GRANULOMA ANNULARE

A REPORT OF FIVE CASES *

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Although the credit of having first described this affection is usually, and properly, ascribed to Colcott Fox who, in 1895, reported a case under the name "ringed eruption," the first case to be found in dermatologic literature is probably the one reported by Radcliffe Crocker a year previously as a case of erythematous lupus resembling lichen planus. Crocker soon recognized his error after seeing other cases, and proposed the name "granuloma annulare," by which it is generally known at present among English and American dermatologists.

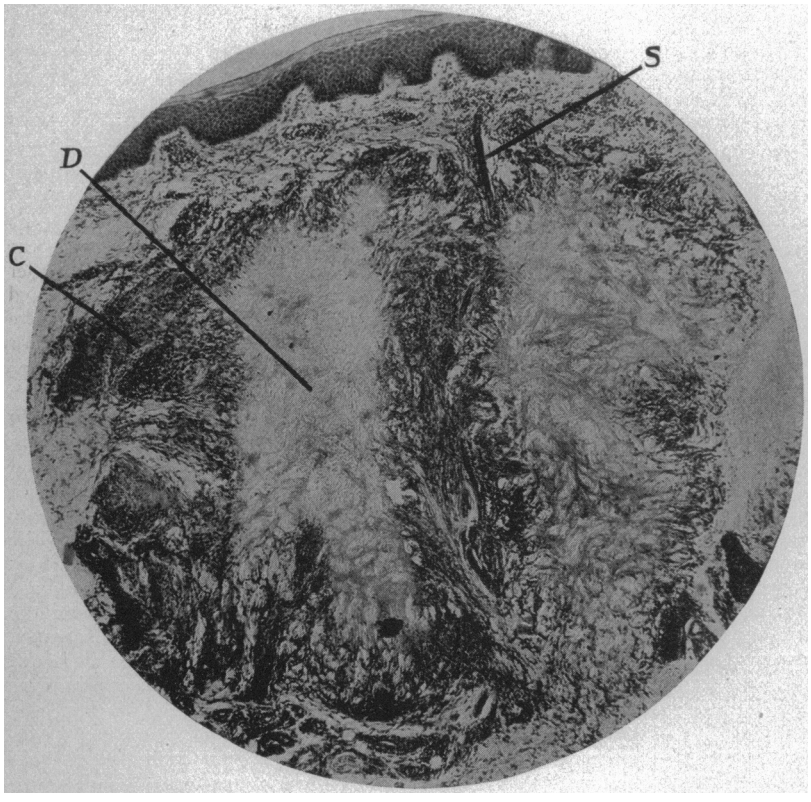

Fig. 1.—Granuloma annulare; section from Case 1; *C*, cell infiltrate; *D*, central area of necrosis; *S*, excretory duct sweat-gland.

Like so many other cutaneous affections, this one has suffered from a veritable plague of names. Ringed eruption, *éruption circinée chronique de la main*, lichen annularis (a most unfortunate name, leading to confusion since it has been already used to describe a variety of lichen planus), sarcoid, benign sarcoid, *néoplasie circinée et nodulaire, érythémato-sclérose du dos des mains, stéréo-phlogose nodulaire et circinée*, helodermia simplex et annularis are some of the names given to the malady by as many authors. The name proposed by Crocker, while not free from criticism, is descriptive, and seems in a fair way to be accepted by the majority of writers.

Although the affection is usually described as rare, Graham Little in an exhaustive paper published in 1908, had collected reports of not less than forty-nine cases, including six of his own, observed by various authors in a period of less than fifteen years; and since the publication of this paper a considerable number of additions to this list have been made by European and American observers. In view of the number of cases now on record, all of them reported within a period of twenty years, it can no longer be properly described as a rare malady. In all probability too, the reported cases by no means represent the frequency of its occurrence since, owing to the usual complete absence of annoying symptoms and the frequent insignificance of the lesions, many cases doubtless never came under the notice of a physician.

Case 1.—The first case which came under my observation occurred in the person of a girl, aged 17, who was brought to me a number of years ago; and I may say at once that it remained for a considerable time among the unclassified cases in my index. On the back of the right hand, and the dorsal surface of the index, middle and little fingers, were a number of shot to pea-sized, firm, whitish nodules, some of them isolated, others arranged in a circular patch. The nodules composing the circular patch which was situated at the base of the index-finger, were arranged about the border of a dime-sized cicatrix which had followed the destruction of a number of the lesions by a caustic of some sort applied by the patient's former medical adviser. The single lesions were the size of a split pea, were scattered about without any particular arrangement, and were situated almost without exception over the joints of the fingers. The disease had existed for two years, new nodules appearing from time to time, usually, but not always, in the neighborhood of the old ones which had been destroyed. Although the condition was not spontaneously painful, the patient complained much of pain if the nodules were pressed on. During the next nine months new lesions, usually single nodules, continued to appear as before, and occasionally one disappeared spontaneously. A considerable number were excised and several were destroyed by a pyrogallol plaster; at the end of another six months the disease had completely disappeared having lasted altogether about three years.

