increased index of suspicion will probably uncover more cases.

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Necrotizing Vasculitis and Ulcerative Colitis

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Skin lesions are frequent extracolonic manifestations of ulcerative colitis, the incidence of such lesions ranging from 6% to 34% of cases (Bockus *et al.*, 1965). We describe a patient with severe ulcerative colitis who developed extensive necrotic skin lesions due to cutaneous vasculitis and survived.

Case Report

The patient, a 26-year-old man had enjoyed good health till May 1972, when a superficial thrombophlebitis occurred in the left popliteal fossa. This healed spontaneously within a few days. From that time on he suffered from a migrating thrombophlebitis affecting alternately the knees and elbows. Five months later his general condition deteriorated; he felt tired and weak and developed low-grade fever. Extensive physical, biochemical, radiological, and serological examination showed nothing abnormal, and skin biopsy of the left elbow showed no underlying disease. Treatment with coumarin was given from December 1972 to July 1973, during which no relapse of migrating thrombophlebitis occurred.

The second day after stopping the coumarin the patient became feverish and developed painful blue spots on both thighs which disappeared spontaneously within a day. Two days later a more extensive bluish area appeared on the inner aspect of the left thigh which did not resolve but instead central haemorrhagic necrosis of the skin developed. Again extensive examination was carried out for a systemic disease but no specific abnormalities were found. Treatment with coumarin was reintroduced but was stopped after three days because of haematuria and bloody stools. At that time the patient also suffered a short-lasting attack of arthritis of the jaw joints. X-ray studies of the thorax and colon and an intravenous pyelogram were thought to show nothing abnormal. At sigmoidoscopy the rectal mucosa appeared to be haemorrhagic. On 16 August two biopsy specimens were taken from indurated remnants of healed thrombophlebitis on the back of the left thigh and upper calf. That evening a large, painful, bluish skin discoloration appeared centred around the previous already necrotic lesion on the left thigh. On 18 August he was transferred to this hospital for investigation of blood-clotting abnormalities.

On admission he appeared ill and pale-looking. Temperature 38.9°C. Examination of the head, neck, lungs, and heart showed nothing abnormal. His abdomen was slightly tender on palpation

but was otherwise normal. On the anterior aspect of the left thigh there was an extensive slightly raised area of bluish purple discoloration. The lesion was sharply and serpigiously circumscribed and surrounded by an erythematous zone. Small vesicles and a few blisters filled with haemorrhagic fluid were present within this area, which surrounded a centrolateral black necrotic patch (fig. 1 a, b). The left side of the scrotum was black and necrotic and surrounded by an erythematous zone. All the peripheral arteries pulsated normally.

FIG. 1—(a) Necrotic skin lesion on anterior aspect of left thigh and scrotum on admission. (b) Small vesicles and blisters filled with haemorrhagic fluid within bluish black skin. (c) and (d) Microscopical appearances of colonic mucosa before treatment. Severe inflammation was confined to mucosal layer, with cryptitis, crypt abscesses, and depletion of mucus. No evidence of vasculitis was present in submucosa (arrows). ($\times 50$). (e) Microscopical appearances of mucosa of colon after one and a half months of treatment. Striking regression of inflammatory reaction had occurred. Epithelium was of normal appearance. ($\times 50$)

Urine analysis and blood chemistry showed nothing abnormal throughout the illness. The E.S.R. was 73 mm in the first hour, haemoglobin 9 g/100 ml, and W.B.C. 20,000/mm³. Fibrin degradation products were increased and the Thrombotest time (Owren) was prolonged; all other coagulation values were normal. No cryoglobulins were detected. Widal, Bang, and Yersinia agglutination reactions were negative. The cytomegalic virus complement fixation titre was 1/16. The antistreptolysin titre was 100 U and the Rose-Waaler and Latex test results were negative, as was the Wasserman reaction. Blood cultures remained sterile on seven occasions. Stool cultures were negative for salmonella, shigella, yersinia, ova, and parasites. Faecal examination for occult blood using benzidine was strongly positive.

The first day in hospital the patient developed arthritis and periarthritis of the right elbow, and 12 hours later the same symptoms appeared in the left elbow with concomitant swelling and oedema of the upper arm. Next day he experienced sharp

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pain in the right hip and within 45 minutes slightly raised purpuric lesions appeared in that area. The purpura quickly became more intense and within a few hours covered an area of 25 by 20 cm. The irregular border of the purpuric zone was sharply demarcated by an erythematous zone. Within several days all the discoloured skin on the left thigh and on the right hip had become black and necrotic with sharp demarcation from the healthy skin (fig. 2 a-d). Together with the skin manifestations appeared a sharp increase in the already raised fibrin degradation products, and a drop in factor V was noted while the platelet and fibrinogen levels remained within the normal range.

