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SYPHILIS AND RAYNAUD'S DISEASE *

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The coincidence of syphilis and Raynaud's disease has occasionally been observed. A few cases have been reported in which the diagnosis of Raynaud's disease was unwarranted, and in which we were dealing with a pure specific obliterative endarteritis; in other cases in which the diagnoses are beyond question, the interdependence is very frail and uncertain, and we might more correctly speak of a simultaneous occurrence; but several instances must be admitted in which the etiologic rôle of an acquired or inherited syphilis is extremely suggestive.

The following case is deemed worthy of record because confusing complications early in the course of the disease obscured the diagnosis, but chiefly because it adds another illustration to this curious group of cases.

History.—The history concerns a colored girl 7 years old, whose present illness began Feb. 5, 1914.

Family History.—The mother has had six miscarriages and a Wassermann test on March 21, 1914, was positive. The father denies lues. A brother and sister of the patient, both younger, seemed normal and showed no luetic stigmata on physical examination.

Past History.—The patient's birth was normal. She had suffered from otorrhea at 2 years of age, and had had spells of earache since then. At 5 years of age she had measles, mumps and whooping cough. Otherwise she had been healthy and normally active.

Present Illness.—Feb. 5, 1914, the mother noticed that the child walked "straddled legged," and examination disclosed a vaginal discharge. Three days later she commenced limping on the right foot and complained of intense pain in her right knee, so that she was confined to her bed, and when seen Feb. 11, 1914, her temperature was 104 F. Vaginal smears showed a Neisser infection. The right knee was swollen, tender, and motion was limited, due to pain. No other joints were involved. Feb. 18, 1914, the patient was admitted to the medical service of the Washington University Hospital. Temperature, 103 F.; leukocytes, 45,000.

Physical Examination.—Forty-six inches long; patient crying, restless, facies show pain, looks ill, is emaciated; muscles small; panniculus absent; complains of cold in a comfortably heated ward. Examination negative except for slightly enlarged tonsils; notched lower incisors; enlarged cervical glands; rapid pulse; and the following interesting condition of the extremities: The right knee

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enlarged and very tender; definite fluctuation; patella floating; left knee not swollen; the right foot shows a black swollen area, including all the foot laterally from the base of the great toe across to the outer side of the heel, including the whole dorsum of the foot as high as the malleoli. There is a sharp line of demarcation with a narrow red margin, especially on the sole. The left foot showed a similar area, extending from between the great and second toes to the middle of the lateral border of the foot, including all four outer toes. Discoloration is dark chocolate over the toes, light brown over the other parts. The ankles are not swollen or tender. The pulse is readily felt in the posterior tibials and dorsalis pedis artery of each foot.

February 20 the Widal test was negative. The right knee was aspirated and about 30 c.c. of a thick purulent fluid removed. Smears showed almost exclusively polymorphonuclear leukocytes. Careful search failed to reveal any organisms and cultures on various media were sterile. Repeated blood cultures were likewise sterile. The fever gradually subsided; the leukocytes falling steadily. Under treatment the vaginal discharge cleared up. The knee was kept in extension from February 24 to March 8 and a roentgenogram of the knee joint taken March 22 showed apparently a normal joint. It seems reasonable to conclude that we were dealing with a gonorrheal vaginitis, complicated by an acute gonorrheal arthritis of the right knee joint.

On admission and for the first four days thereafter, the patient exhibited a peculiar craving for carbohydate foods, constantly crying for bread, crackers and cake, even asking for them when in pain and even at night. The first three days after admission the patient's urine showed a partial reduction of Fehling's solution, an atypical Nylander's test, was fermented by yeast, and polarized light to the right. Repeated examinations since that time have been consistently negative for sugar, even though on one occasion 100 gm. of white bread were given at a single meal. Thus we were dealing with a transient glycosuria probably alimentary.

Two days after admission the Wassermann test gave complete fixation of complement and the patient's serum was again strongly positive April 11 and June 23. With the positive Wassermann of the mother and a history of six miscarriages we are justified in a diagnosis of congenital lues.

We now come to the chief feature of interest, the discoloration of the feet, which eventually developed into a perfectly symmetrical gangrene. Just before admission there had been a spell of very cold weather with considerable snow on the ground. Thinking the condition might be frost bite, careful inquiries were made from the family as to the possibility of exposure to cold. They insisted that the house had been warm and felt reasonably certain that the child had not been in the snow.

