

THE NECROBIOTIC NODULES OF RHEUMATOID ARTHRITIS

CASE IN WHICH THE SCALP, ABDOMINAL WALL (INVOLVING STRIPED MUSCLE), LARYNX, PERICARDIUM (INVOLVING MYOCARDIUM), PLEURAE (INVOLVING LUNGS), AND PERITONEUM WERE AFFECTED

BY

RONALD W. RAVEN, F. PARKES WEBER, and L. WOODHOUSE PRICE

Much has been written about the nodules of rheumatoid arthritis, which, though present in less than a quarter of the patients, may nevertheless be regarded as constituting an important, if not the most important, feature from the pathological point of view. Collins (1937) and others, including Parkes Weber (1943, 1944), Kersley and others (1946) have shown that the characteristic subcutaneous nodules consist of foci of fibrinoid degeneration and necrosis, surrounded by a border of tissue reaction, notably by a palisade-like radiate arrangement of fibroblasts. Somewhat similar microscopic appearances have been described in pathological conditions of a different nature (granuloma annulare, necrobiosis lipoidica), but even if the histological features of the nodules of rheumatoid arthritis were absolutely pathognomonic, one would still be far from the discovery of the essential pathogenic agent.

Allison and Ghormley (1931) made a great point of what they called "focal collections of lymphocytes" in the synovial membrane of joints being almost pathognomonic of "proliferative arthritis of uncertain origin"—that is to say, of rheumatoid arthritis. But if one looks at their illustrations (for instance, p. 147, fig. 4; p. 169, fig. 3; and Plate VIII) one recognizes the presence (in these "focal collections") of so-called "germ-centres" of Flemming. Now, surely such lymphadenoid foci with typical "germ-centres" can hardly be considered as pathognomonic of any special disease. Apart from their conspicuous presence in normal lymphadenoid tissue (lymph glands, tonsils, the walls of the vermiform appendix and intestines, the Malpighian corpuscles of the spleen), they form a special feature in so-called lymphadenoid goitres, and are also not rarely found in thyroids from patients with Graves' disease. One of us (Parkes

Weber) has seen them in abnormal salivary glands. They constitute a conspicuous feature of cutaneous lymphocytomata (Epstein, 1935), and may be found in various other pathological conditions (Parkes Weber, 1947).

Similarly, there is nothing absolutely pathognomonic in the painless lymphadenopathy of the superficial lymph-glands, which is present during active periods in many cases of rheumatoid arthritis, though seldom noticed by the patients themselves and often not looked for by the examining doctor. It is "non-specific follicular lymphadenopathy" of toxic or infective origin, with marked enlargement of the "germ-centres" of Flemming (not to be confused with "follicular lymphoblastoma" of neoplastic nature), and tends to disappear when the patient's general and articular condition improves and the disease becomes quiescent (Parkes Weber, 1947, p. 38, case 4). Rochu (1946) thinks that this lymphadenopathy, together with the articular changes and occasional splenomegaly, indicates that what we in England call rheumatoid arthritis—which cannot be separated from the Chauffard-Still-Felty syndrome—is much more than a joint disease and that the reticulo-endothelial system is obviously involved.

As to possible pathogenic relationship between rheumatoid arthritis and rheumatic fever and between their respective nodules (cf. Bennett and others, 1940), there has been much discussion. Most of those who have studied the question apparently have come to the conclusion that the two diseases are clinically distinct and probably not due to the same (still unknown) pathogenic agent. Dawson (1933), however, in his "Comparative study of Subcutaneous Nodules in Rheumatic Fever and Rheumatoid Arthritis" wrote: "These studies . . . lend further support to the conception that

rheumatic fever and rheumatoid arthritis are intimately related and possibly different responses of affected individuals to the same aetiological agent."

In rheumatic fever the nodules mostly remain small and soon disappear. Small nodules in rheumatoid arthritis also sometimes disappear rapidly, but most of the nodules, especially the larger ones, become chronic and are only slowly, if at all, absorbed—doubtless owing to the formation of the characteristic necrotic foci surrounded by chronic reactive inflammatory and firm fibrous tissue. Fresh nodules may appear—a sign of renewed activity—even in old quiescent and apparently "burnt-out" cases.

Case Report

History.—The patient, a woman, aged 62, was admitted to the Royal Cancer Hospital under one of us (R. W. Raven) on March 14, 1947, on account of increasing difficulty in breathing. This commenced about January, 1946, and steadily progressed with increasing inspiratory stridor. Eventually the patient was suffering from breathlessness whilst at rest.

In April, 1946, there was onset of dysphagia, with special difficulty in the swallowing of fluids, which were often regurgitated. There was also progressive loss of voice, which became more and more indistinct and of a croaking character.

In December, 1946, the patient noticed the appearance of multiple lumps on her head. Whilst under observation similar lumps developed over the abdomen. There were also nodules on the elbow-joints and hands, some of which probably dated from the commencement of rheumatoid arthritis in 1916.

From October, 1946, there was increasing difficulty in vision, associated with gross conjunctivitis, which later progressed until, by the middle of March, 1947, she could only vaguely appreciate any object. There was marked loss of weight and energy, and the appetite was poor. No symptoms related to the colon or gastrointestinal tract were noted.

The patient had no children, but had had five miscarriages. She had had rheumatic fever in 1905, and in 1916 showed the onset of progressive chronic rheumatoid arthritis.

Condition on Examination.—Arthritic changes involved the joints of the arms and legs, with gross deformity. The patient was noticed to breathe with a marked inspiratory stridor, with all the accessory respiratory muscles in action. There was obvious great loss of weight.

Numerous nodules were present in the subcutaneous tissues of the scalp, some of which were attached to the skin and some attached deeply to the epicranial aponeurosis. The nodules were most marked on the forehead, but were scattered throughout the scalp. They varied in size from 1 cm. to 3 cm. in diameter.

The conjunctivae were pale, and there was an extensive ulcerative scleritis with corneal involvement which, in

the left eye especially, had the clinical appearance of a Mooren's ulcer.

There were numerous hard nodules about the elbow joints, attached to the skin, and on the left side ulcerated.*

The subcutaneous tissue of the abdomen showed multiple scattered nodules, whereas none was seen over the chest.

There was a painless lymphadenopathy of the superficial lymph-glands, such as is often present during the active stages of rheumatoid arthritis (see above).

There was a patch of dry gangrene on the tip of the right great toe, and no pulsation could be felt in either *arteria dorsalis pedis*.

