the more superficial muscle groups. It is known from the experiments of Kellgren, McGowan, and Hughes (1948) that pain in such structures is related to the local temperature. Such an effect must presumably depend on absorption of adrenaline into the general circulation, as penetration to site tissues by direct spread would be unlikely. This would explain the identical relief felt on both sides when adrenaline is applied to only one half of the back (Bywaters, 1951).

The delay in recovery which, as our figures indicate, follows the use of adrenaline cream may be due to interference with the pain-defence mechanism. A similar effect on recovery times has been noted when procaine is injected repeatedly into a site of pain in muscle or connective tissue. Whether dry massage produces a similar delay is at present uncertain, but is under investigation.

Summary

Adrenaline cream applied locally in a number of rheumatic diseases gives greater relief than a simple cream. Dry massage also gives greater relief than massage with simple cream or no massage at all. No significant difference was noted between the effects of dry massage and massage with adrenaline cream.

Repeated application of adrenaline cream appears to delay recovery in rheumatic diseases.

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SEZARY'S RETICULOSIS WITH EXFOLIATIVE DERMATITIS*

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The original account of this condition is contained in an article by Sézary and Bouvrain (1938). Their patient, a woman of 58, presented as a case of mild pruritus of the trunk and limbs, which became steadily more severe and extensive and was followed in two or three months by the appearance of erythematous plaques on the affected area. Fine scales developed on these plaques, and they gradually increased in size to produce a generalized erythrodermia. Microscopical examination of her skin showed a considerable infiltration of the dermis. The infiltrate consisted of round or polygonal cells with a round or oval nucleus and an indistinct nucleolus. Repeated blood examinations gave a red-cell count which varied from 3,500,000 to 4,490,000 and a white count ranging from 6,000 to 14,400 per c.mm. The blood film showed from time to time the presence of an unusual type of giant cell in numbers varying from 2 to 56 per hundred white cells. These *cellules mon-*

streuses, 12 to 14 μ in diameter, contained a large nucleus surrounded by a thin band of cytoplasm. The nucleus varied in shape, was sometimes oval or occasionally bilobed, rectangular, or lanceolate. The bone marrow contained none of these cells. Sézary believed them to be of mesenchymatous origin, but had never previously seen any similar cells.

In the discussion following the presentation of this case Civatte stated that he had seen this type of cell on three occasions. The patients in whom it was found all ultimately developed cutaneous tumours, and Civatte was undecided whether they should be regarded as examples of atypical mycosis fungoides, Hodgkin's disease, or leucosarcoma. Two further cases (Sézary, Horowitz, and Maschas, 1938; Sézary and Bolgert, 1942) closely resembled the original one, as did a fourth reported by Baccaredda (1939). All these patients died in 18 to 40 months without developing cutaneous tumours. Sézary thought it probable that the condition was related to mycosis fungoides, but felt that no more definite opinion could be given until further evidence became available.

Case History

A retired clerk aged 67 had suffered from transient rashes on the arms and legs for 16 years. The rash would last a few weeks and then clear, leaving a few residual eczematous patches which caused him no discomfort. Within one or two months there would be an exacerbation. This state of affairs continued until March, 1949, when he developed an unusually severe attack, accompanied by oedema of the legs. He was admitted to Paddington Hospital on March 14, 1949. A few days later he developed a small ulcer on the right ankle. Three weeks after this his face became red and swollen. Within a week scaling developed on the face and was rapidly followed by a similar scaling eruption on the scalp and limbs. The trunk was later affected, but not so severely as the face and limbs. There was moderate itching and considerable burning of the skin. He had had "barber's rash" when aged 45, gastric ulcer when aged 50, and seborrhoeic dermatitis causing his admission to hospital on three occasions when aged 55. His mother's brother suffered from industrial dermatitis. One brother suffers from asthma and occasional eczema.

FIG. 1.—The patient, aged 67; showing oedema of skin, pigmentation, and pseudo-ptosis. The photograph is the copyright of the Royal Society of Medicine.

Examination showed him to be a small frail elderly man weighing 8 st. 12 oz. (51.1 kg.). His temperature ranged between 97 and 100° F. (36.1 and 37.8° C.), and pulse from 96 to 108. He was melancholy and apathetic. The skin of the face was thickened, and both eyelids were distended with oedema, which gave an appearance of ptosis and collected in pockets below the eyes (Fig. 1). There was considerable scaling over the face, scalp, and limbs. On the trunk the skin was thickened and covered with fine

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branny scales, larger on the arms and legs than on the abdomen. Superficial oedema obliterated the abdominal folds. There was no scaling in the axillae or groins. The whole skin was red; there was mottled brown pigmentation, particularly on the back and limbs. Many excoriation marks were seen on the legs, some weeping patches, and several superficial ulcers, all of which showed signs of healing. The hair was sparse, but the finger-nails and toenails were unaffected. The cervical, axillary, and inguinal glands were moderately enlarged. The patient was edentulous, the mucosa of the mouth was normal, and the tongue was unaffected. No abnormality was found on general examination. The spleen and liver were not palpable.

