FIG. 1.—Photograph of simple ulcer removed from greater curvature of the stomach, showing a probe in the eroded artery.

Comment

A total of eighty-eight cases of benign greater curve gastric ulcers have now been published. This is the first in which the patient was receiving steroid therapy. The increased incidence of peptic ulceration in patients receiving steroid therapy is well established and it is possible that with the increase in the therapeutic use of these substances, benign peptic ulcers of the greater curvature of the stomach may be seen more frequently.

Addendum

Since this paper was prepared, Low (1962) has described four patients in whom a greater curvature gastric ulcer was demonstrated radiologically whilst they were receiving steroid therapy. Further barium studies showed evidence of healing ulceration, but in no case was the lesion proved histologically.

I am grateful to Mr. A. J. Heriot and Dr. J. L. Livingstone for permission to publish this case and to Dr. F. E. Dische for the histology report. I should like to thank the Department of Medical Photography at the Southern Group Laboratory for the photograph and Mrs. R. M. Springall for her secretarial assistance.

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PULMONARY DETERIORATION IN WEGENER'S GRANULOMATOSIS DURING STEROID THERAPY

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THE treatment of Wegener's granulomatosis is unsatisfactory and the prognosis poor (Walton, 1958). Steroids have been recommended (Moore, Beard, Thoburn and Williams, 1951; Cutler, 1955), but their potential harmful effects must be considered. Although involvement of the respiratory tract is frequent and cavitation may occur, extensive cavitation is unusual. In the patient described, widespread pulmonary cavitation developed during

a course of steroid therapy while the patient remained very well generally, and it is likely that the pulmonary deterioration resulted, at least in part, from the administration of the prednisolone.

Case Report

Mrs. M. S., a housewife, aged 46 years, presented on 20.9.61 with a three-week history of pain over the maxillary sinuses, nasal congestion, earache, malaise and nocturnal sweats. In addition, she admitted to a

FIG. 1.—Chest radiograph. Note diffuse infiltration and cavity left apex.

productive cough and loss of weight for two months. There were no urinary symptoms, no history of taking any specific drugs prior to her illness, and nothing relevant in the past or family history.

On examination she was febrile and tender on pressure over the maxillary antra; there was partial nasal obstruction, but no septal ulceration was noted. There was an inflamed left ear drum. Conjunctivitis was present. Inspiratory crepitations were heard over both upper lobes and at the left base, but there was no clinical evidence of consolidation or cavitation. There was no lymphadenopathy and the cardiovascular, alimentary and nervous systems were normal.

Investigations. Hb 72%. WBC 11,100/cu. mm., with 64% polymorphonuclears, ESR 125 mm/hr. The chest radiograph showed diffuse, woolly opacities over both lung fields, with a small, thin-walled cavity containing a fluid level at the left apex. These appearances suggested an acute tuberculous infection (Fig. 1). A radiograph of the sinuses was normal. Sputum examination showed persistent *E. coli* infection and tubercle bacilli were not isolated. Serum proteins (including electrophoresis), calcium, phosphorus and urea were normal. Mantoux test 1:1,000 was negative. Slight proteinuria was present, but there were no red cells or casts. The L.E. phenomenon was not demonstrated in the serum.

Course. In view of the pulmonary involvement, eye changes and negative Mantoux test, a diagnosis of sarcoidosis was considered possible, although cavitation is rare in this condition, and a Kveim test was initiated. Meanwhile, on 4.10.61 prednisolone, 10 mg./t.d.s., was started, together with tetracycline, 250 mg./q.d.s. The temperature fell rapidly, there was an improvement in general well-being, and the ESR fell to 60 mm./hr. within seven days. Slight radiological improvement occurred and she was discharged on 1.11.61 on pred-

FIG. 2.—Chest radiograph shows new cavitation at left apex and cavitation in right mid and lower zones.