Further inquiries elicited the important fact that on Jan. 15, 1914, the patient's left hand became cold and swollen suddenly, the fingers showing a sharply demarcated black discoloration. After two or three days this disappeared only to reappear two days later. This same phenomenon occurred in the hospital, the first time February 24, lasting ten days, with pain, swelling, redness, tenderness and itching of all the fingers going on almost to blackness of the index finger of the left hand. The radial vessels were pulsating; the same condition recurred April 7, clearing up over night.

The process on both feet gradually progressed, the skin becoming ashen gray, finally black, dry, shriveled, the gangrene extending proximally and the line of demarcation assuming a permanent position March 28, almost six weeks after the onset of symptoms. The great toe of the left foot amputated itself April 2, the remainder up to the proximal phalanges dropped off April 15. The process was slower on the right foot, but a symmetrical portion was involved and was removed by a little manipulation June 29. The final result illustrated the wisdom in a case of dry gangrene of permitting a natural demarcation in preference to an amputation. Had a surgical attempt been made it would have

been necessary to sacrifice a great deal more of the feet than the patient was able to save for herself.

Antiluetic treatment was instituted soon after admission and consisted in mercurial inunctions for almost three months. June 29, 0.2 gm. old salvarsan was administered intravenously, 0.25 gm. on July 8, 0.3 gm., July 14, and 0.3 gm., July 29. This therapy had no effect in curing or checking the disease of the feet, and such a result could not be reasonably expected, even if the congenital lues were held responsible for the Raynaud's symptom complex; for the damage was already beyond repair when antiluetic treatment was begun. It is significant to note that an attack of local asphyxia of the fingers occurred April 7, although this attack was much briefer and milder than the previous ones.

DISCUSSION

To summarize, then, the case presents symmetrical gangrene of the feet, and four unquestioned attacks of local asphyxia of the fingers, without exposure to unusual cold. The transient nature of the glycosuria rules out diabetes as the etiologic factor. A gonorrheal vaginitis with probable arthritis occurred, and a gonorrheal septicemia with emboli might be held responsible for the gangrene of the lower extremities; but the question of such sepsis was never proved and does not seem probable clinically. The patient had congenital syphilis, and an obliterative endarteritis could cause the condition. But the vasomotor attacks of the fingers, combined with the symmetrical gangrene of the feet is so typical of Raynaud's disease that the latter diagnosis must be very seriously considered. In fact it seems justifiable to conclude that the patient simultaneously suffered from three diseases—gonorrheal vaginitis with arthritis, congenital syphilis and Raynaud's disease. It remains to discuss what relation, if any, existed between these maladies. Were we dealing with a pure time coincidence, a simultaneous occurrence without interdependence, or did the syphilis, or the gonorrhea, or both, act in relation to the Raynaud's symptoms as the *"Auslösendes Moment?"*

It is not within the scope of this paper to include more than a brief summary of the literature. A complete bibliography of those publications which specifically consider the relation between syphilis and Raynaud's disease has been added for those more fully interested. Raynaud's disease is uncommon, yet its occurrence is not so extremely infrequent as to relegate it to the category of medical rarities. Cassirer saw 56 cases, and including a careful review of the literature up to 1911, has gathered together over 300 unquestioned instances of the disease. Coming now to the group of cases in which an hereditary or acquired lues is present, we find a considerable discrepancy in the figures published. Monro would allow only 2.8 per cent., while Castellino and Cardi find 22 cases of syphilis in 306 cases of Raynaud's disease. Probably the proportion is still higher. The appended 54 references contain more than 22 cases. Perhaps 10 per cent. will not be too high an estimate.

Raynaud himself seemed not to attach any importance to the presence of syphilis, though he mentions an observation to that effect by Portal (1836) and Henry (1857). Defranc notes an early record of this combination described by Liston in 1836, before Raynaud had written his treatise. As Cassirer correctly points out, Morgan in 1889 was probably the first to direct attention to the possible interdependence of syphilis and Raynaud's disease. Cases illustrating this coincidence in acquired lues, have been reported by Amann, Klotz, Morgan, Castellino and Cardi, Elsenberg, Fordyce, Giovanni, Germer, Jacoby, Morton, Nash, Ornellas, Puzey, Riva, Tounton, Balzer and Fouquet, Lustgarten, Cassirer, Phelps, Schuster, Gaucher, Gougerot and Meaux Saint Mare, and Semon. To these must be added those cases of congenital lues, exhibiting a Raynaud's symptom complex, namely, the reports of Hutchinson, Marsh, Humphrey, Krisowski, Young, Wherry, Dyce Duckworth, Pasteur, Rietschel, Schiff, Spieler, Stoltzner, Glaser, Brocq (quoted by Gaucher), Bosanyi, Durantes, Beck, and the case that forms the basis of this report.