Radiographic Investigations.—Radiographs of the chest showed bronchitic changes in the lungs and some cardiac enlargement. No abnormality detected on radiographic examination of the skull.

There were advanced changes of rheumatoid arthritis in all the joints, with marked osteoporosis and skeletal deformity. A radiograph of the larynx showed a projection from the posterior wall at the level of the epiglottis.

Haematology.—There were 4,660,000 red blood cells and 8,000 white blood cells per c.mm. The Hb was 75 per cent.; Wassermann and Kahn reactions were negative. The erythrocyte sedimentation rate was 40 mm. in one hour (Westergren).

Blood urea, blood uric acid, serum calcium, serum inorganic phosphorus, and serum phosphatase were all within normal limits. There was nothing abnormal in the urine.

Progress.—The patient developed signs of pneumonia. Her condition deteriorated, and she died on March 30, 1947.

This patient had been seen by one of us (F. Parkes Weber), who agreed that the case was one of advanced chronic nodular necrobiosis of the rheumatoid arthritis type. The biopsy tissue (see below) had been found superficially to resemble that of a gumma.

Post-mortem Report

External Examination.—The body was that of a poorly developed, poorly nourished, and extremely deformed woman of about 60 years of age. A small surgical incision was seen on the anterior aspect of the right temple. In the left temporal region were three or four small, firm, circumscribed subcutaneous nodules. They did not fluctuate, and were not attached to the overlying skin. A number of smaller nodules were seen and felt beneath the skin round the elbow and wrist joints and in the anterior abdominal wall. The degree of joint deformity was considerable, and the wrists and hands displayed an exaggerated ulnar deviation with wasting of the interosseous muscles, presenting a picture of advanced rheumatoid arthritis. In the legs it was hardly possible to move the ankle joints, and the left tibia showed an almost complete backward dislocation.

Internal Examination.—The scalp showed no abnormality, apart from that already mentioned, and the skull appeared to be of normal thickness. The brain was

* One of us (F. Parkes Weber) has since heard of two (unpublished) cases with ulcerated nodules of the rheumatoid arthritis type.

normal in appearance. There was no meningitis or flattening of the cerebral convolutions. The ventricles contained a normal amount of cerebrospinal fluid, and the arteries at the base of the brain did not present any gross evidence of atheroma.

The mouth was edentulous and the tongue, larynx, pharynx, thyroid, and trachea presented no obvious macroscopic evidence of pathological change, excepting a few small submucous nodular thickenings in the region of the glottis, particularly one on the epiglottis.

The left lung was adherent at its apex. It was partly collapsed by a left basal effusion and the visceral pleura was covered by a fairly thick fibrinous exudate. The cut surface of this lung showed the characteristic appearance of collapse, and there was some evidence of bronchitis. Pulmonary emboli were not found.

The right lung was also adherent to the parietal pleura and a small amount of turbid fluid was found at its base. This lung also was covered by fibrinous exudate which had involved the mediastinum and pericardium; on the left side the diaphragm and the splenic capsule were involved, producing an obvious perisplenitis.

The pericardium was adherent over the anterior surface of the heart; and, on forcible removal, both visceral and (to a less extent) parietal pericardium were found to be studded with raised, whitish firm nodules of 1 to 10 mm. in diameter. There was apparently no calcification. The heart was normal in size and it showed some dilatation of the left auricle with a moderate degree of mitral stenosis. On the endocardial surface of the left auricle there were some nodules of a similar nature to those found on the pericardium, although the process in this instance appeared to be of a minor degree. Further dissection of the heart was not done, with a view to preserving it as a museum specimen, but what could be seen of the aorta and aortic valve did not show any obvious evidence of syphilitic aortitis. The heart muscle, in so far as it was examined, did not appear macroscopically grossly abnormal.

The diaphragm was thickened by a fibrinous exudate which, although penetrating on the left side to involve the spleen, had not produced on the right side any noticeable peri-hepatitis.

The liver was normal in size. Its cut surface did not present any abnormal features and the gall-bladder contained about 3 c.cm. of bile. Gall-stones were not found. The bile-ducts were patent. The gastrointestinal tract appeared normal throughout. The adrenals were normal.

The kidneys were normal in size and the renal pelvis showed no evidence of pyelitis; the capsules were easily stripped off, showing some degree of granulation of the kidney cortex. The ureters and urinary bladder appeared normal.

The uterus and ovaries, together with their ligaments, did not show any abnormal features.

Cause of Death.—The cardiac condition was thought to have been the cause of death.

Summary of Naked-Eye Pathological Findings.—Naked-eye pathological examination showed pericarditis, endocarditis, and mediastinitis; bilateral pleural effusion; perisplenitis; and rheumatoid arthritis.

Histological Examination

Lung and Pleura.—The latter showed fibrous thickening, in which there were several areas of necrosis of varying size from about 0.1 mm. up to 5 mm. These showed some peripheral palisading of nuclei, but in general the appearances were not so characteristic as in the nodules in the heart muscle. Giant cells were inconspicuous.

In sections stained with Orcein much fragmentation of elastic fibres by the necrotic process was discernible.

Rectus Abdominis Muscle.—This showed very clearly demarcated necrobiotic nodules. Muscle bundles were separated, and in several instances the sarcolemma sheath was either destroyed or invaded by proliferating cells.

Heart Muscle.—Sections stained with Van Gieson showed interstitial fibrosis of the muscle fibres, partly in association with necrobiotic nodules, but more frequently remote from the immediate vicinity of such nodules. In addition there was some deposition of calcium salts. The nodules in the heart muscle were sharply demarcated and of characteristic appearance, the peripheral zone of radiating fibroblasts being particularly clear.

A careful search of the heart muscle remote from the necrobiotic nodules failed to reveal any characteristic Aschoff's nodes in the perivascular zones.

Spleen.—The splenic pulp was markedly congested, and the arterioles showed well-marked hyaline degeneration of their medial coats. Some perivascular fibrosis was present, and slight atheromatous changes were seen. A notable feature was the presence of multiple confluent areas of necrobiosis in the thickened capsule. These presented the characteristic morphology of the necrobiotic nodules of rheumatoid arthritis, though giant cells were inconspicuous. The Malpighian bodies were prominent.

Liver.—Brown atrophy was present, and there was a mild degree of cloudy swelling. Certain areas showed congestion, but there was no gross pathological change. No fibrosis was discernible other than a mild degree in certain portal areas.