nisolone, 5 mg. daily. The Kveim test was later found to be negative. She remained clinically well, apart from occasional nasal catarrh, until 13.3.62. At this time she had an attack of sinusitis and the ESR was found to be 83 mm./hr. A chest radiograph showed considerable deterioration, as cavitation had now occurred in the right mid-zone, with surrounding lung parenchymal infiltration, and a new cavity had developed in the left upper zone (Fig. 2). She was readmitted to hospital. Nasal examination then showed crusting and mucosal ulceration over the septum, and biopsy revealed well-marked granulomatous infiltration with giant cells and vascular necrosis (Fig. 3). A diagnosis of Wegener's granulomatosis was made. Slight thickening of the left antral mucosa was present on radiographs of the nasal sinuses. She was treated with bed rest and antibiotics and improved clinically, although there was no radiological improvement. She was discharged on 28.5.62, and she has remained clinically well since, but the ESR has been persistently high, and on her most recent chest radiograph, on 20.9.62, the cavities were increased in size and, in spite of their chronicity, had not developed thick walls, while surrounding lung infiltration persisted (Fig. 4).

Discussion

Wegener's granulomatosis is a condition of unknown aetiology, characterized by extensive granulomatous involvement, initially of the naso-respiratory tract and ultimately affecting many other systems, including the blood vessels, skin, nervous system, joints and kidneys (Godman and Churg, 1954). Death from respiratory or renal failure is common and usually occurs within six months (Walton, 1959), although rarely the condition can last up to four years (Walton, 1958). The essential

FIG. 3.—Biopsy of nasal septum, showing vascular necrosis, giant cells and granulomatous infiltration with endothelial cells, lymphocytes and plasma cells ($\times 330$).

histological pattern shows granulomatous infiltration with endothelial cells, plasma cells, lymphocytes and numerous giant cells, and widespread necrosis; blood vessels may be involved, but only by virtue of proximity to the granulomatous infiltration. This picture is well seen in Fig. 3.

The common radiological findings are rounded shadows in one or both lungs, and although central cavitation may be found on postmortem examination, radiological evidence of extensive cavitation is less common. When rapid spontaneous progression of the disease does occur, constitutional effects are marked, and the patient usually has persistent malaise, fever, and weakness (Walton, 1958). In the patient described, the absence of any constitutional disturbance was notable, in spite of extensive pulmonary cavitation, supporting the view that the pulmonary changes were aggravated by the prednisolone, and did not solely develop in the natural course of the disease. The possibility that the prednisolone masked the constitutional disturbances while natural progression of the disease occurred, was considered, but was thought unlikely in view of her favourable progress to date, with lack of clinical evidence of involvement of other systems.

Extensive necrotizing granulomatous lesions, often with hæmorrhagic suppuration in the upper respiratory tract, are frequently the presenting feature in Wegener's granulomatosis (Wegener, 1936 and 1939), but sometimes pulmonary symptoms may predominate (Weinberg, 1946, and Godman and Churg, 1954). In our patient, nasopharyngeal involvement was limited to persistent mild sinusitis, with only minimal crusting on the nasal septum. The disproportion between the nasopharyngeal and pulmonary lesions may also be partly due to the influence of steroid therapy.

FIG. 4.—Chest radiograph shows enlargement of cavities at right mid and lower zones and left apex.

The prognosis in Wegener's granulomatosis is uniformly bad, and death usually occurs within six or twelve months (Walton, 1959, Aubin, Duperrat and Debain, 1958). Treatment is unsatisfactory. Antibiotics may be used to control secondary respiratory infection. Local radiotherapy to the nasopharynx appears to be the most effective local measure (Walton, 1958). Steroids have been used on the basis of a possible hypersensitivity mechanism underlying the disease (Leggat and Walton, 1956). However, any hypersensitivity involved would probably account only for the later systemic features of the disease, and not for the local respiratory manifestations. The two dangers inherent in steroid therapy in Wegener's granulomatosis are encouraging secondary infection and delaying healing of the necrotic lesions. The progress of the pulmonary lesions in our patient was probably mainly due to the inhibitory effect of prednisolone on the healing process, since there was no evidence of continued secondary infection during the progressive pulmonary deterioration.

In conclusion, we would suggest that if steroids are used to treat patients with Wegener's granulomatosis, they should be reserved for the later systemic manifestations and not given when only respiratory tract involvement is present.