Case 2.—Anna K., aged 14, came to the skin dispensary of University Hospital in November, 1909, for advice concerning a cutaneous affection consisting of circinate patches made up of small firm, whitish nodules situated on the backs of the hands, one patch on each hand. The right-hand patch, situated over the knuckle of the index-finger formed a complete circle to which was attached a curved line about half an inch long, made up of discrete and confluent nodules; the patch on the left hand was semicircular, and was situated over the knuckle of the middle finger. The disease was not accompanied by any annoying symptoms, and had lasted about one year. After five Roentgen-ray exposures of from five to seven minutes' duration, the patch on the right hand had completely disappeared, and a similar result followed four exposures of the left-hand patch.

Case 3.—May L., aged 3, also a patient in the University Skin Dispensary, had six or eight finger-nail-sized annular patches composed of small, solid, pinkish nodules, scattered over the arms, abdomen and legs. These patches, some of which showed signs of involution, had been present for two years. The child was apparently in perfect health, and was in no way incommoded by the affection. Special inquiry was made concerning the presence of tuberculosis in any member, near or remote, of the patient's family, but the his-

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tory was entirely negative in this respect. After a few visits to the dispensary the child was lost sight of, and the further history of the case is unknown.

CASE 4.—Miss B., aged 24, who was referred to me by her family physician, for two years had had a number of dime to dollar-sized nodular, ring-shaped patches situated on the back of the left hand, the flexor surface of the left wrist, both elbows and the outer side of the left ankle. All these patches, with the exception of the one on the left elbow, were made up of small bright-red, quite solid, well-defined nodules; but the nodules in the patch on the left elbow were of a dull violaceous hue, quite deep-seated, much less well defined than those in the other patches, and quite as large as small peas. Although the eruption was not accompanied by any troublesome symptoms, the patient was greatly annoyed by its presence and was extremely anxious to have it removed. After a year of somewhat indifferent treatment under her family physician but little change had taken place except that the patch on the left elbow had lost its violaceous color, being almost the color of the normal skin, and the nodules composing it were much more sharply defined than formerly. Roentgen-ray treatment was now begun, and after six or eight exposures the patch on the back of the hand had almost completely disappeared and the one on the elbow was undergoing involution. As it was extremely inconvenient for the patient to continue under my care owing to the distance at which she lived from Philadelphia, she was transferred to a physician nearer her home who was to continue the treatment. What the final result of the treatment was I have not learned.

CASE 5.—In all the preceding cases the annular disposition of the nodules making up the patches was one of the most striking clinical features, although there were single nodules as well as rings in the first case. In this case, which occurred in a boy aged 6, a patient in the University Skin Dispensary, there were neither rings nor nodules, but flat, irregularly shaped and oval, pinkish plaques varying in size from a finger-nail to a Lima bean, situated on the back of the neck, the back of the hand and on the outer side of the right leg. These plaques, which were unaccompanied by any subjective sensations, had appeared rather suddenly about six weeks before the patient's visit to the dispensary. A diagnosis of erythema elevatum diutinum was made, as the case corresponded closely in its clinical features with the disease described by Crocker under that name; but the microscopic examination of an excised lesion at once made it apparent that the affection was histologically at least, identical with granuloma annulare, and it is for this reason included here. As the patient ceased attendance at the dispensary after two or three visits, the further course of the case is unknown.

Microscopic examination of several of the discrete nodules and a portion of the annular patch removed from the hand of the first case showed that the pathologic alterations were confined exclusively to the corium. Beginning in the subpapillary portion and extending down to the hypoderm was a moderately dense, fairly well-circumscribed cellular exudate composed chiefly of lymphocytes and spindle-cells of the connective-tissue type with a few polymorphonuclears and some large epithelioid cells. The exudate was densest about the vessels and the coil-glands and their ducts, the cells being especially numerous in the latter situation. Neither giant- nor plasma-cells were seen in any of the many sections examined. The most striking feature, however, was an area of necrosis occupying the central part of the exudate from which all traces of cell-elements had disappeared, and about which were numerous oval and spindle-cells arranged in radiating lines. This necrotic area was present in every section of every lesion examined, the area involved being apparently in proportion to the age of the lesion, since in lesions a few weeks old it was quite small. The elastic and collagenous tissues were apparently but little affected except in the areas of necrosis where the former had entirely disappeared and the fibers of the latter had lost their sharpness of outline, were granular in places, and stained poorly.