Kidney.—The cortex showed patches of fibrosis and lymphocytic infiltration associated with glomerular sclerosis and arteriolar sclerosis. The renal tubules showed well-marked stellate lumina produced by cloudy swelling.

Brain and Pituitary.—These showed no gross pathological change.

Larynx: Epiglottic Nodule.—The sagittal section in the midline was passed through the epiglottis and base of the tongue.

Microscopic examination showed multiple foci of necrobiosis in the sub-epithelial zones of the epiglottis, and also in the musculature of the tongue. These foci presented the characteristic histological picture as described in the note on the general histology of these nodules (see further on). Several areas showed hyaline degeneration. Nuclear hyperchromia and pyknosis were well marked. Nuclear palisading was present, and giant cells of the Touton type were frequent. The characteristic lesions were well marked among mucin-secreting accessory salivary glands. The involved tongue

musculature showed interstitial fibrosis, atrophy, and hyaline change.

Nodule from the Forehead.—A nodule from the forehead (biopsy) showed necrobiotic foci surrounded by reactive cellular areas, containing multi-nuclear giant cells (some of Touton type).

Histology of the Nodules.—Characteristically the change was multifocal. Typical lesions from the heart muscle showed numerous minute foci of necrosis. These were approximately 0.5×1 mm. in diameter. The central zone showed pyknosis, karyorrhexis, karyolysis, and a fine powdery deposition of calcium salts.

External to this there was a narrow zone where all structure was lost and which remained almost unstained by eosin. Immediately external to this structureless zone there was some cellular concentration which tended to show palisading of the nuclei and which gave the general effect of cells radiating centrifugally from the central necrotic area. The cells concerned comprised lymphocytes, plasma cells, histiocytes, and small multinucleated giant cells. Some of the latter were of Touton form with a more or less complete peripheral ring of hyperchromic nuclei; others bore a slight resemblance to the tuberculous giant cell.

These centres of necrobiosis were in some cases isolated and occurred in small groups, each separated from its neighbour by normal adipose or muscular tissue. In other instances the necrotic foci became confluent, giving rise to elongated and tortuous masses which presented the characteristic histological features from within outwards, as above described.

We are greatly indebted to Professor D. S. Russell for the following report.

"The specimens received had been fixed in formaldehyde and consisted of (1) a portion of heart muscle, with pericardium, measuring $2.8 \times 1.1 \times 1$ cm. The pericardium was expanded by two opaque greyish-white firm nodules, the larger of which measured 0.7 cm. The muscle showed no naked-eye changes. (2) A portion of skin and subcutaneous tissues, from the elbow, measuring $3.2 \times 1.4 \times 1$ cm. Beneath the skin lay a nodular mass, 1.4 cm. in diameter, of firm opaque greyish-white tissue of tough, somewhat fibrous consistency.

One half of each specimen was embedded in paraffin wax; frozen sections were prepared from the remainder and were stained with Sudan III. Unstained frozen sections were mounted for examination with polarized light.

Microscopic Examination

(1) *Heart.*—The visceral pericardium is everywhere thickened by a slight increase of collagenous fibres, sparse infiltration with small lymphocytes and plasma cells, and an increase in small blood vessels which are engorged. There is great focal expansion of this layer by three nodules. The largest shows a large central acellular area of serpiginous outline; much of it appears fibrinoid, but in places, especially towards the periphery, there are many delicate collagenous fibres, and in places ill-defined granular areas packed with fragmented leucocytes. This acellular central area is surrounded by a dense zone of short spindle, and angular, polymorphic

cells with round, oval, rod, or occasionally lobed, nuclei and abundant basophil cytoplasm. These cells are often arranged as a palisade, their long axes radiating towards the central area. Small multinucleated giant cells are occasionally present. There are no foam cells. The cells are supported by delicate collagen fibres, which in places coalesce to form small hyaline foci. At the periphery of the nodule is an indefinite zone of infiltration with small round cells blending with that in the remainder of the pericardium.

Frozen sections stained for fat show sparse, fine extra-cellular granules throughout the central necrotic area. Intra-cellular droplets of larger size are numerous within the cells immediately surrounding the necrosis, thereby rendering the zone conspicuous under low powers of the microscope. None is to be found in the periphery of the nodule.

With polarized light some of the intracellular Sudanophil material appears doubly refractive, but the central extra-cellular granules are isotropic.

The myocardium shows, in the interstitial tissue at the extreme edge of the block, a nodule resembling the largest focus in the pericardium. It is almost completely surrounded by bundles of muscle fibres, but, from the curvature of the section, it must lie close beneath the pericardium. The muscle is normal, apart from granules of lipofuscin at the poles of the fibre nuclei.

(2) *The subcutaneous lesion* from the elbow expands the dermis and is composed of aggregated nodules of varying size separated by narrow strands of connective tissue. The largest nodules, measuring up to 8 mm., are central and are composed almost entirely of hyaline collagenous tissue. Many areas are devoid of cells; elsewhere sparse fibroblasts separate the fibres. Near the centres of these larger nodules there are, however, a few ill-defined acellular fibrinoid foci occasionally containing angular spaces. The margins of these foci contain delicate collagenous fibres.

Eight smaller nodules, occupying the periphery of the conglomerate mass, are lenticular and are far more cellular. Though all are rich in collagen, the fibres are more delicate. Central necrosis of a fibrinoid character is visible in six, and the general appearances in these are closely similar to those already noted in the pericardium. Several giant cells of Touton type are present in one of the remaining nodules, and in the compressed adjacent tissues of the dermis, which show a diffuse, mainly perivascular infiltration with lymphocytes, plasma cells, and large mononuclear cells. *A few of the giant cells unassociated with nodules are conspicuously foamy, but apart from these no foam cells are present.* The infiltration extends about the appendages to the deep borders of the overlying epidermis. The walls of blood vessels are unaltered.

In frozen sections the large hyaline nodules are for the most part devoid of Sudanophil material, but finely-granular aggregates occupy areas corresponding to the necrotic fibrinoid foci; they are associated with large, unstained acicular and rhomboid cholesterol crystals. In the smaller nodules the amount and distribution of Sudanophil lipid corresponds to that already described for the pericardium.

