PYODERMA GANGRENOSUM COMPLICATING A SIMPLE SKIN GRAFT

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A 43-year-old female, when first seen, had an ulcer on the outer side of the left leg about 3 inches above the level of the ankle joint. The ulcer was deep, extended down to the deep fascia and was approximately $3\frac{1}{2}$ inches long by $2\frac{3}{4}$ inches broad. The surrounding skin and subcutaneous tissues were thickened and inflamed, the edges and base of the ulcer were irregular, unhealthy looking and undermined. There were small blisters on 2 areas of the skin edge at the upper end of the ulcer.

The ulcer had been present for 5 weeks. It commenced with a very small irritable blister which the patient noticed shortly after rubbing an itchy spot which she assumed to be an insect bite. A ring of blisters formed around the orignal affected area; they soon burst and a scab formed. A week later, she says, she went down with 'blood poisoning', accompanied by a high temperature, aching limbs, enlarged and painful glands in the left groin, severe pain at the site of the blisters and much swelling of the ankle region. A deep ulcer now formed at the orignal infected site.

An injection of penicillin was given but, as it caused a severe reaction, it was not repeated. In spite of this reaction she took penicillin by mouth. The temperature subsided and the glands in the groin became reduced in size. The ulcer, however, remained extremely painful and continued to spread. The following dressings were applied: Ichthyol ointment, acriflavine emulsion, penicillin tulle, jelonet and furacin ointment. She says that whatever dressing was put on made the ulcer worse until furacin ointment was used. This dressing gave some relief but did not stop the ulcer from spreading.

Before the commencement of the ulceration the patient had been a very active, healthy and energetic woman, seldom ill, always busy with her home and children. In her spare time she helped in a store and shouldered the burdens and illnesses of her husband's employees and those of her neighbours. Her only departure from robust health had been septic infection of the tonsils on about 5 occasions in the previous 2 years. There was no apparent cause for the ulcer. Insect bites, such as that of a poisonous spider, were excluded on the history and absence of pain at the commencement. There was no sign or symptom suggesting a vascular cause.

The patient was admitted to hospital. A diphtheric infection was suggested as a possible cause and swabs were taken for culture and examination. The day following admission to hospital the tonsils became inflamed and a membrane formed on them lending strong support to the presumptive diagnosis. Swabs were taken from the throat. Direct examination and culture showed no diphtheria bacilli, but staphylococci and streptococci were found in both the ulcer and the throat.

Special Investigations

The following investigations, including excision of a portion of the edge of the ulcer for biopsy, were carried out with results as shown:

Throat swab (29 *June* 1957): Microscopic examination showed moderate mixed bacteria, mainly gram-positive cocci and scanty pus cells. Cultivation yielded a profuse mixed growth of non-haemolytic streptococci and *Staphylococcus aureus*.

Cultures from wound (2 *July* 1957): Microscopic examination of cultures from the new ulcerated area showed numerous pus cells and gram-positive cocci resembling staphylococci and scanty streptococci. Cultivation yielded a profuse growth of *Staphylococcus aureus* together with scanty non-haemolytic streptococci. Microscopic examination of cultures from the old ulcerated area showed numerous pus cells and scanty staphylococci. Cultivation yielded a profuse growth of *Staphylococcus aureus* together with scanty non-haemolytic streptococci.

Blood count (9 *July* 1957): Haemoglobin 82·5% (12·2 g.%), colour index 1·01, erythrocytes 4,000,000 per c.mm., leucocytes 12,250 per c.mm., neutrophils 55%, monocytes 1%, lymphocytes 34·5%, eosinophils 9·5%, basophils nil and PCV 35%. The red cells were normal in appearance. There was an eosinophilia.

Swabs (9 *July* 1957): The results of a number of sensitivity tests are given in Table I.

TABLE I. RESULTS OF SENSITIVITY TESTS

Antibiotics	*Staphylococcus aureus*	*B. proteus*	*Streptococci*
Erythromycin	++		−
Terramycin	+		++
Novobiocin	++	++	++
Chloromycetin	++	+	+
Aureomycin	+	−	++
Penicillin	−		−
Streptomycin		++	
Sulphatriad	−	+	+
Sulphamezathine		+	
Gantrisin		+	

Key: ++ Very sensitive. + Sensitive. − Resistant.

Blood count (25 *July* 1957): The following are the results of a subsequent blood count. Haemoglobin 88% (13·0 g.%), colour index 1·0, erythrocytes 4,400,000 per c.mm., leucocytes 11,800 per c.mm., neutrophils 50·5%, monocytes 4·5%, lymphocytes 33·5%, eosinophils 11·5%, basophils nil and PCV 37%. The red cells showed anisocytosis. There was an eosinophilia.

Pus (26 *July* 1957): Microscopic examination showed numerous pus cells and gram-positive cocci. Cultivation yielded a profuse growth of *Staphylococcus aureus*.

Blood (27 *July* 1957): The fragility of the red cells was within normal limits.

Culture from wound (31 *July* 1957): Cultivation for fungi was negative.

Faeces (2 *August* 1957): The ultraviolet light test for porphyrins gave a negative result on this specimen.

Diagnosis and Treatment

Several attempts were made to find and culture anaerobic organisms with negative result. Chronic infection, such as tuberculosis and syphilis, were considered and excluded on the short history, rapid progression of the ulcer and absence of physical signs of such diseases in other parts of the body. The W. R. was negative. Allergy was considered as a possible cause, though it was hard to see to what she could be allergic. There was no history of any other allergic manifestation in her past history. Her reaction to penicillin occurred only after the trouble had commenced. It was concluded that she had lost resistance for some reason, possibly connected with her recurrent tonsillar infection. She was kept in bed with the leg slightly elevated. Saline dressings were applied and as the ulcer, after a few days, began to show signs of healthy granulations, arrangements

were made for a skin-grafting operation as soon as local conditions appeared satisfactory.