As already mentioned, sections were also made and examined of the plaque on the back of the hand of the case in which a clinical diagnosis of erythema elevatum diutinum had been made. The most cursory examination of these sections showed that the histologic features of the lesion were practically the same as those observed in the ringed lesions of the first case: there was the same perivascular and periglandular cellular exudate composed of round cells and spindle-cells, and the same central area of necrosis, although this was much less in extent than in the sections made from the first case, owing doubtless to the much shorter duration of the lesion, which was only a few weeks old. There was one notable difference, however, and that was the presence of many small mast-cells, a variety of cell not seen at all in the first case.

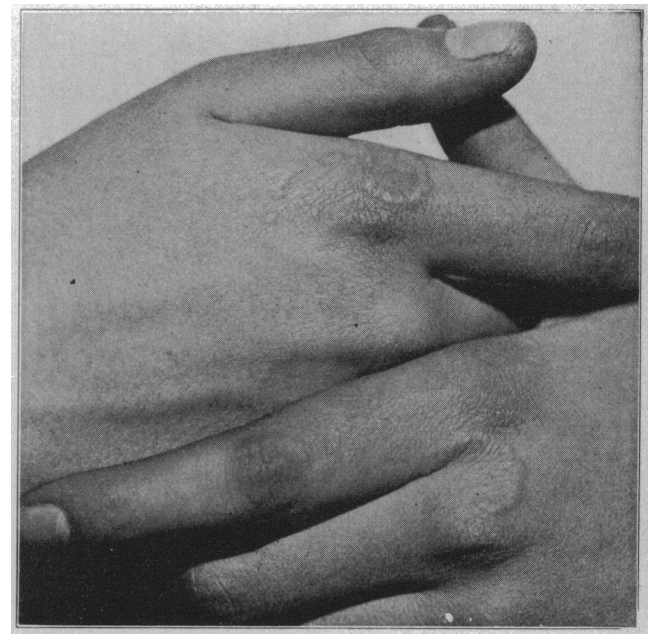

Fig. 2.—Granuloma annulare in Case 2.

A few words as to the relationship of this very interesting neoplasm to other affections.

The case reported by Rasch and Gregersen, in 1909, was regarded by them as a new type of sarcoid tumor; and Galewsky likewise described the case which he reported in the third fasciculus of the Ikonographia Dermatologica with an excellent colored portrait, as benign sarcoid tumor of the skin. Later observers, however, are practically in accord in rejecting this view of the character of the affection; indeed, its histopathology leaves but little doubt that it is in no way related to the malady described by Boeck as sarcoid.

Graham Little, to whose exhaustive study of the malady I have already referred, is strongly of the opinion that it is in some way closely related to tuberculosis, but the evidence which he presents in support of this opinion is far from conclusive; indeed, it seems to me quite the contrary. In only four of the forty-nine cases, reports of which were collected by this

author — or in five out of fifty if we include a case presented later at a meeting of the Dermatological Section of the Royal Medical Society — was there a history of tuberculosis in the patient's family, and in but a single instance did the patient himself present signs of tuberculosis.

The observations of Wende, Graham Little and my own more recent study have quite convinced me that the so-called erythema elevatum diutinum of Crocker is simply a clinical variety of granuloma annulare; histologically, there is no essential difference between the two affections.

As to the essential nature of this curious malady, little or nothing definite is known. The objection which has been made to the name "granuloma annulare" that it is not a granuloma, is apparently supported by its histopathology, which is much more that of a connective-tissue neoplasm than of a granuloma. Some observers, it is true, have found plasma and giant-cells, usually in very small numbers, but this finding is decidedly the exception rather than the rule. Halle thinks it a chronic inflammation of the middle and deep portions of the corium, while Dalla Favera believes it dependent wholly and alone on the blood-vessels; none of these views, however, explain in the least the peculiarities of the neoplasm. My own belief is that it is an affection *sui generis*, not related, so far as our present imperfect knowledge permits us to form an opinion, to any other. As to its etiology we cannot furnish even a reasonable conjecture.

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ABSTRACT OF DISCUSSION

DR. CHARLES J. WHITE, Boston: One case of granuloma annulare which I had the pleasure of studying proved rebellious to many sorts of medication, but yielded to the Roentgen-ray treatment, unfortunately, however, only to recur in a few weeks.