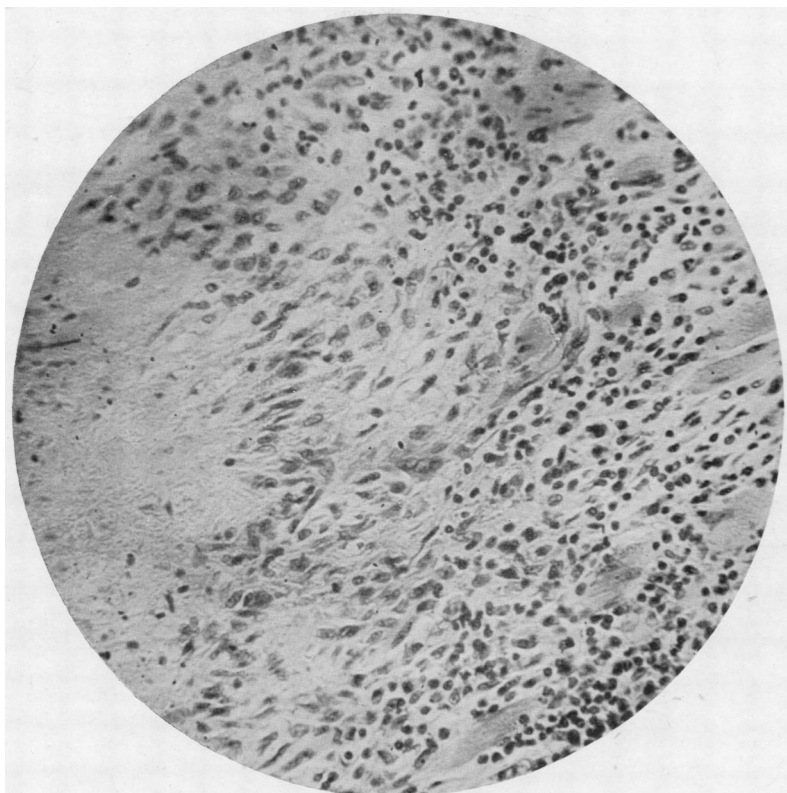


FIG. 2.—High-power view ($\times 220$) of part of Fig. 1. A typical necrobiotic focus in heart muscle. Note the clear, structureless zone. External to the latter the palisading of the nuclei and the cellular infiltration are well shown.

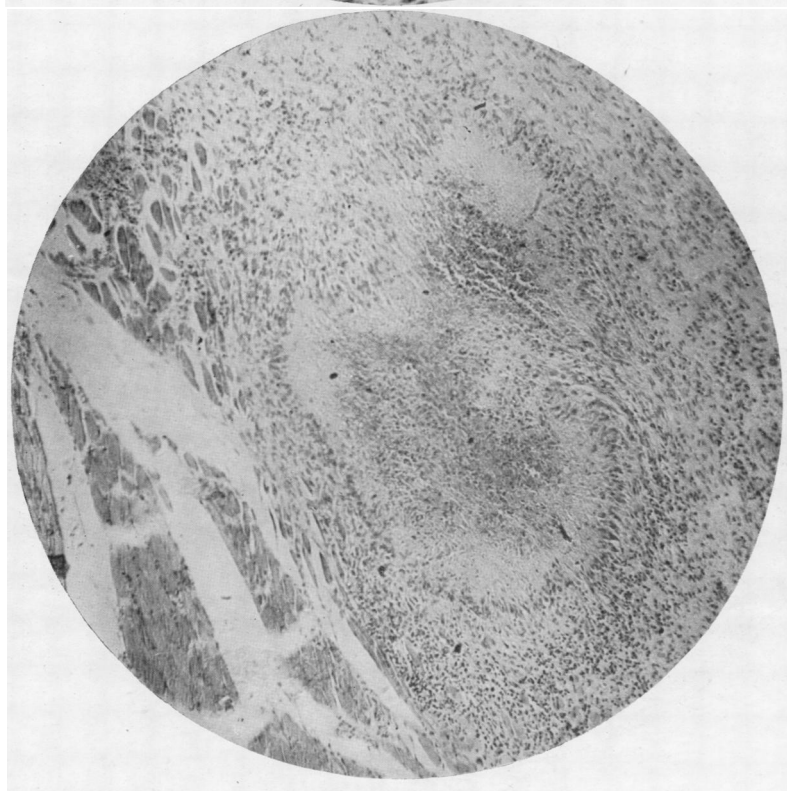


FIG. 1.—Low-power view ($\times 45$) of heart nodule, showing nuclear palisading and cellular infiltration external to the clear, structureless zone.

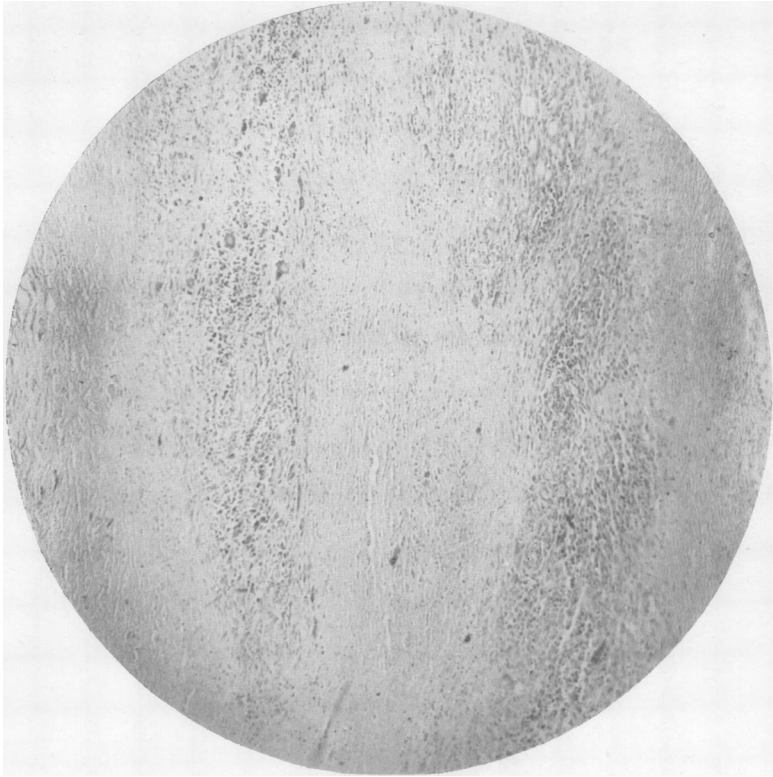


FIG. 4.—Confluent necrobiotic foci in heart muscle, showing giant cells.
Low magnification ($\times 45$).

