria.

Dr. Milne: I should say it entirely depends on the distribution of the lesion. If the glomeruli are involved obviously albuminuria will occur and I think we saw from Dr. Goodwin's Table that the renal lesions are, if not the commonest, very high up in the list and therefore the great majority of cases have albuminuria; but many of course come to autopsy without any renal lesions whatsoever.

Dr. Fraser: I was meaning in this microscopic type where it seems to me it was implied you always have renal lesions. You do not think that is so?

Dr. Milne: I would not like to be dogmatic. This type has been described recently by Davson who is particularly interested in the kidney and I take it it is conceivable that such types might occur without involving the kidney, but as far as I know this has not been described.

Dr. Lennox: There has been at least one article describing microscopic arteritis limited to the appendix. I take it you would assume that in those cases there would be no albuminuria!

BIBLIOGRAPHY


SAMPSON, R. S., and HERSON, R. N. (1949), Ibid., 18, 123.


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