DR. A. RAVOGLI, Cincinnati: I have never seen a case of typical granuloma annulare in this country. I can recall a few cases in Italy; in those the lesions were typical, being limited to the hands and the fingers, in form of rings, near the joints, and giving rise to no itching nor other discomfort. I am inclined to regard this eruption as a localized lichen planus rather than to associate it with lupus erythematosus, tuberculosis or sarcoid. It is exceedingly stubborn, and I know of no remedy that will permanently relieve it. The Roentgen ray may hide it for a time, but there are cases in which it may aggravate the trouble.

DR. FRANK E. SIMPSON, Chicago: I have seen one case of this affection with Dr. Joseph Zeisler, which disappeared, apparently permanently, under the use of carbon dioxid snow.

DR. FRANK W. GREGOR, Indianapolis: Before listening to Dr. Hartzell's paper, I had almost come to the conclusion that granuloma annulare was not a dermatologic entity. Of two cases I can recall that were regarded as examples of this affection, one proved to be a case of syphilis; the other a case of lichen ruber planus in which I was subsequently able to demonstrate the typical lesions of that disease on the buccal mucous membrane.

DR. RICHARD L. SUTTON, Kansas City: I have under my care a case of granuloma annulare in a girl, 2½ years old, who instead of improving under Roentgen-ray treatment, grew distinctly worse. I then tried the carbon dioxid snow, without knowing that Dr. Simpson had previously employed it in this affection. The results apparently, were very good, but it is still too early to make any definite statement concerning the final outcome.

DR. M. B. HARTZELL, Philadelphia: Of course, an experience with only two cases does not prove very much. In one the lesions disappeared absolutely and did not return. It should be borne in mind, however, that these lesions sometimes disappear spontaneously, but in this instance it followed so promptly after the use of the Roentgen ray that the patient could but attribute it to the treatment. These lesions show a certain predilection for the neighborhood of the joints. The eruption is most common in children, and occurs most frequently on the hands, particularly about the knuckles. As to its relationship to tuberculosis, I think that is a purely gratuitous assumption which is entirely negatived by the histologic picture. To repeat, I regard it as a disease *sui generis*.

THE PINEAL GLAND IN RELATION TO SOMATIC, SEXUAL AND MENTAL DEVELOPMENT *

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From tumors involving the pineal gland, two distinct systems of symptoms and signs ensue, the neurologic and the metabolic. The neurologic manifestations arise from the encroachment of the neoplasm on the intracranial contents and are indications of changes in pressure, in placement and of destruction of tissue. Such changes are the consequence of pineal tumors at any age of the patient; but in pineal tumors appearing in prepuberal life a second group of changes arise, the metabolic. These metabolic alterations are referable to disturbance in the gland's secretory function. Apparently only in young males is this syndrome complete.[1] It consists of (1) early sexual development evidenced in the enlarged sex organs, pubic hair, general body hair, early changes in voice; (2) precocious mental development evidenced in the maturity of thought and speech, and (3) general body overgrowth to the extent that a child of 5 or 6 years may have the appearance of a child of 11 or 12.

A case reported by Machell[2] presents these changes in a striking manner. The patient was a boy less than 6 years old at the time of the publication. At the age of 5 months there was pubic hair, erections at 17 months, emissions at 30 months. The patient's weight was 7½ pounds above normal at 4 months of age, 12 pounds in excess at 8 months, 20 pounds in excess at 3 years. When the patient was 44 months old, his height was 8½ inches above normal for a child of that age. At 48 months the circumference of the head was over 2 inches in excess of normal. The voice was a deep bass. Mental precocity was very marked and the general bearing and language was that of a much older person.

On account of the difficulties attending experimentation on this vestigial organ, the clinical findings with subsequent necropsy records have been the prime factor in the formulation of the prevailing ideas as to this gland's functions. The conception of this gland's function, however, has in part been developed from laboratory studies, notably from the results concomitant to the extirpation of the organ. This has been attempted frequently, but the situation of the gland is such that in the greater number of instances death followed the operative procedure, from hemorrhage or injury to the vermis or the occipital lobes. By operating on a large number of animals some workers have had a few animals survive. No changes attended the

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1. For review of clinical cases see Bailey, Pearce, and Jelliffe, Smith Ely: Tumors of the Pineal Body, Arch. Int. Med., December, 1911, p. 851. For Physiology and Anatomy, see Vincent Swale: Internal Secretion and Ductless Glands, 1912.

2. Abstract taken from Medical Chronicle, 1912, lvii, 154.