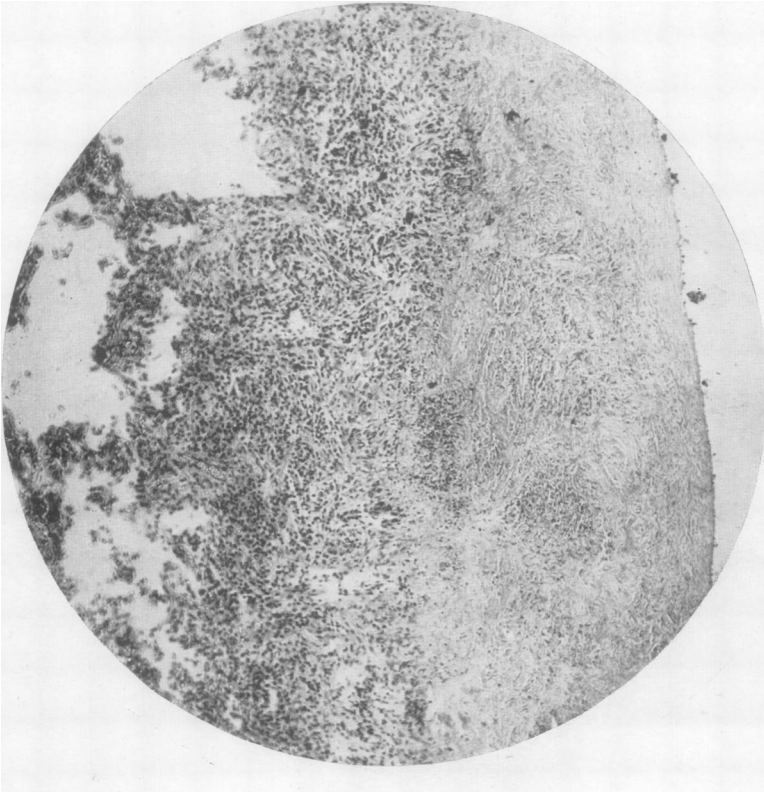
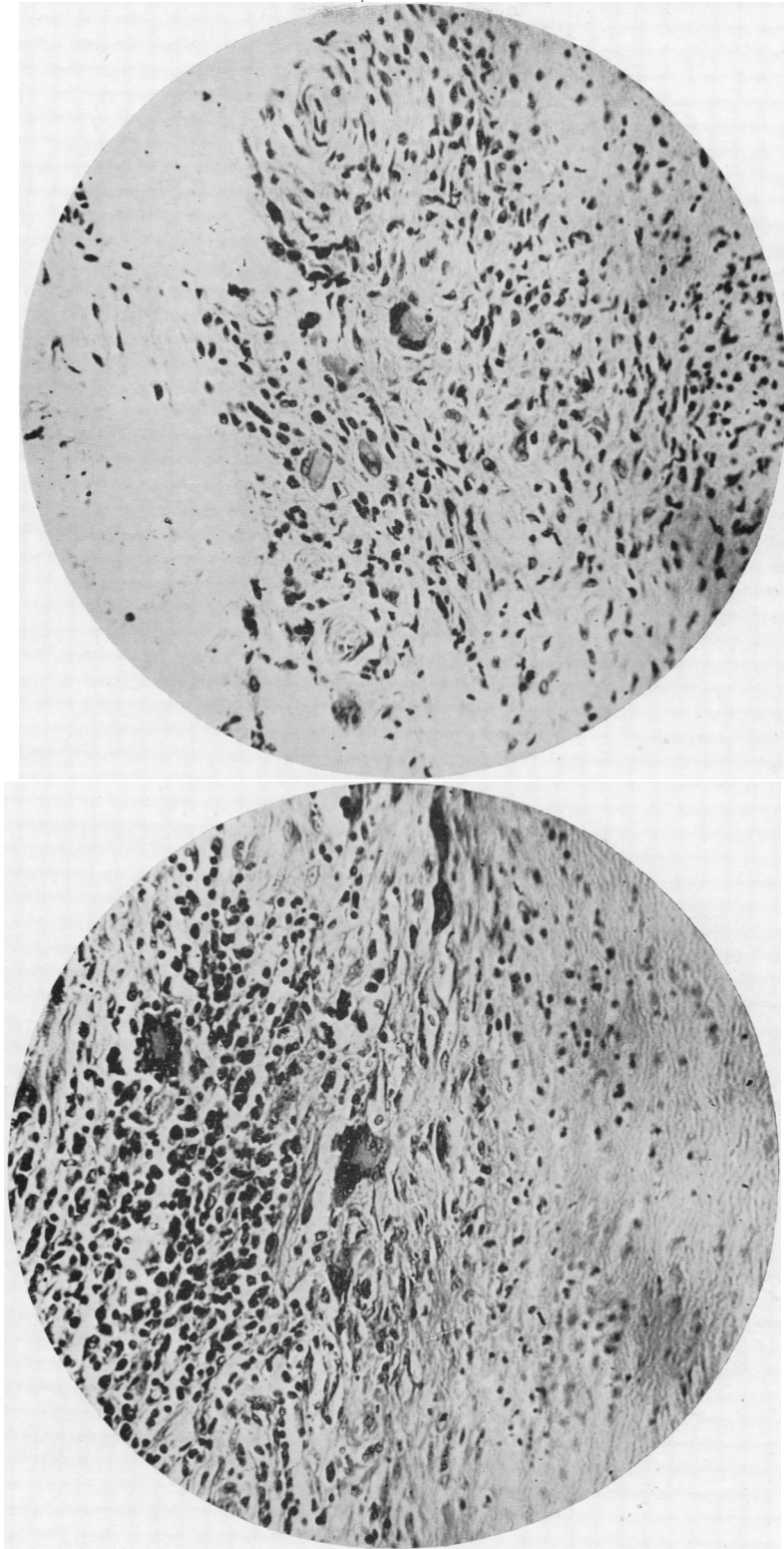


FIG. 3.—Multiple necrotic foci in the pleura. These lesions are at an earlier stage of development than those shown in Figs. 1 and 2 ($\times 220$).



FIGS. 5 and 6.—Showing typical multinucleated giant cells in heart lesions under high magnification ($\times 220$).