He was treated with an initial course of intramuscular injections of penicillin, 250,000 units six-hourly, and later with amphetamine, 10 mg. daily, and local applications of boric ointment.

While in hospital his skin condition remained substantially unchanged except for an increase in pigmentation. Six months after admission his liver became enlarged and

FIG. 2.—Biopsy of skin, showing dermal infiltration.

was palpable two fingerbreadths below the costal margin. About the same time he developed contractures of the legs, which were thought to have resulted from disuse, and a small trophic ulcer over the sacrum. He was discharged home in June, 1950. His condition remained unchanged until his death from cardiac failure in September, 1950, eighteen months from the onset of the disease. A post-mortem examination was not made.

Investigations.—A biopsy of the skin was made on August 4, 1949. The epidermis showed parakeratosis and acanthosis, with spongiosis, vesicle formation, and immigration of round cells. The upper third of the corium was oedematous and showed an increase of vessels and an infiltrate which was partly perivascular and partly diffuse (Fig. 2). The infiltrate itself was composed chiefly of round cells and a few histiocytes. X-ray examination of the chest showed no abnormality. The Wassermann reaction was negative. The urine showed no abnormalities. On November 29, 1949, serum protein was 6.9 g.%—albumin 3.9 g.%; globulin 3 g.%; albumin/globulin ratio 1.3/1.

Haematological Findings

Routine examination up to August, 1949, revealed a mild normochromic anaemia, haemoglobin 82–92% (11.4–13 g. per 100 ml.); a constant thrombocythaemia, platelets 730,000–820,000 per c.mm.; a constant leucocytosis, white blood cells 10,000–20,000 per c.mm. The differential white count varied considerably (see Table).

At this time large nucleated cells, numbering 1–2% of the total nucleated cells, were seen in the film of the peripheral blood. These cells, 15–25 μ in diameter, were irregularly ovoid in shape, and often drawn out into pseudo-

Date	W.B.C.	Poly-morphs	Eos.	Baso.	Lymphs	Monos
4/5/49 ..	17,800	84	4	1	10	1
31/5/49 ..	18,800	51	6	1	32	10
14/7/49 ..	10,200	58	—	—	40	2
21/7/49 ..	16,000	84	—	—	15	1
27/7/49 ..	14,000	72	5	—	19	4
10/8/49 ..	16,800	50	4	—	44	2

podium-like processes. The rounded nucleus, occupying rather more than half the cell, showed a uniform open meshwork chromatin structure, a well-defined margin, and two or three variably distinct nucleoli. The delicately foamy and tenuous cytoplasm stained very faintly blue with Leishman, and sometimes contained many small azurophil granules. These large cells were clearly of reticulum type (Fig. 3). In a small proportion, convolution of the nucleus was pronounced and gave some resemblance to primitive monocytes. Following this initial observation these reticulum cells were seen in almost all subsequent films. The

FIG. 3.—Peripheral blood film. (a) Reticulum cell, (b) binucleate reticulum cell, (c) mitosis in reticulum cell.

leucocytosis continued and at most examinations the number of reticulum cells seen was few. On two subsequent occasions, however, large numbers of these abnormal cells appeared in the peripheral blood and then disappeared after a few days. They were seen in venous as well as in capillary blood. These showers of reticulum cells were accompanied by an increase of lymphocytes and a decrease of polymorphs.

Leucocyte Counts.—December 14, 1949: W.B.C. 23,800 per c.mm. (polys 41%, eos. 2%, lymphs 48%, monos 9%). "There are numerous reticulum cells present, of the type previously described; many of the lymphocytes show primitive characters with nucleolar remnants." January 2: W.B.C. 21,200 (polys 68%, eos. 4%, lymphs 22%, monos 5%, baso. 1%). January 10: W.B.C. 17,800 (polys 29%, eos. 3%, lymphs 50%, monos 1%, reticulum cells 17%). "The film shows a remarkable picture; many mitoses are seen amongst the reticulum cells; many lymphocytes again show immature characters." January 21: W.B.C. 19,000 (polys 67%, lymphs 32%, monos 1%).

The mild anaemia slowly deteriorated to haemoglobin 75% (10.5 g. per 100 ml.) in October, 1949. No nucleated red blood cells were seen at any time in the peripheral blood and a sternal marrow puncture on November 5 showed normal cellularity and normal distribution of the nucleated cells.

The reticulum cells included haemocytoblasts 1%; myeloblasts 3%; promyelocytes 1%; neutrophil myelocytes 16.5%; eosinophil myelocytes 2%; metamyelocytes 24%; eosinophil metamyelocytes 1%; polymorphs 29.5%; eosinophils 1.5%; lymphocytes 5%; plasma cells 0.5%; pro-

erythroblasts nil; basophil normoblasts 2%; polychromatic normoblasts 9.5%; orthochromic normoblasts 3.5%.

Lymph-node Biopsy.—Dr. H. Haber reported: "The structure of the lymph node is changed, the follicles being atrophic and the sinuses showing a hyperplasia of reticulum cells which contain vacuoles and melanin. There is also an admixture of eosinophils demonstrable. Histological appearance of lipomelanin lymphadenopathy."

