WEGENER'S GRANULOMATOSIS

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THIS disease is now well recognized and documented. First described in 1931 by Klinger, it acquired its eponym when Wegener, in 1936 and 1939, presented three cases characterized by destructive lesions of the nose, pulmonary symptoms, glomerulonephritis, and generalized angiitis. The nature of the disease and its classification, in relation to other granulomatous conditions of the nose on the one hand, and to periarteritis on the other, remain the subjects of dispute. The rhinologist still wishes to know whether there is a valid distinction to be made between the generalized disease and the locally destructive lethal midline granuloma. The solution of this nosological problem must depend, among other things, on the careful analysis of the recorded clinical features of authenticated cases, and for this reason a further instance of this rare and fatal condition is recorded here.

Many authors believe that Wegener's granuloma represents one example of a spectrum of disease, ranging from purely necrotizing granulomatous conditions of the upper respiratory tract, through mixed forms, to a generalized condition of vasculitis without granuloma formation. Such was the opinion of Godman and Churg, who, in 1954, defined clinico-pathological criteria enabling Wegener's granulomatosis to be diagnosed as an entity, and to be segregated from allied granulomatous conditions, and from the miscellaneous category of vascular diseases called periarteritis nodosa. Their criteria have been accepted and used by most writers on this subject since then; they are:

(1) Necrotizing granulomatous lesions in the upper air passages, or in the lower respiratory tract, or both.

(2) Generalized focal necrotizing vasculitis, involving both arteries and veins, almost always in the lungs, and more or less widely disseminated in other sites.

(3) Glomerulitis characterized by necrosis (and thrombosis) of loops or lobes of the capillary tuft, capsular adhesion, and evolution as a granulomatous lesion.

Walton, writing in 1958, found 58 cases satisfying these criteria, but remarked that many other cases had to be excluded because of insufficient data. His pathological description was detailed and comprehensive, telling how the lesions have a constant pattern irrespective of site, and how focal

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vascular lesions, showing fibrinoid necrosis of all layers of the vessel wall, occur independently of granulomata. He believes that this condition is distinct from periarteritis, suggesting that the primary lesion is granulomatous ulceration in the respiratory tract, to which the angiitis is a secondary hypersensitivity phenomenon. There is evidence for believing that periarteritis arises as an abnormal immunological response; the granulomata resemble those of experimentally induced serum sickness, and the disease is associated with such features of allergic conditions as eosinophilia, raised serum gamma globulins, and purpuric skin rashes.

Friedmann, in 1955, commenting on the difficulties that have beset classification, remarked that rhinologists have often failed to exclude general disease in cases of nasal granuloma; while general physicians have frequently paid scant attention to lesions in the upper respiratory tract, when writing about periarteritis nodosa. As regards outcome, he divided malignant granulomas of the nose into two groups:

(1) A "classical" type, with external ulceration of the face, and no polyarteritis, in which giant cells are absent from the lesions.

(2) A form with no external ulceration, with widespread necrotizing angiitis and granulomatosis, resulting in death from uræmia, and in the lesions of which giant cells may often be found. He held the opinion that both types are probably identical in nature.

Brown and Woolner (1960) reported six new cases and suggested that no distinction should be drawn between Wegener's granuloma and lethal midline granuloma. They could find no record in which biopsy revealed definite vascular involvement, even when vasculitis was seen later in post-mortem specimens.

The frequency with which this disease occurs is difficult to determine. Pirogova and Shapiro (1960) analysed 80 authenticated cases, while Richards, Razavi, and Leftwich, in 1962, said that the number of accepted cases reported between 1939 and 1960, varied greatly in the writings of different authors, the highest estimate being 84.

The case presented here showed most of the features that may be seen in this protean disease, was diagnosed during life, and showed vascular involvement in a biopsy taken from the area of nasal ulceration.

The patient, a man of 67, had no nasal symptoms until the middle of October, 1962, when he became troubled by nasal obstruction and daily nose bleeds. Before he was seen at King's College Hospital, a swelling of the nasal septum had been incised, in the belief that it was an abscess. In 1951 an operation had been performed to remove bladder papillomata, which were revealed, by subsequent inquiry, to contain low-grade carcinomatous changes. For many winters he had suffered from bronchitis.

He was admitted to King's College Hospital on December 11th, 1962. During the week before his admission, he had become increasingly breathless, and had suffered joint pains in the left knee and ankle, and both

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elbows. He was an ill, sallow man, dyspnœic at rest, and with slight cyanosis. There was no fever and he was not clinically anæmic. Splinter hæmorrhages were seen under his fingernails. The liver edge was just palpable below his costal margin, and the abdomen bore a vertical suprapubic scar. Generalized bronchial breathing was heard in the chest, and moist sounds were present over both upper lobes. His speech was sluggish and his concentration poor. Both elbow joints, and the left knee and ankle, were stiff, hot, swollen, and painful. There was a purpuric rash over the elbows.

The mouth and pharynx were dry and dirty, the tongue coated. His nasal septum was deviated into the left nasal cavity, and in its concavity, on the right-hand side, was a shallow, irregular, ulcer, mainly over the cartilaginous part, but extending back onto the bony septum. The postnasal space was partly obstructed by blood-stained crusts.