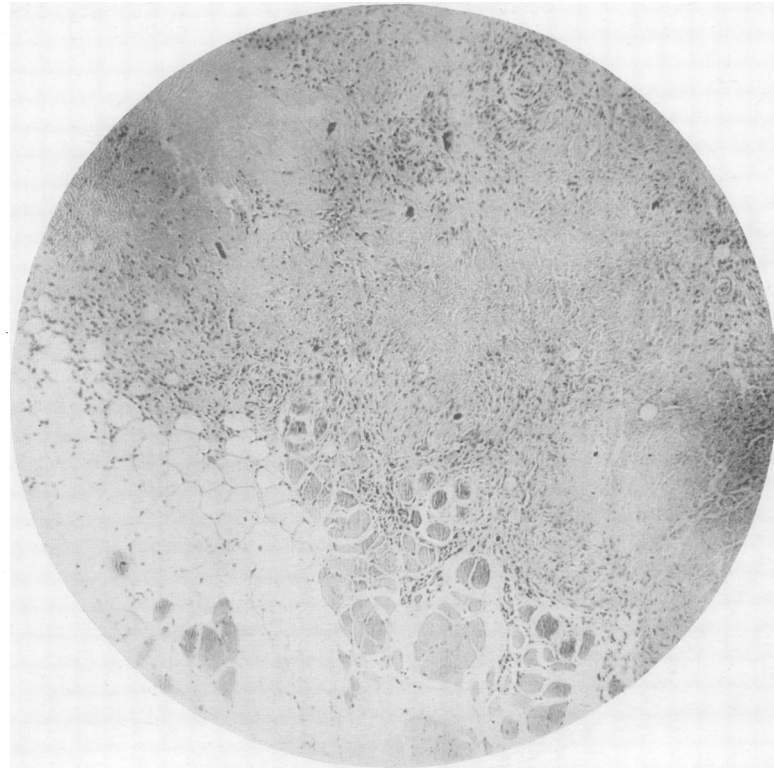


FIG. 7.—Showing necrobiotic changes affecting fat and heart muscle. Low magnification ($\times 45$).

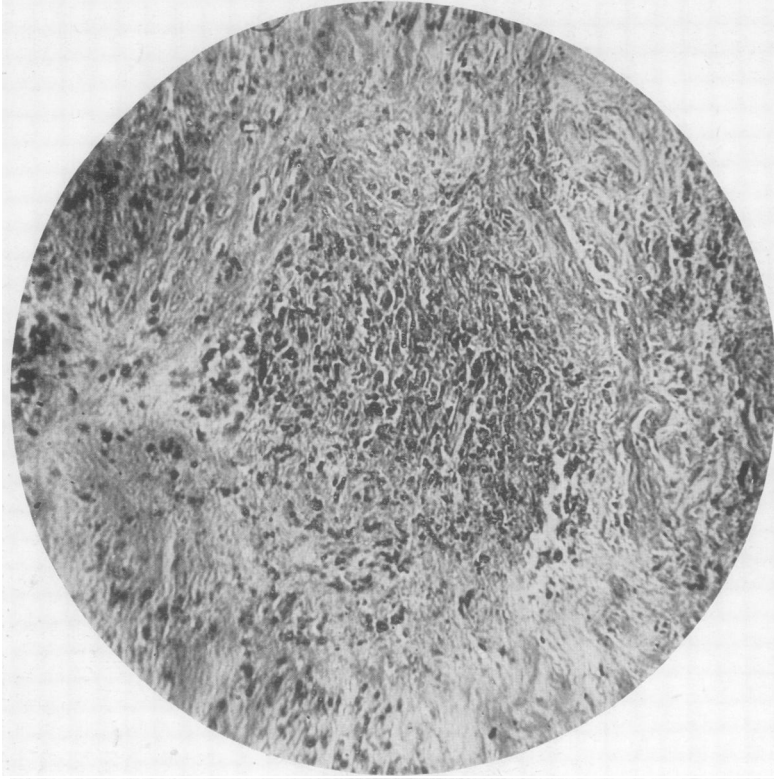


FIG. 8.—A focus of necrobiosis in pleura. Low magnification ($\times 45$).



FIG. 9.—Nodules on the patient's forehead.



FIG. 10.—Nodules on the patient's abdomen.



FIG. 11.—Showing nodules on patient's right elbow and deformity of wrist.

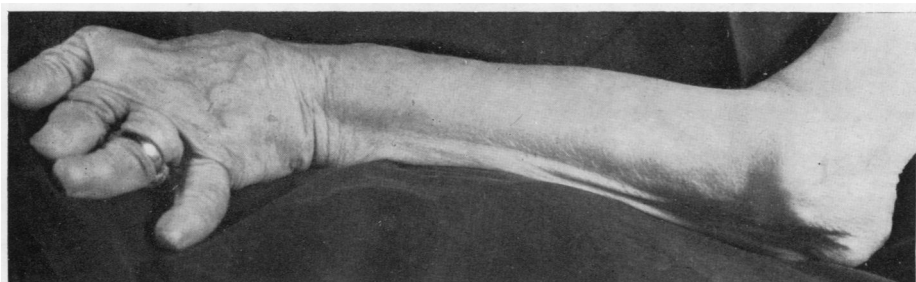


FIG. 12.—Showing gross deformity of patient's left hand and wrist.

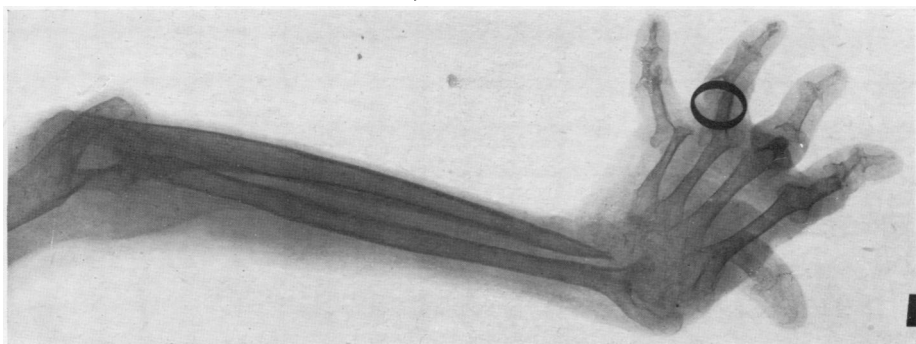


FIG. 13.—Radiograph showing gross deformity of left hand and wrist with osteoporosis.

