CHRONIC LEG ULCERS IN NON-THROMBOCYTOPENIC PURPURA

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Apart from a probable case reported by Osler in 1914, we have been unable to find in the literature any account of leg ulcers occurring in non-thrombocytopenic purpura. As we have seen three such cases in the last two years we think it worth while to report them.

Case 1

A married butcher aged 57 first came to the out-patient department in December, 1953, with a complaint of swollen joints for 10 days. He had a history of developing painful swollen joints 30 years previously while serving in the Army in Egypt. They became normal in six months with no residual disability (he was later a racing cyclist). In 1943 he was treated for a prolapsed intervertebral disk by laminectomy, and post-operatively developed a thrombosis of the left small saphenous vein. Following this episode he was subject to mild ankle oedema after standing for prolonged periods, but no other disability. His present illness began suddenly with swelling of the right knee and a blotchy rash on the skin surrounding that joint. In the course of the next few days, the left knee, right ankle, both elbows, and right wrist also became swollen and painful. At the same time the rash spread over both legs, and, to a less extent, on the trunk. It came as a series of crops, and the patient noticed that the spots were raised above the skin and did not itch. There was no past history of any allergic disorder and he had never taken any drugs.

On examination he was well nourished, with a purpuric rash in which there was an urticarial component, richly distributed over the legs, buttocks, and extensor surfaces of the arms, and more sparsely over the trunk. Several joints were swollen and painful on movement—namely, both knees, both ankles, both elbows, both wrists, and the left shoulder. The spleen was not palpable. Small, discrete, painless lymph nodes were felt in the occipital, the cervical, and both axillary regions. The left small saphenous vein was represented by a firm cord-like structure, which was evidently the sequel of his post-operative venous thrombosis ten years earlier. The left long saphenous vein was prominent, but there was no evidence of varicosity; and the skin was healthy apart from the purpura. In other respects, physical examination was negative. A diagnosis of Schönlein-Henoch purpura was made, and he was admitted to hospital for further investigation and treatment.

While in hospital he was found to have a persistent albuminuria with occasional red blood cells. Apart from a moderately raised E.S.R. (17 mm. in one hour by the Wintrobe method) his blood picture was in all respects normal—namely, platelets, 557,000 per c.mm.; red cells, 4,810,000 per c.mm.; haemoglobin, 14.4 g. per 100 ml.; white cells, 3,900 per c.mm. on one occasion and 8,600 on another, with a normal differential distribution. The bleeding-time (Duke) was

one minute and the clotting-time (Lee and White) 6½ minutes. The one-stage prothrombin time was normal. The report on a bone-marrow examination by Dr. S. T. E. Callender was as follows: "The marrow is moderately cellular. Eosinophils are fairly frequent. Apart from this, there is no definite abnormality." The tourniquet test caused increase in size of the existing purpuric lesions, but no fresh petechiae occurred.

During his stay in hospital he developed cramp-like abdominal pain and was found to have large amounts of occult blood in the stools. Thus the classical picture of anaphylactoid purpura was complete.

He was in hospital for two months following this admission. During this time he received treatment with cortisone by mouth in a total dose of 4.2 g. over a period of three weeks. The disease was unaffected. The purpura persisted, fresh crops of lesions occurring intermittently, and there was no notable improvement in his joints. He later showed gradual improvement, with his joints returning slowly to normal and the petechial rash diminishing. As already mentioned, gross albuminuria persisted, but he remained normotensive and his blood urea was normal. The tourniquet test became strongly positive during the latter part of his stay in hospital. He was discharged from hospital on February 16, 1954, with no joint symptoms or bowel symptoms, but with a scanty petechial eruption.

He was then regularly seen in the out-patient department. He continued to have recurrent crops of purpura, mainly over the legs, with both ankles particularly affected. In March, 1954, he developed an ulcer of the left ankle at the site of a patch of profuse purpura. The ulcer persisted and became more extensive, and he was readmitted to hospital in June. At that time there were two shallow ulcers, each about 2.5 cm. in diameter, in the region of the left medial malleolus and one shallow ulcer about 7 by 1 cm. in the region of the left lateral malleolus. There was a fading purpuric eruption on the legs. Investigations at this time gave the following results: haemoglobin, 13.6 g. per 100 ml.; white cells, 6,000 per c.mm.; platelets, 248,000 per c.mm. The urine contained albumin, red blood cells, and occasional granular casts. The blood urea was 35 mg. per 100 ml.; plasma proteins, 5.4 g. per 100 ml., with albumin 3.2 g. The tourniquet test was strongly positive on admission and later became negative. With rest in bed the ulcers healed and he was discharged in 24 days, having had no fresh purpuric eruption.