A chest X-ray, shortly after admission, showed opacities, in both mid-zones, radiating from the hila. The appearances were considered to be due to inflammatory changes, or to pulmonary œdema. Sinus X-rays showed polypoid thickening of the mucosa in the left antrum. His hæmoglobin was 80 per cent., with anisocytosis of red cells, and there was a moderate neutrophil leukocytosis, with a slight shift to the left. Platelets were present in sufficient numbers. His blood urea, at this time, was 176 mg./100 ml.

On the following day the patient became increasingly drowsy and developed signs of a deep vein thrombosis in the muscles of the left calf. At this time, his breathlessness was thought to be the result of repeated pulmonary infarcts.

By now, after twenty-four hours in hospital, he had passed no urine. The bladder was not palpable in the abdomen, and catheterization produced only one to two ounces of cloudy urine. This specimen contained large quantities of albumen, red and white blood cells, granular casts, and organisms. A clear account of his urinary activity, during the preceding days, was not obtainable, but, in view of his past history of bladder disease, the possibility of a postrenal cause for the anuria seemed high. A straight X-ray of the abdomen did not show renal calculi. In the early morning of December 13th, a cystoscopy was performed, ureteric catheters passed, and, by means of retrograde pyelography, the postrenal urinary tract was shown to be without abnormality.

His blood pressure was 180/85, and there was no reason to suspect that a period of hypotension might have determined the onset of a prerenal anuria.

The only satisfactory way to explain the sudden onset of renal failure, the dyspnœa with X-ray opacities in the lungs, and the presence of ulceration in the nasal cavities, without invoking multiple pathological processes, was by a diagnosis of Wegener's granulomatosis.

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Under local anæsthesia, a biopsy was taken from the nasal septum. Histological examination of the material removed was reported on as follows: "Sections show fibrinoid material and numerous acute inflammatory cells. Foreign body type giant cells are present. A number of vessels are present in the specimen and their walls are probably also involved in this fibrinoid degeneration. No acid-fast bacilli can be seen in a section stained by Ziehl-Neelson's method. The appearances are essentially non-specific, but are compatible with a diagnosis of Wegener's granulomatosis (Fig. 1).

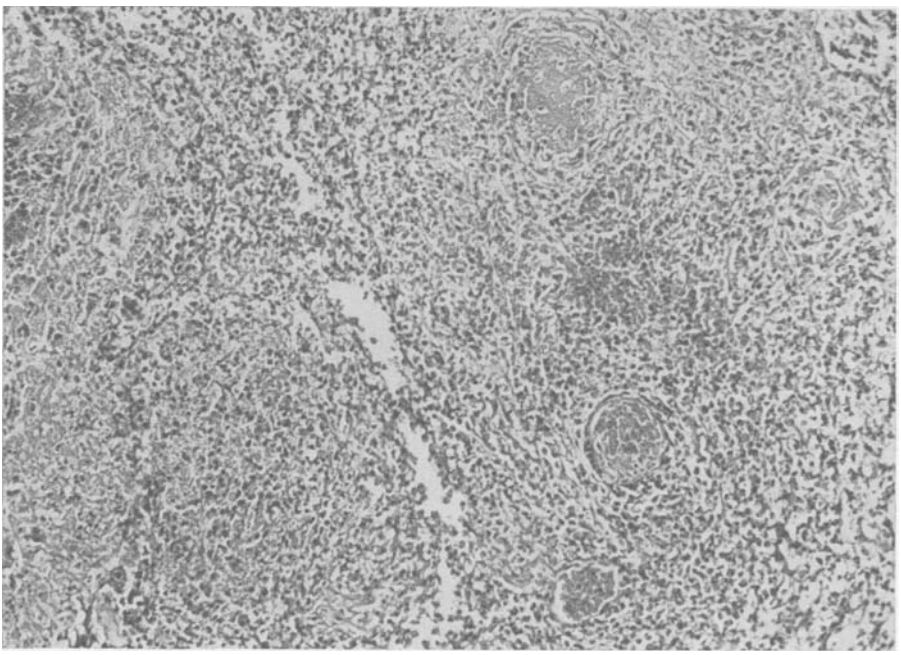


FIG. 1.
Section of biopsy from nasal lesion, ×150 showing blood vessels with degenerative changes.

By the following morning his blood urea had risen to 381 mg./100 ml. and he was put on an artificial kidney. Dialysis was abandoned after one and a half hours, when a sudden and severe fall in blood pressure occurred. He gradually deteriorated and died on the morning of December 17th.