Three weeks after her admission to hospital, a Thiersch skin-grafting operation was done, the donor area being the outer and anterior part of the thigh. No undue symptoms occurred for a week—then she began to complain of pain in the thigh. When the dressings were removed 2 days later, the donor area was seen to be heavily infected—the thigh around the area was swollen and inflamed, the temperature rose rapidly and once again the glands in the groin became enlarged and very tender. The graft appeared to have taken in part, though later it sloughed off completely. Two deep ulcers rapidly appeared on the donor area and spread down to the fascia lata of the thigh, and large sloughs of subcutaneous tissue formed under the intervening and surrounding skin.

The ulcer on the leg began to spread again and all the grafted skin sloughed off. Her condition became alarming, with general signs of a severe septicaemia developing. She was put on treatment with meticorten, 5 mg. *t.i.d.* Saline dressings were continued both on the original ulcer and on the new ulcerated area on the thigh. The response was satisfactory, but after 2 days, as she was still running an irregular temperature, novobiocin, 500 mg. was given in addition. A suggestion was now made that this was a case of pyoderma gangrenosum, due to agammaglobulinaemia or hypogammaglobulinaemia. A paper-electrophoretic test of blood proteins was at once carried out with the following result: Albumin fraction normal, alpha 2 globulin raised, Alpha 1 beta and gamma globulin normal. Estimation of blood proteins showed total protein 6·5 g. per 100 cc. albumin 4 g., glubulin 2·5 g. The only abnormality shown was the rise in the alpha 2 globulin, the significance of which is apparently unknown.

Under the influence of the new line of treatment the patient made rapid and satisfactory progress. The signs of septicaemia disappeared. The ulcers on the donor area filled in with remarkable rapidity once the sloughs came away. The original ulcer on the leg took on a healthy appearance with granulations, and comparatively slowly, but surely, began to heal from the edges towards the centre. Sixteen days after commencing the meticorten treatment the ulcers were so nearly healed and were making such good progress that she was able to return home.

She continued on the same treatment for 3 weeks. Her condition then became stationary, with a small unhealed area on both the leg and the thigh. It was then suggested that gamma globulin should be tried and accordingly injections of 20 cc. were given twice weekly for 2 weeks. There was no marked improvement locally, though the patient said she felt better after the injections. The position became static for the time being. It was then decided to try local cortisone treatment. She was put on terra-cortril ointment, and instructed to use only a very small quantity to cover the ulcers as thinly as possible. The result was dramatic and pleasing. She says that the pain was immediately relieved and that for the first time in 5 months she was able to sleep all night without any pain or discomfort.

This treatment was continued until the beginning of December, when the ulcers finally healed. When seen at the beginning of March this year, the patient had put on weight, felt well, was full of energy and enjoyed life once more. There had been no return of tonsillitis or other septic infections. The scars on the leg and thigh were sound though bluish in colour.

DISCUSSION

The remarkable ulceration which occurred in this patient spontaneously in the leg and followed a simple surgical operation to the thigh, and the failure to respond to antibiotics and conservative treatment, is characteristic of pyoderma gangrenosum (phagadena). The presence of spreading ulceration associated with pus and marked destruction of tissue is consistent with the diagnosis. The apparent inability of the patient to overcome infection and the recurrent attacks of purulent tonsillitis, suggest a low resistance to infection.

Pyoderma gangrenosum characteristically occurs in ulcerative colitis, but may occur without the latter. It may or may not be associated with an absence or lowering of the gamma globulins in the blood. The initial lesion may be an ulcer of the leg, which may extend, or new lesions may develop in other parts of the body, e.g. boils or furuncles, which rapidly break down and become gangrenous.

In our patient full blood counts did not reveal any evidence of any of the blood dyscrasias which may be associated with leg ulceration, e.g. leukaemia, sickle-cell anaemia, haemolytic jaundice, etc. General examination failed to reveal an enlarged spleen, liver or generalized adenopathy. Culture from the thigh and leg revealed staphylococci, on several occasions but on no occasion were anaerobic bacteria isolated. In spite of antibiotic therapy there was no evidence of improvement until prednisone was given. In order not to confuse the issue, when the latter was started all antibiotics were discontinued. There was a dramatic improvement in the appearance of both ulcers on prednisone therapy. An antibiotic, novobiocin, was only added later because of the possibility of spreading sepsis and the fact that we did not have the courage to continue without the cover of an antibiotic.

In view of the clinical picture and history of recurrent attacks of tonsillitis, the possibility of agammaglobulinaemia or hypogammaglobulinaemia was considered. A single blood examination revealed normal values. This is not considered a contraindication to gamma-globulin therapy by Sulzberger[1]. It was therefore decided to try injections of gamma globulin, and the patient was given 20 cc. weekly for 2 weeks. She stated that she felt much better, but there was no observable clinical improvement in the local condition of the ulcers. No inference can be drawn as the dosage was small in comparison to amounts which have been tried in similar cases.

SUMMARY

A case of pyoderma gangrenosum (phagadena), following a skin-grafting operation, is described. This patient showed a dramatic improvement only on prednisone therapy and was finally cured by the local use of hydrocortisone under cover of an antibiotic. Gamma-globulin therapy did not appear to have any beneficial effect on the ulcers.

REFERENCE

1. Sulzberger, E. (1957): Amer. J. Derm., 75, 917.