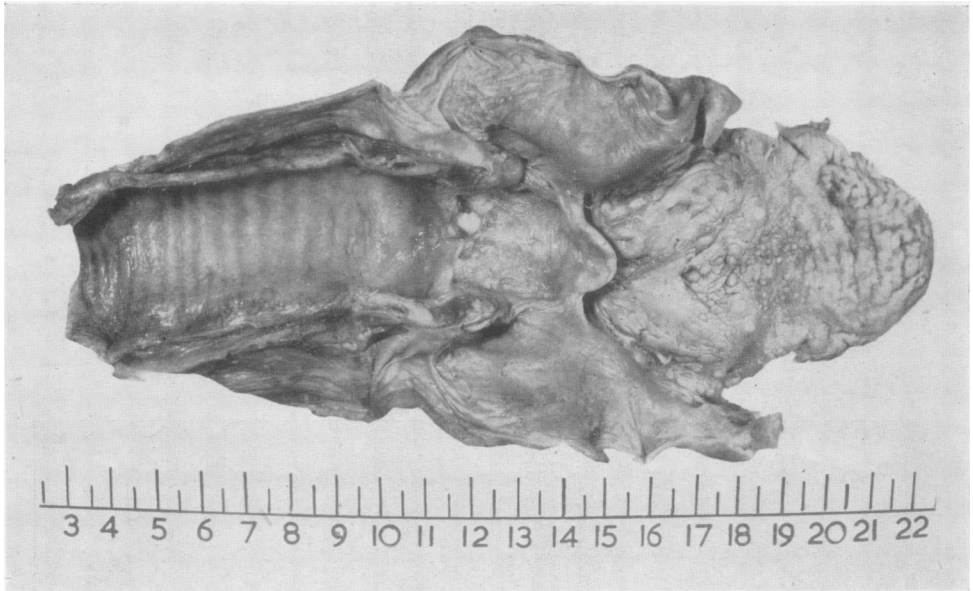


FIG. 14.—Showing small nodules in glottis, and particularly one rather larger one on the epiglottis

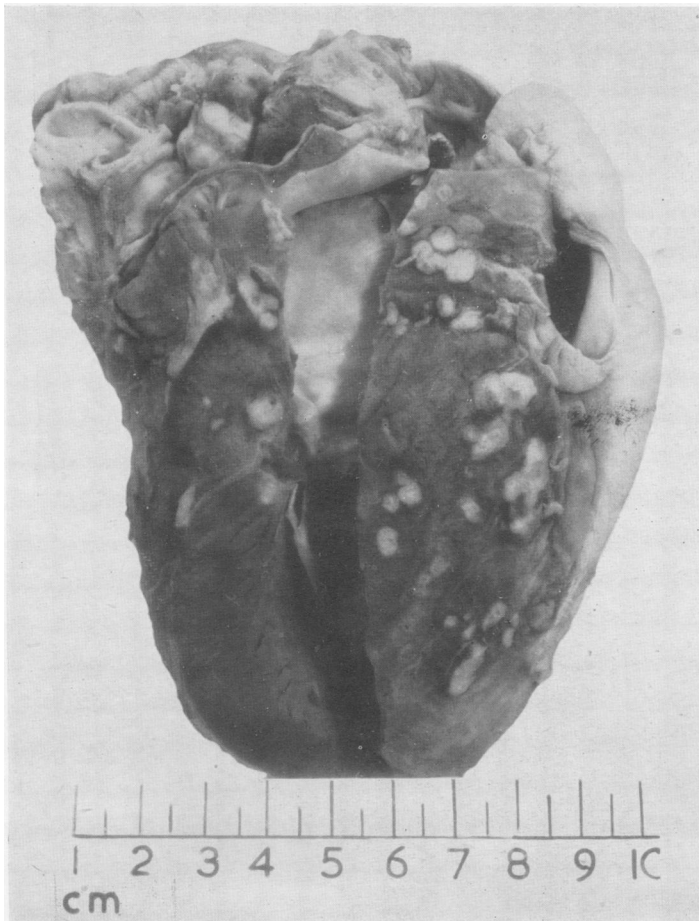


FIG. 15.—Heart, showing multiple epicardial nodules.

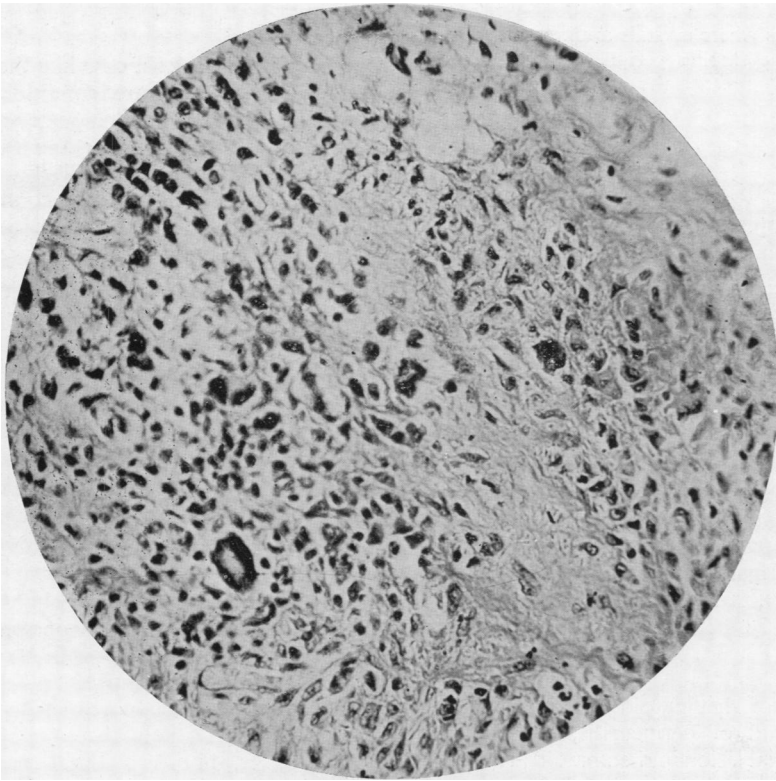


FIG. 17.—Part of Fig. 16 under high power ($\times 220$).



FIG. 16.—Nodule from larynx. Low power ($\times 45$). Several giant cells are discernible. Palisading indistinct.

With polarized light there is abundant doubly refractive lipid in the areas where crystals are present. Unfortunately few of the smaller peripheral nodules are represented; in those present the amount of doubly refractive lipid appears somewhat greater than in the pericardial nodule."

Discussion

A case like our present one, in which the main feature during the latter part of the patient's life consisted in the almost universally distributed (both superficial and visceral) characteristic nodules of the rheumatoid arthritis type, makes one wonder whether rheumatoid arthritis should not be classified with the infective granulomata, together with tuberculosis, syphilis, and lepra, though the infective agent still remains unknown. A varying allergic-like reaction towards the infective agent (whatever it may be) almost certainly plays an important part in the symptomatology.