At a post-mortem examination, the following abnormalities were noted. There was a shallow ulcer, in the trachea, just above the bifurcation, similar in appearance to that on the nasal septum. Both lungs were congested, with reddened bronchi filled with mucus and blood. In the middle lobe of the right lung, there was a firm whitish area. The pericardium was the seat of a slight fibrinous pericarditis. The spleen showed recent infarcts and white specks. Both kidneys were congested, with

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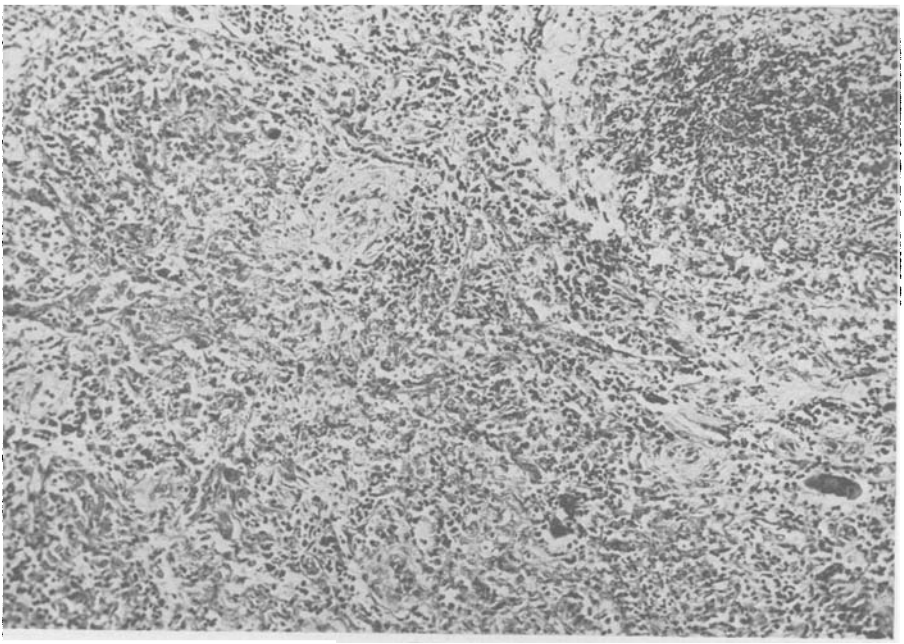


FIG. 2.
Section of granulomatous lesion from lung ×150 showing necrotic granuloma and giant cells.

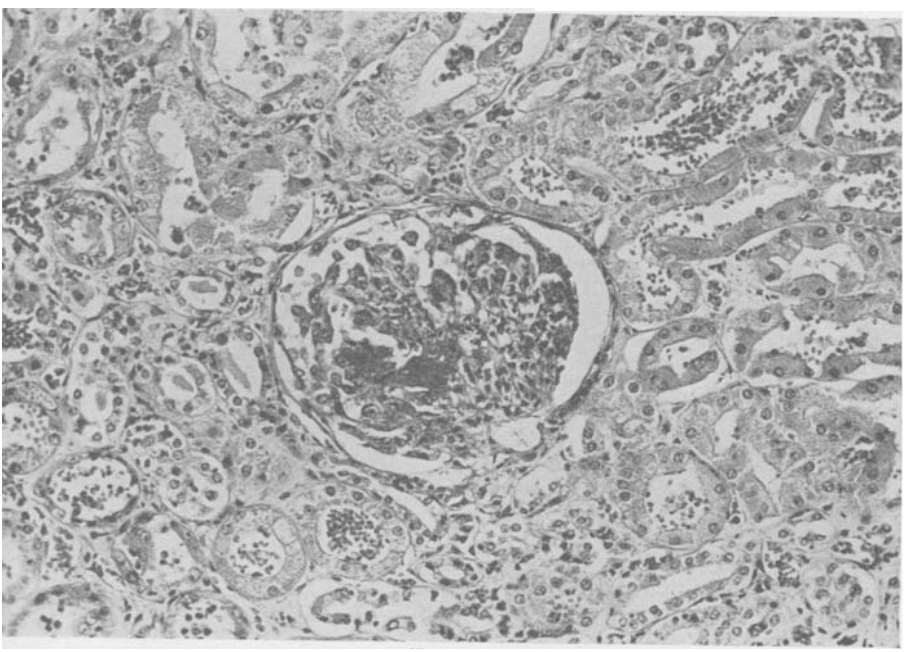


FIG. 3.
Section from kidney ×200 showing the changes of glomerulitis.

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minute, white, multiple areas under the cortices; there was an infarct in the right one.

Histological examination of the lungs showed several necrotic granulomatous lesions, with a patchy infiltrate of both acute and chronic inflammatory cells. There were no follicular lesions, and acid-fast bacilli were not seen by Ziehl-Neelson's method of staining. Several small arteries showed an acute panarteritis.

The microscopic abnormalities in the kidneys were an acute focal glomerulitis involving nearly all the glomeruli, of a kind that is typical of the glomerular type of polyarteritis, and recent infarction. There was moderate arteriosclerosis. An occasional small granulomatous lesion was seen in the renal medulla, closely resembling the lesions in the lung. The spleen contained an infarct and the changes of acute panarteritis. Skeletal muscle sections showed patchy degeneration of muscle fibres, and an occasional vessel with a thickened wall and a cuff of neutrophils, eosinophils, lymphocytes, and plasma cells. The liver was the seat of mild chronic venous congestion, and fatty change.

Summary

The difficulties associated with the classification and description of Wegener's granulomatosis, and related conditions, are briefly reviewed. A further case, satisfying the accepted criteria, is described.

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