Discussion

The occasional association between a disturbance of the reticulo-endothelial system and generalized redness and scaling of the skin is well known. The original account of mycosis fungoides (Alibert, 1832) refers to a scaling premycotic phase, the importance of which was later recognized by Brocq (1889). Under the title lymphoderma perniciosum a case was reported (Kaposi, 1885) in which there was exfoliative dermatitis with cutaneous tumours and a blood picture suggesting lymphatic leukaemia. There are many records of chronic erythrodermia associated with a clinical and haematological picture of leukaemia (Elsenberg, 1887; Riehl, 1892; Arndt, 1914; Ketron and Gay, 1923; Barney, 1928; MacCormac and Whitby, 1936). There was leukaemic infiltration of the dermis in most of these patients; a few (Sweitzer, 1916; Wise, 1917) showed cutaneous infiltration with a normal blood picture; and in one (Lutz, 1937) there was a leukaemic blood picture and a dermal infiltrate, but no post-mortem evidence of leukaemic changes elsewhere. Lutz therefore suggested that leukaemia might originate in the skin.

Exfoliative dermatitis has also been described with monocytic leukaemia (Montgomery and Watkins, 1938), Hodgkin's disease (Symmers, 1924; Miller, 1928; Wigley, 1937; Epstein and MacEachern, 1937), and giant follicular lymphadenopathy (Symmers, 1938; Combes and Bluefarb, 1941). In lymphoblastic erythrodermia (Sequeira and Pantan, 1921) there was erythrodermia with lymphadenopathy and lymphocytosis, but no evidence of leukaemia.

Reviewing the four published cases of his *nouvelle reticulose*, Sézary (1949) described the following symptoms: intense itching of the skin and burning of the tongue and buccal mucosa, sensations of cold and sweating, but no impairment of the general health until the disease was well advanced. The skin was found to be red and pigmented, warm to the touch, and thickened, having a pasty consistency. There was oedema sufficient to produce puffiness of the eyelids, a leonine facies, obliteration of the normal abdominal folds, and swelling of the legs. The conjunctivae were often suffused. Two cases showed dystrophic changes of the nails. There was enlargement of the superficial lymph nodes in all cases, splenomegaly in two, and hepatomegaly in one.

Much of this detailed description might apply to any case of generalized exfoliative dermatitis. There are, however, several distinctive clinical features. Involvement of the mucosa is unusual in the more chronic cases, although it has been described in the acute scarlatiniform erythrodermia of Féréol. Some oedema of the legs is evident in most cases of exfoliative dermatitis, but gross oedema of the face and abdominal wall is rare. Injection of the conjunctivae is not uncommon in erythrodermia resulting from arsenic or phenobarbitone, but does not usually occur apart from this. The combination of scaling, pigmentation, oedema of the skin, and pseudo-ptosis gave a facies, illustrated by Sézary, which was remarkably reproduced in the present case.

In addition to these clinical features Sézary's cases showed particular haematological changes, including the appearances of *cellules monstreuses* in the peripheral blood. Sézary was unable to classify this cell, and the nearest approach he cared to make was "monocytoid." Most of the abnormal cells seen in the present case do not appear, from the published illustrations and Sézary's description, to be identical with his, although both are clearly primitive

reticulum in type. A few cells, however, more closely resembled Sézary's *cellules monstreuses* in the convoluted character of the nucleus and clearer cytoplasm, and it is possible that they represent varying stages of development or activity of a common cell type. Sézary emphasized the intermittent flooding of the peripheral blood with these cells and the accompanying fall in the numbers of circulating polymorphs with an increase in lymphocytes. These features were also seen in the present case.

The clinical findings, the course of the disease, and the haematological picture described by Sézary are clearly reproduced in this case, and we have no hesitation in calling this a fifth example of Sézary's cutaneous reticulosis with erythrodermia. We feel, however, rather diffident in using the term "reticulosis" in this connexion. Insufficient consideration has been given in the past, in these so-called dermal reticuloses, to the point of view that the cellular features represent a non-specific response to the gross disorder in the dermis and epidermis which is not, at least to begin with, malignant in character. A similar consideration affects the so-called lipomelanin reticulosis of Pautrier and Woringer (1937), in which the changes in the superficial lymph nodes are now generally thought to be a non-specific reaction to the cutaneous disturbance. Until further evidence is available concerning the nature of the disease we suggest the noncommittal title of "exfoliative dermatitis with reticulaemia."

Summary

A case of exfoliative dermatitis in a patient who gave a long history of eczema is described. Large reticulum cells were found in the peripheral blood. The patient died without developing any of the characteristics of the known reticuloses. The clinical and haematological features were similar to those described by Sézary as a new cutaneous reticulosis, and the case is the first to be reported in this country.

We should like to thank Dr. J. E. M. Wigley, under whose care this patient was admitted, for permission to report this case.

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About 180 general practitioners are employed by the London County Council on a sessional basis. About 65 of these work in the school health service, and the remainder are employed at ante- and post-natal clinics, child welfare centres, vaccination and immunization clinics, and at dental clinics as anaesthetists. On an average these general practitioners attend two sessions a week each, and are responsible for about one-third of all the sessions worked under the National Health Service Act.