Staff Meeting Bulletin
Hospitals of the » » »
University of Minnesota

Leukemia Cutis

Volume IX | Friday, March 4, 1938 | Number 19

STAFF MEETING BULLETIN
HOSPITALS OF THE . . .
UNIVERSITY OF MINNESOTA

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Published for the General Staff Meeting each week during the school year, October to May, inclusive.

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William A. O'Brien

I. LAST WEEK

Date: February 25, 1938

Place: Recreation Room
Nurses' Hall

Time: 12:15 to 1:15 P.M.

Program: Movie: "New Schools for Old"

Diabetes Mellitus
B. A. Watson

Discussion: Willis Thompson
Geo. Fahr

Present: 117

Corrections:

Page 228, Col. 2, Par. 1, 2, 3: "glycogenolysis" instead of "glycogenesis"

Par. 1: "hyperglycemia" instead of "hypoglycemia"

Gertrude Gunn,
Record Librarian

II. MOVIE:

Title: "Lonesome Ghosts"

Released by: R-K-O

III. AUTHORS

1. LAST WEEK

Bernard Alec Watson

Born in Three Forks, Michigan, graduate of University of Michigan, M.D. '29; Intern and Resident, Montreal General Hospital. Service of I. M. Rabinowitch. Physician of Health Service, '31. Assistant Professor of Medicine; Service - University of Minnesota Health Service, University of Minnesota Hospitals.

2. THIS WEEK

Francis Watson Lynch

Born in Winona, Minnesota; Graduate of University of Minnesota, B.S.; M.B.; M.D. '30; M.S. '33. Intern, University of Minnesota Hospitals. Resident in Dermatology, Minneapolis General Hospital. Thesis: Dermatologic Disease of Fetus. Assistant Professor of Dermatology and Syphilology, Medical School. Services: University of Minnesota Hospitals; Ancker Hospital, St. Paul; University of Minnesota Health Service.

IV. TRIP

Why not take advantage of the excellent rate offered by Dr. Arild Hansen for the meeting of the Federated Societies of Biological Science, to be held in Baltimore March 30th? You do not have to attend the meetings but you can get a 10-day round trip fare to Washington and return for $35.00. The party will leave on the Burlington Zephyr at 8:00 A.M. Tuesday, March 29th, and arrive in Baltimore or Washington the morning of Wednesday, March 30th. You can make your return trip to suit yourself. Please see Dr. Hansen, Department of Pediatrics Office, immediately if you are interested.

V. VENEREAL DISEASE

Please use the special white venereal disease card in reporting cases to the State Department of Health and the manila venereal disease card for reporting cases to the Minneapolis Division of Public Health. Some have been using the contagious disease report card for this purpose. For further information see Dr. Philip D. Kernan, Hospital Health Officer, or inquire at the Record Room.

VI. LEUKEMIA CUTIS

Francis Lynch

Lymphoblastoma

The term lymphoblastoma has enjoyed wide usage with reference to the leukemias and allied conditions. When it was introduced by Mallory he referred only to diseases involving tissues and cells of lymphoid nature. In the dermatologic field Warthin, Wile and Keim have supported its use for a group of conditions (lymphatic leukemia, lymphosarcoma, Hodgkin's disease and mycosis fungoides). Because many of these cases possess features of two or more of these conditions, these and other authors believe that they are but different manifestations of a single underlying process. They believe that one variety may merge into another. This attitude has aided in pointing out the relationships between these diseases.

Ewing, Ormsby and many others believe that more is to be accomplished by separating these diseases into distinct entities. Admitting the common features and inter-relationships, they believe that apparent transitions from one to the other are the result of misinterpretation of the diagnostic features at one time or the other. (The tendency in our department has been to accept this theory.)

Though use of the term lymphoblastoma has many practical advantages it is etymologically incorrect when applied to myelogenous and monocytic leukemia and probably to reticulo-endotheliosis and mycosis fungoides, at least until the cellular pathogenesis of these latter diseases is clearly established.

Lymphatic Leukemia

By far the most numerous examples of cutaneous lesions associated with leukemia are those seen with lymphatic leukemia. There are two main divisions of such lesions: (1) non-specific eruptions (leukemides), and (2) specific eruptions (leukemia cutis). Determination of the nature of the cutaneous involvement is dependent on the microscopic pathology. The non-specific lesions show a banal inflammatory reaction; the specific lesions are pathologically identical with those observed in other organs (lymph nodes, etc.).

From a clinical standpoint, too, these lesions differ. The non-specific involvement is not clinically diagnostic although the proper diagnosis may be suggested to the trained observer. The specific lesions present clinical characteristics that frequently allow exact diagnosis before general physical examination, microscopic study or other laboratory studies.