As regards the pathologic anatomy of Raynaud's disease, Dehio's statement in 1893 obtains today, namely, that none of the published pathologic investigations, where negative findings have been reported, are complete and detailed enough to justify the conclusion that this malady has no recognizable lesions. The positive findings include changes in the nervous system and circulatory system, either separately or in both. But such changes have been very inconstant, and their etiologic relationship to the Raynaud's disease rather indefinite, while the majority of cases autopsied have failed to reveal any lesions whatsoever. The theories as to the pathogenesis of the disease are briefly:

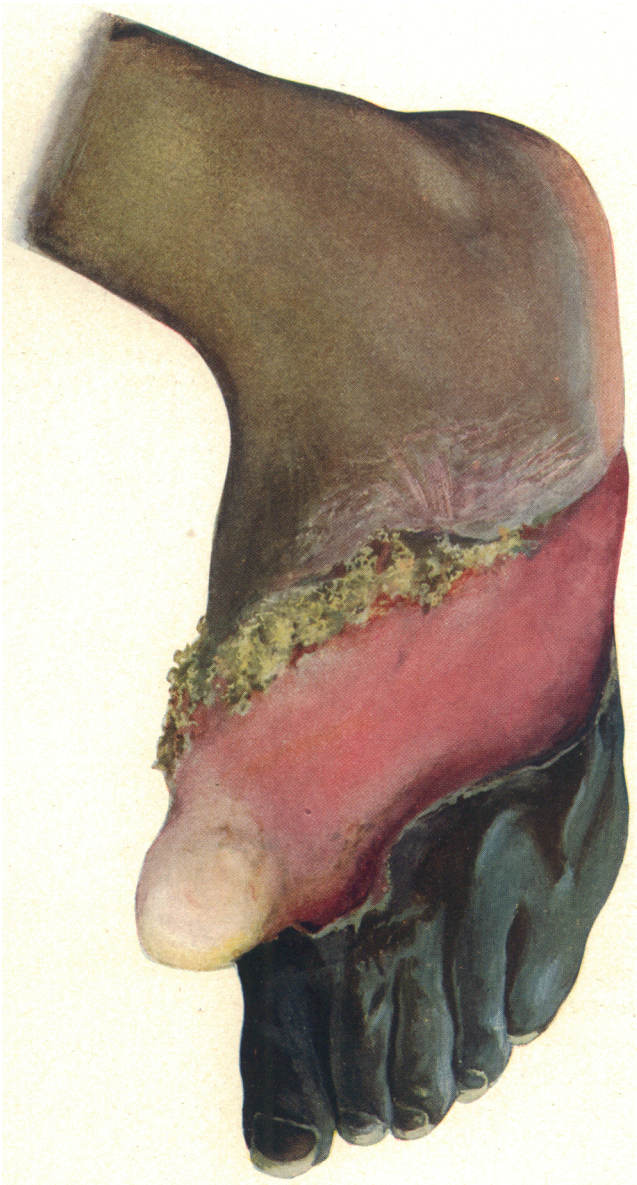
THEORIES AS TO PATHOGENESIS

1. The theory of Raynaud himself. He would classify the syndrome as a central vasomotor neurosis, due to direct or reflex stimuli on the vasomotor center. The majority of writers agree in this conception, modifying it only in certain details.

2. There are those (Pitres and Noesske, etc.) who insist that a peripheral neuritis is the cause of the disease.

3. In disease of the peripheral arteries some have found their etiologic agent.

4. Concerning a case of acquired lues with Raynaud's disease, Gaucher, Gougerot and Meaux Saint Mare offer the following explanation: Either vascular spasm, caused by a syphilitic peripheral neuritis or a central vasomotor disturbance, as the primary feature, a secondary endarteritis from prolonged vasoconstriction sufficing to complete the clinical picture; or more probably, a primary luetic endarteritis, remain-



Appearance of gangrenous foot in author's case.

Illustrating Article by Hans Lisser, A.B., M.D.
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ing latent symptomatically until a spasm set up through the nerve channels determines the onset of local asphyxia and subsequent gangrene.