Shortly after leaving hospital fresh purpuric crops occurred and he had occasional abdominal pain and painful joints. By September the purpura had become more severe and ulceration of the left ankle had recurred (see Fig.). He was readmitted to hospital, where rest in bed and eusol

Photographs of Case 1, showing large areas of ulceration and surrounding purpuric lesions.

dressings brought improvement of the ulcers. His purpura became less severe, but albuminuria persisted. When last seen, in October, the ulcers were covered by scabs and appeared to be healing well. The purpura was then absent.

Comment.—The history, physical signs, and results of investigation leave no doubt that this patient suffers from Schönlein-Henoch purpura. The only doubt that exists is whether the venous thrombosis he sustained ten years previously played any large part in the genesis of his leg ulceration. We do not think this likely, for the following reasons. He had been working for those ten years as a butcher, standing a great deal, with negligible symptoms. The ulceration occurred when he was living the life of a semi-invalid involving less need for a perfect venous return. Secondly, the ulcers were not surrounded by the eczematous changes in the skin which almost invariably accompany varicose ulceration. Finally, the ulceration occurred at a site where the purpura was so dense as to be confluent.

Case 2

A clergyman aged 62 was under our care for severe rheumatoid arthritis, which began in 1934, and later made him dependent upon an electric chair for mobility. From April, 1952, until March, 1953, we treated him with large doses of sodium salicylate with relief of his joint symptoms, but only at the expense of troublesome deafness. In March, 1953, salicylate therapy was stopped and he was put on to treatment with phenylbutazone by mouth in a dose of 200 mg. four times a day. He continued on this therapy, and on August 13 he noticed purple spots on his legs. The eruption became more profuse and he was admitted to hospital ten days later.

On examination at that time he had a profuse purpuric eruption covering both legs, buttocks, and the extensor surfaces of both arms. His joints showed evidence of longstanding rheumatoid arthritis. The spleen was not felt. All other systems were normal. Investigations gave the following: platelets, 745,000 per c.mm.; red blood cells, 4,380,000 per c.mm.; haemoglobin, 14.4 g. per 100 ml.; white cells, 8,000 per c.mm., with a normal differential distribution; bleeding time (Duke), $3\frac{1}{2}$ minutes; E.S.R., 32 mm. in one hour. The tourniquet test was negative. The phenylbutazone had been discontinued before admission on the assumption that it was the agent responsible for the purpura and he was treated with calcium aspirin. The purpura appeared to be subsiding and he left hospital after one week, being anxious to return to his parish.

When seen in the out-patient department a week later several of the purpuric patches on his legs appeared to be about to slough and arrangements were made for his readmission. By the time he was admitted to hospital, a week later, painful ulcers had developed on his legs, three on the right and two on the left. On the anterior surface of the shins there were two ulcers on the right side and one on the left. Both medial malleoli were the site of ulceration. The symmetrical distribution of the lesions was notable. The surrounding skin was inflamed. At this time the purpuric eruption was confined to the legs below the knees. The results of investigations were similar to those on his previous admission, except that the tourniquet test had become positive.

The ulcers were treated with eusol dressings, and after three weeks complete healing had occurred and he was discharged from hospital on October 5.

A week later, when seen as an out-patient, the ulcers of the legs had recurred. He was unwilling to be admitted to hospital, but was seen frequently as an out-patient. From October, 1953, until February, 1954, he had several severe exacerbations of the purpura, with occasional ecchymoses. Throughout this period the ulcers repeatedly healed and broke down; they were extremely painful. Complete bed rest at home assisted the ulcers to heal, but made the stiff-

ness of his joints much worse, so that a satisfactory regime was difficult to achieve.