We would like to thank Dr. S. E. Tanner and Dr. C. W. Lawson for permission to publish this case report, and also Dr. J. L. Freer and Dr. T. Lodge for their advice and encouragement.

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FATAL APLASTIC ANAEMIA FOLLOWING SULPHAPHENAZOLE (ORISULF) THERAPY

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WINTROBE (1961) classifies sulphonamides among the rarer causes of pancytopenia. Nevertheless, aplastic anaemia due to sulphonamides occurred in 5.3% of Welch's series (Welch, Lewis and Kerlan 1954), 8.7% of Wolff's 334 cases (Wolff and others 1959), and once in Scott's series of 39 cases (Scott, Cartwright and Wintrobe 1959). Similarly the shorter-acting sulphonamide preparations have appeared individually in the literature from time to time as causing aplastic anaemia viz. sulphathiazole (Strauss, 1943; Meyer and Perlmutter, 1942), sulphanilamide and sulphadiazine (Denny and Menten, 1946), sulphabutin (Wagner and Sterz, 1961), and sulphapyridine (Scott and others, 1959). The sulphonated nitrobenzene nucleus of the sulphonamide compounds has been blamed for the bone marrow depression and this indeed would seem to be the case, as structurally related compounds like carbutamide, tolbutamide, acetazolamide and thiosemicarbazone have all been associated with the development of aplastic anaemia. (see Wintrobe (1961) for references).

There have, however, been few reports of this complication following the use of the newer, longer acting sulphonamides.

The first of these drugs, sulphamethoxypyridazine was first reported to have caused aplastic anaemia in 1958 (Holsinger, Hanlon and Welch). A further report followed in 1961 (Johnson and Korst).

A sulphonamide with a similar prolonged action is 3-(p-amino benzene sulphonamido)-2-phenylpyrazole (sulphaphenazole, 'orisulf', 'orisul') which has the following structural formula:—

The case reported here suggests a possible association between the administration of this drug and the development of aplastic anaemia.

Case Report

The patient was a 66-year-old housewife who lived in Jersey. For 15 years she had suffered from asthma and chronic bronchitis. On May 26, 1961, she went to see her general practitioner with breathlessness which had not responded to aminophyllin and ephedrine. Severe bronchospasm was diagnosed and betamethazone prescribed; initially 2 mg was given daily in divided doses, reducing to 0.5 mg daily by the 10th June, 1961 when 'Amesec' was introduced.

In July 1961 a diagnosis of acute bronchitis was made and a 4 day course of 'Orisulf' given—1 g twice a day for the first 2 days, and 0.5 g twice a day for the next two.

The patient was next seen by her doctor on August 16, 1961 when she had had no drugs for 4 weeks. She had been feeling well but petechiae were noticed by the doctor. Ascorbic acid was given pending investigation.

Early in October 1961, in addition to petechiae in the skin and hard palate, there were ecchymoses in the skin and Hess's test was strongly positive. At this time the patient was receiving Histryl spansules (Diphenylpyraline hydrochloride) for vasomotor rhinitis.

Blood count: Hb. 62%; wbc 4,700/cu.mm.; polymorphs 30%, eosinophils 6%, lymphocytes 63%, monocytes 1%, PCV 30%; MCHC 30.5%, platelets 220,000/cu.mm.

On October 25, 1961 the patient was admitted to the General Hospital, Jersey. A few days before her admission she had become lethargic and anorexic and had developed soreness of the tip of her tongue. A further blood count showed: Hb. 26%; wbc 3,200/cu.mm.; reticulocytes 0.3%, PCV 13%; MCHC 29.5%; ESR 75 mm hr (Wintrobe). The sternal marrow was hypoplastic and acellular. An occasional normoblast was present. One myelocyte was seen in 20 /12 inch fields.

In addition to blood transfusions, ACTH, prednisone, iron, ascorbic acid and Vitamin B₁₂ were given. On February 12, 1962, the patient was transferred to the Westminster Hospital for consideration of bone marrow infusion.