FIG. 2—Development and evolution of necrotizing vasculitis of skin and subcutaneous tissue of right hip. (a) Palpable purpura which appeared 45 minutes after pain in right hip. Local skin oedema became evident. (b) More intense and confluent purpura after six hours. Purpuric area was sharply and serpiginously circumscribed and surrounded by erythematous zone. (c) Seven days later. Skin was black, necrotic, and sharply demarcated from uninvolved skin. (d) Two weeks after onset of lesion. Flat defect about 1 cm deep remained after removal of necrotic debris.

The history of migrating thrombophlebitis, arthritis, and skin lesions apparently vasculitic in origin was suggestive of a systemic or underlying disease. On careful questioning the patient recalled that he had experienced several episodes of diarrhoea during the previous few years. He had not paid much attention to this because he often had loose bowel movements in stress situations such as university exams. Only during the last two months on coumarin treatment had he observed blood in his stools. Sigmoidoscopy was therefore performed on 21 August. The mucosa was oedematous and swollen, covered by a thick mucopurulent exudate, and exhibited numerous haemorrhagic spots. Scattered throughout the bowel were tiny superficial erosions. The mucosa was friable and bled easily. This macroscopic appearance of the rectocolonic mucosa was strongly suggestive of a severe ulcerative colitis. Multiple biopsy specimens from different levels of the rectum and colon showed microscopical evidence of active inflammation confined to the mucosal layer, with crypt abscesses, epithelial abnormalities, erosions, and depletion of mucus compatible with severe inflammation as seen in ulcerative colitis. No evidence of vasculitis was seen in any of the biopsy specimens removed at sigmoidoscopy or in several rectal suction specimens (fig. 1 c, d).

The patient was initially treated with 3 g sulphasalazine, 50 mg prednisone, and a short course of ampicillin. The ethanol gelation test for detection of fibrin monomers, which gave a negative result before treatment, gave repeatedly positive results after starting the prednisone treatment. He was therefore also treated with intravenous heparin for 10 days. After heparinization the ethanol gelation test gave negative results. New purpuric lesions appeared on two occasions. On the left upper arm a purpuric lesion developed into a superficial necrosis confined to the skin without affecting the subcutaneous tissues. On the lateral aspect of the right thigh a second purpuric lesion healed without necrosis. While

the patient was slowly improving the necrotic areas on the left thigh and right hip persisted but were limited to skin and subcutaneous tissues. After removing the necrotic debris a flat defect about 1 cm deep remained (fig. 2 d). These wounds healed by granulation and on 13 October the remaining defect was covered by skin grafts. In the meantime the patient continued to improve. His temperature became normal, his appetite returned, and he gained weight. No new skin necrosis appeared. On 6 September, however, he developed thrombosis of a deep vein of the left leg and on 14 September thrombophlebitis of the dorsal superficial vein of the penis. Coumarin treatment was started again. The condition resolved and no other thrombotic phenomena occurred.

On 10 October, about one and a half months after starting treatment, sigmoidoscopy was again performed. The macroscopic appearance of the mucosa was almost normal. The normal vascular pattern was clearly visible, there were no haemorrhages, and there was no increased friability of the mucosa. Histological examination of several specimens from different areas showed a striking regression of the previous inflammation (fig. 1 e). The dose of prednisone, already being gradually reduced, was cut to 15 mg a day. On 9 November the patient was discharged in good general health. At follow-up in May 1974 he had remained in excellent condition as judged clinically and by sigmoidoscopy.

Comment

This patient, whose severe skin lesions were preceded for more than a year by migrating thrombophlebitis, appeared to have ulcerative colitis. The appearance and evolution of the skin lesions gave rise to a suspicion of necrotizing vasculitis (Rook *et al.*, 1969). Such skin lesions must be differentiated from coumarin necrosis (Verhagen, 1954; Koch-Weser, 1968). In our patient the lesions developed after stopping the coumarin treatment. The appearance of the lesions was reminiscent of purpura fulminans (Dudgeon *et al.*, 1971). There was, however, no evidence of acute infection. Haematoma as the cause of skin necrosis can be ruled out. Pyoderma gangrenosum differs from necrotizing vasculitis by its appearance and mode of onset and development (Johnson and Wilson, 1969). We have found only one description of a similar case (Goldgraber and Kirsner, 1960), in which the colitis was detected only at necropsy. Vasculitis is an uncommon complication of ulcerative colitis. Kehoe and Newcomer (1964) described a patient with ulcerative colitis who developed necrosis of the glans penis due to vasculitis. Isenberg *et al.* (1968) reported pulmonary vasculitis in a patient who had ulcerative colitis for 15 years.

The relation between ulcerative colitis and vasculitis remains hypothetical. It has recently been suggested that antigen-antibody complexes may be present in the sera of patients with ulcerative colitis (Doe *et al.*, 1973; Jewell and MacLennan, 1973). It is possible that such circulating immune complexes can produce vasculitis.

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