In April he overcame his reluctance to desert his parish and was readmitted to hospital, where it was hoped to combine treatment in bed with active physiotherapy for his joints. On examination there were fresh petechiae of the legs superimposed on areas of fading purpura. There were several ulcers of both legs, about 2.5 cm. in diameter, from which came a purulent discharge. They were treated with eusol dressings and later with tulle gras, and healed well in the course of the next few weeks. The results of investigations on this admission were: platelets, 343,000 per c.mm.; red cells, 4,290,000 per c.mm.; haemoglobin, 12.8 g.; white cells, 6,000 per c.mm., with a normal differential distribution; bleeding-time (Duke), two minutes; clotting-time (Lee and White), eight minutes; one-stage prothrombin time, normal; E.S.R. (Westergren), 52 mm. in one hour. A patch test with phenylbutazone was negative.

He was discharged from hospital in June. He has been seen since and the ulcers have not returned.

Comment.—There is no doubt that in this patient the purpura was responsible for the ulceration of the legs. The cause of the purpura is uncertain, but it is highly probable that it was a toxic effect of phenylbutazone. Non-thrombocytopenic purpura is a rare complication of phenylbutazone therapy, occurring in 4 out of 800 patients studied by Kuzell *et al.* (1953).

Case 3

A housewife aged 66 attended the skin department, Radcliffe Infirmary, in August, 1952, complaining of a painful localized swelling on the inner side of the right lower leg which had been present for three months. Three weeks later a purpuric rash developed on both arms, and later became generalized. She was referred to us and was found to have the following signs. There was a generalized purpuric rash, which was most pronounced on the extensor surfaces of the arms and on the trunk. The petechiae were discrete and raised above the surface. There was an indurated erythematous area, about 7.5 cm. in diameter, on the front of each lower leg. The distribution was symmetrical. Each area contained several ulcers which were covered with hard scabs. Apart from a palpable liver, there was no other abnormality on clinical examination.

She was later admitted to hospital, when investigations were essentially negative—namely, platelets varied from 193,000 up to 667,000 per c.mm.; haemoglobin, 11.7 g. per 100 ml.; red cells, 4,200,000 per c.mm.; white cells, 7,200 per c.mm., with a normal differential distribution; bleeding-time (Duke), $2\frac{1}{2}$ minutes; clotting-time (Lee and White), $6\frac{1}{2}$ minutes; one-stage prothrombin time, normal; clot retraction (Marfarlane), 50% (normal); plasma proteins, normal. Liver function tests: plasma bilirubin, 0.4 mg. per 100 ml.; flocculation tests, normal. Coombs test, the Wassermann and Kahn reactions, and the tourniquet test were negative.

She was discharged after one week at her own request to care for her invalid husband, with no change in her clinical state. In December, when she was seen as an out-patient, the purpura was still present but less intense. The ulcerated area on her left leg had healed, but that on the right was still active. Blood investigations were negative, with the exception of the E.S.R., which was 102 mm. in one hour (Westergren). She refused to enter hospital for cortisone therapy and failed to attend the out-patient department until five months later (May, 1953). Her purpuric rash had by then completely disappeared, and the ulcers of the legs were healed. She refused to have a blood examination, so that we do not know whether the E.S.R. had become normal.

According to her family doctor, she remained well and free of purpura until August, 1953, when he was called in because she had died suddenly in her bed at night. The cause of death was certified as coronary thrombosis.

Comment.—It is probable that this patient's non-thrombocytopenic purpura was an example of so-called anaphylactoid purpura. It is noteworthy that she developed indurated areas of both legs before the onset of the purpura and that these subsequently ulcerated. The most reasonable conjecture would appear to be that both the indurated areas and the purpura were independent manifestations of the same underlying allergic state.

Discussion

We have no doubt that leg ulcers which persist for several months are decidedly rare in non-thrombocytopenic purpura. Davis (1948) reported 44 cases of Schönlein-Henoch purpura without mentioning ulceration among the skin lesions. Gendel (1948), in a review of the reported cases of chronic leg ulcer in diseases of the blood, likewise does not mention this association. Chronic leg ulcers have been observed in a number of blood dyscrasias, such as congenital haemolytic anaemia, sickle-cell anaemia, polycythaemia, splenic anaemia, thrombocytopenic purpura, and Gaucher's disease, in all of which splenomegaly is a frequent finding, and it has been usual to attribute the liability to leg ulceration to some abnormal action of the spleen.