In regard to the involvement (in the present case) both of skeletal striped muscle (abdominal wall) and of heart muscle, it is interesting to study the paper by Steiner and others (1946) on "Lesions of Skeletal Muscles in Rheumatoid Arthritis". These authors describe a condition of "nodular polymyositis" in cases of rheumatoid arthritis, which, together with a kind of perineuritis, constitutes, they claim, an essential lesion in rheumatoid arthritis, for which they propose the term "nodular neuro-myositis". The size of the nodules varied from those easily seen by naked-eye inspection in stained sections to very small (microscopic) ones. "Lymphocytes and plasma cells were abundant, mast cells occasional, and polymorphonuclear cells and eosinophils rare or absent." All the various lesions of rheumatoid arthritis they regard as of an inflammatory and granulomatous nature. The muscular lesions, they find, differ from those found in other diseases. They obviously differ in degree from the relatively gross necrobiotic nodules in our case.

As to the pericardial and heart lesions in the present case, one may remember that clinical signs of heart involvement of some kind are found in a great many cases of rheumatoid arthritis at various periods of the disease. Feiring (1945) reported an incidence of 29 per cent. ("carditis") in twenty-seven cases of rheumatoid arthritis. It may be remembered that in Still's disease, which is an infantile or juvenile type of rheumatoid arthritis, Still himself reported the occurrence of pericarditis.

Incidentally, our case illustrates a point urged by Steiner and others (1946), namely, that in old quiescent and apparently "burnt-out" cases of rheumatoid arthritis one can never be sure that the

disease may not burst out again with renewed virulence.

One may ask whether a case like the present may be related to certain rare conditions classed as examples of "disseminated lupus erythematosus", a disease, according to Baehr and Pollack (1947), expressing itself morphologically as a fibrinoid degeneration of the collagen of the connective tissues. This, they say, "is but the structural symptom of the disease, whose essential nature is yet to be disclosed". These authors speak of areas of fibrinoid degeneration in the subendothelial connective tissue of the epicardium, which are responsible for pericarditis; of the pleura, responsible for pleuritis; of the peritoneum, responsible for peri-splenitis or peri-hepatitis. In our present case we found no verrucose endocardial lesions of the so-called Libman type, nor the vascular lesions mentioned by these authors. Clinically, indeed, commencing dry gangrene of the right big toe was noted, but unfortunately the corresponding blood vessels were not examined post mortem.

Finally, in regard to lipoidal changes connected with the nodules, a lipoidosis of some kind may undoubtedly be associated with symptoms and lesions of rheumatoid arthritis. As in the present case and cases described by Fletcher (1946), and Kersley and others (1946), there may be, and probably usually is, lipid material present in the necrobiotic nodules of rheumatoid arthritis type; Professor Russell is convinced that the sudanophil substances present in the nodules of our cases are no greater in amount, nor different in character, from what one might expect in such lesions with central necrosis. Secondly, there are rare cases which may be termed "lipoid rheumatism" or "xanthomatous rheumatism" (Parkes Weber and Freudenthal, 1937; Parkes Weber, 1943, and 1948; Layani, 1939; Layani and others, 1939). Graham and Stansfeld (1946) described an exceedingly puzzling case as one of "A Hitherto Undescribed Lipoidosis simulating Rheumatoid Arthritis".

Addendum: January, 1948

Since this paper was completed, one of us (F. Parkes Weber), through the kindness of Dr. G. B. Dowling, has seen a middle-aged man with a typical nodular lesion over the left ulna, near the elbow, of the rheumatoid arthritis type. The patient likewise had a ringed swelling resembling granuloma annulare over the knuckle of the right index finger. This, like the elbow lesion, had gradually developed during the last two years. Both lesions were subcutaneous and situated over prominent bones, and both felt to palpation as if they consisted of multiple small nodules, each nodule probably representing a minute necrobiotic focus surrounded by an area of

inflammatory and fibroblastic reaction. There had also been pain in muscles and joints. Dr. Dowling had seen two similar cases, suggesting that at least some cases of granuloma annulare are of the same nature as the nodular lesions of rheumatoid arthritis, with a similar aetiological factor, not merely a histological resemblance. Even when characteristic arthritic symptoms are absent, nodules of the rheumatoid arthritis type and granuloma annulare may perhaps both be regarded as incomplete forms of what one might term the "rheumatoid arthritis syndrome".

Summary

A case of rheumatoid arthritis is described, in which the characteristic necrobiotic nodules were of extensive distribution. Arthritis changes involved the joints of the arms and legs with gross deformity, and typical lesions were found in the larynx, in the muscles, and in the subcutaneous tissues. Moreover, the internal organs, including the lungs, pleurae, pericardium, and heart muscle, showed macroscopic nodules of characteristic histology.

Attention is drawn to the fact that some of the necrobiotic lesions were associated with giant cells, but that they were not universally present.

In regard to similar cases, which are likely sooner or later to be met with, it is hardly necessary to stress the importance of clinical estimation of phosphatase and phosphorus in the blood, and, if there should be a necropsy, the microscopical examination of the pituitary and parathyroid glands.

Our thanks are due to Mr. S. O. Aylett, F.R.C.S., Surgical Registrar to the Royal Cancer Hospital, for helpful suggestions; and to Professor Dorothy S. Russell, Pathologist to the London Hospital, for most valuable help in the histological examination of the nodules. We also thank Miss Hunt for the clinical photographs; Mr. Chadwin for histological preparations; and Mr. Cowles for photomicrographs.

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Les Nodules Necrobiotiques dans l'Arthrite Rhumatismale

RÉSUMÉ

Cet article décrit un cas d'arthrite rhumatismale dans laquelle les nodules nécrobiotiques étaient très largement distribués. Les modifications arthritiques atteignaient les articulations des bras et des jambes qui présentaient des déformations importantes, et l'on a trouvé des lésions caractéristiques dans le larynx, dans les muscles, et dans les tissus sous-cutanés. De plus les organes internes, y compris les poumons, les plèvres, le péricarde et le muscle cardiaque présentaient des nodules macroscopiques caractéristiques histologiquement.

On attire l'attention sur le fait que les lésions nécrobiotiques étaient associées avec des cellules géantes, mais qu'elles n'étaient pas présentes partout.