5. Some authors (Hochenegg, Fuchs) find it necessary to assume a special as yet unknown trophic center, through disease of which or the nerves leading from which, Raynaud's symptom complex follows.

6. Bearing syringomyelia in mind, some are tempted to seek a similar origin, in the spinal cord for Raynaud's disease (Bender, Tscherback, Lyle and Grieve). Oppenheim would suggest that a group of cases at least are due to lesions of the posterior and lateral columns.

7. Still others (Moebius, Solis-Cohen, Levi, Rothschild) ascribe a causal rôle to the glands of internal secretion, especially the thyroid.

It is worth noting that Raynaud's symptom complex has been observed as a complication in some fifty different diseases, including acute and chronic infectious diseases, intoxications, mental and nervous maladies, disorders of the circulatory system and ductless glands, etc. These widely divergent types of disease cannot all be responsible for the unique and singular syndrome of Raynaud. This very fact is one of the most suggestive arguments in support of its being a clinical entity. That Raynaud's disease (probably 10 per cent. of all cases) occurs very frequently in syphilitic patients, might superficially suggest an intimate relationship. However, this statistical preponderance is not surprising, in view of the prevalence of syphilis. A similar case might be made out for tuberculosis. This frequency, then, can have no weight in establishing any relationship between the two diseases.

In discussing the coincidence of these diseases, we can suppose the following possibilities:

1. The symmetrical gangrene and, more important, the other signs and symptoms, may be caused directly by a syphilitic lesion of blood vessels or the nerve supply to such blood vessels. For the final proof of such a contention, the *Spirochaeta pallida* must be demonstrated in the lesion, just as the gonococcus has been found in the tissues of a gonorrheal arthritis, or the spirochete by Noguchi in the cords of tabetics and brains of paretics. Probably many cases of myocardial weakness were suspected of a luetic origin, even though no gummatous process was histologically discernible; but positive statement of fact had to await Warthin's demonstration of the spirochete in the heart muscle.

2. Raynaud's symptom complex may be caused indirectly by the syphilitic toxin. The number of conditions in which this toxin is the etiologic agent are becoming increasingly appreciated. We are coming to recognize a larger number of arthropathies as luetic, even though

the histology is not characteristically syphilitic, nor the signs and symptoms sufficiently typical to permit invariably of a correct diagnosis. Clinicians are becoming convinced that lues of the lung is not as rare as hitherto supposed. We have come to regard an aortitis confined to the arch of the aorta as almost always luetic, even though no gummatous change is present at necropsy. In the conditions mentioned, the history of syphilitic infection, the Wassermann reaction and the response to specific therapy have been the basis for the diagnosis. To what extent do these standards apply to the combination, lues and Raynaud's disease? Some cases of Raynaud's disease have been ascribed to a luetic basis, merely because of a positive Wassermann or history. This is quite unjustifiable. The positive Wassermann and history merely indicated that the patient had syphilis, but not that the Raynaud's disease was an expression of active syphilis.

Those who defend an interdependence between the two diseases advance as their strongest argument, the disappearance of the Raynaud's signs and symptoms under vigorous specific medication. Some of the most striking instances are those reported by Krisowski, Morgan and Bosanyi. Naturally such cases are extremely suggestive, but are they conclusive? It would seem preposterous to doubt such evidence, and yet when one recalls how suddenly and without warning a local asphyxia or local syncope may disappear, a certain skepticism may be permitted as to the rôle played by the specific therapy. In those cases in which local syncope and asphyxia never occurred, and merely a symmetrical gangrene was favorably influenced by mercury or salvarsan, we may actually question the diagnosis of Raynaud's disease and wonder whether a specific endarteritis was not the pathologic basis of the gangrene.

3. We may suppose that syphilis may so lower the bodily resistance as indirectly to make the individual more susceptible to Raynaud's disease. If this were the only relation between the two diseases it would be the same and no more important than the influence of the many other acute and chronic infectious diseases, intoxications, etc., in which Raynaud's syndrome has been observed as a complication.

Morgan concludes concerning his case: "that Raynaud's symptoms appeared as manifestations of tertiary syphilis." Bosanyi concludes similarly concerning his two cases: "Raynaud's disease can develop as a symptom of hereditary lues." But the final proof of such a point of view is still lacking.

It is a pleasure to acknowledge the kindness of Professor Dock in permitting me to report this case.

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