In thrombocytopenic purpura the occurrence of leg ulcers is also rare, being reported for the first time by Witts (1942). It is worth mentioning that the two cases which he reported did not show splenomegaly and that splenectomy carried out on one of them had no effect upon the ulcers.

The only reference to the occurrence of leg ulcers in non-thrombocytopenic purpura appears to be the one made by Osler (1914), who states that necrotic areas may occur in purpuric states. "When a localized infiltration of blood and serum is very intense in a patch [of purpura] of considerable size, bullae form and the superficial layers of skin necrose, leaving an open ulcer." In describing a number of cases, he includes that of a girl aged 14 years who was treated in the Radcliffe Infirmary for Henoch's purpura. Although no platelet count is recorded, there seems to be little doubt from the clinical description that the diagnosis was correct. She suffered from pains in the legs, purpura, haematuria, and albuminuria. There were extensive haemorrhagic lesions on the legs, many of which broke down, leaving ulcers which took a long time to heal.

Osler's description of the genesis of skin ulceration in purpura is an apt account of how ulceration developed in Cases 1 and 2 of the present series. In Case 1 there was the possibility that a previous venous thrombosis may have been an additional cause, but we have given reasons for concluding that this was not a major element. Case 3 is totally different in that ulceration developed in indurated erythematous areas which appeared on the legs some months before the onset of purpura.

Summary

Three cases of leg ulceration in non-thrombocytopenic purpura are described.

The aetiology of the purpura was different in the three cases, one being a classical example of Schönlein-Henoch purpura, one a toxic purpura, presumably due to phenylbutazone, and one possibly a manifestation of an obscure allergic state.

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POST-PUERPERAL RECURRENT DEPRESSION

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The purpose of this paper is to draw the attention of practitioners to a form of illness which is not uncommon and which is important, not only because of the distress and incapacity which it inflicts upon the patient, but also because of the repercussions which it produces within the family group.

There are few references in the literature to the sequelae of puerperal depression. Hemphill (1952) mentions "a periodic affective illness . . . after childbirth, with subsequent attacks related to menstruation." There is little doubt that he had in mind patients such as those I am about to describe. Linford Rees (1953) has observed that "in some patients with children it was found that premenstrual tension had developed or had become worse after childbirth." These, however, are merely the passing remarks of writers who were dealing with a different theme.

Summaries of seven cases are here presented of women with a history of puerperal depressive illness some years previously, following which full health has never been regained and recurrent sharp phases of depression, tension, and irritability have occurred, with short interludes of comparative well-being. The resemblances which these patients bear to one another in their history and symptomatology appear to class them as a distinct group, to which it is proposed to attach the name "post-puerperal recurrent depression."

These patients tend to take a moral rather than a medical standpoint towards the alteration in their feelings and behaviour. While they are not rare as visitors to psychiatric clinics (5 in the last 300 new patients seen), it is probable that many of them do not seek medical advice, or, if they do, are not sent for psychiatric examination.

Typical History.—A woman of pyknic build and cyclothymic temperament suffers from a relatively mild puerperal depressive illness in her thirties or late twenties. Emotional stress or an infective illness may have coincided with the puerperium. She appears to make a good recovery from her depression, but within a short time becomes unwell again. Thenceforward, for years, she suffers from recurrent phases of depression, irritability, and tension, with phobias, obsessive fears, or hypochondriasis. The severity of her symptoms is related to the menstrual cycle, usually the premenstrual phase. Irregularity of the menses is a concomitant feature. Her moodiness, unpredictability, and loss of temper are reacted to by the children and the husband, the family atmosphere becomes clouded and unstable, and the family ceases to function as a unified group.

Case 1

Observation period, All Saints' Clinic, seven years; personal observation, two years. Large-framed woman of pyknic build, aged 38. Facial pallor. Expression morose. Para-3.

Her present illness began in 1943; after birth of her second child lacked confidence to go out and about. Within a few days of birth of third child in October, 1945, became depressed and agitated. Had a mild febrile illness attributed to throat infection at this time. Three attacks of