Leukemides

In cases of leukemia one frequently observes pruritus, dermatitis or cutaneous hemorrhages. The pruritus is characterized by its persistence and intractability. The dermatitis may be papular or papulo-vesicular in nature. These lesions are usually grouped and may be transitory or persistent. Their distribution is suggestive only in that there is no predilection for the areas usually involved in dermatitis or eczema. The hemorrhages may be small (petechiae) or large (hematomas), single or multiple.

Angina, stomatitis and hemorrhages from the mucous membranes are common examples of non-specific involvement of the mucosae.

Leukemides may appear early or late in the course of leukemia. They are less frequently of diagnostic aid than enthusiastic authors and lecturers have suggested. More often the correct diagnosis has been established as a result of general medical study and the leukemide must be regarded as a complication. In a few cases, however, the eruption is seen sufficiently early to be of diagnostic importance.

Generalized dermatitis as an example of the leukemides is of greater

significance and deserves separate discussion (see erythroderma).

Leukemia Cutis

The specific cutaneous involvement associated with lymphatic leukemia may be circumscribed or diffuse and generalized. The former is far more common. Circumscribed eruptions may consist of papules, nodules or tumors. The papular lesions are more often extensive in their distribution and may resemble papular syphilides. Single large tumors are seldom observed as manifestations of lymphatic leukemia. Such lesions ulcerate readily and resemble malignant growths.

The nodular eruptions are the most characteristic feature of leukemia cutis. They are red to brown in color, often presenting a bluish tint because of the hemorrhagic tendency. They are moderately firm and palpation of the surface often results in a rather characteristic velvety sensation.

The location of the specific lesions of leukemia cutis is quite characteristic, the face being a favorite site. Involvement of the ears, nose and eyebrows may result in a leonine facies suggestive of leprosy.

The course of the individual lesion varies. Starting as a papule or as deeper infiltration, there is progression to a nodule and then to larger plaques (and occasionally to tumors). Spontaneous regression may be observed at any time previous to the formation of tumors.

The eruption itself usually begins on the face and may remain limited to this region. Dissemination results in lesions on the scalp, the trunk and particularly the extensor surfaces of the extremities.

Specific cutaneous lesions are much more often associated with the chronic than the acute form of lymphatic leukemia. This is also true of the leukemides with the exception of hemorrhages which are frequently observed as early signs of acute leukemia.

Treatment

The leukemides are notoriously unresponsive to local therapy. When the systemic disease is treated effectually the leukemides usually disappear.

Specific leukemic lesions of the skin require roentgen therapy and may thus be controlled to the same extent as the other lesions of this disease.

Significance

1. Leukemia cutis is of particular interest when it is associated with the aleukemic phase of lymphatic leukemia. In such cases the proper diagnosis can be established, prognosis offered, the eruption treated and early signs of lymph node and visceral involvement awaited (and treated early). Contact with such eruptions stimulates dermatologic interest.

2. There exists a fairly general belief that in those cases of lymphatic leukemia having specific cutaneous eruptions the course is more prolonged than when such involvement is absent. It is our opinion that this belief has resulted from the fact that in these cases the diagnosis is likely to be established earlier in the course of the disease than might otherwise be possible.

3. For many years there was considerable controversy as to the pathogenesis of the individual lesions of leukemia cutis. The older theory favored their development as metastatic lesions, resulting from the deposit of immature cells from the blood stream. The more recent and more generally accepted theory is that these cellular masses arise at the site of cutaneous lymphatic depots (primitive lymph nodes) as a result of the same stimulus that results in the cellular proliferation in the lymph nodes and other organs.

Myelogenous Leukemia

Cutaneous lesions of all types are much less often associated with myelogenous leukemia than with lymphatic leukemia. Their general nature is similar but the hemorrhagic tendency is more pronounced. Proved and accepted examples of such specific cutaneous lesions are sufficiently rare to be reported singly in the literature. We have been fortunate enough to observe several such cases on the medical service of this hospital.

Specific lesions tend to develop very late in the course of the disease, usually appearing as nodules having no characteristic areas of localization. They tend to be more deeply situated than the cutaneous nodes of lymphatic leukemia. It is often difficult to differentiate clinically between subcutaneous hemorrhages and these specific lesions of myelogenous leukemia.

Microscopically these specific nodules are characterized by the presence of immature cells of the myeloid series.

Monocytic Leukemia

Both specific and non-specific cutaneous lesions are commonly associated with monocytic leukemia. There are two types of this disease, (1) the Schilling type which is a distinct disease, comparable with lymphatic and myelogenous leukemia, and (2) the Naegeli type in which immature cells of both the myeloid and monocytic series are present (probably a form of myelogenous leukemia). It is interesting to note that cutaneous lesions appear more frequently with this Naegeli type of leukemia than with the "ordinary" form of myelogenous leukemia.

In the Schilling type of monocytic leukemia cutaneous lesions are present with even greater frequency than in lymphatic leukemia. The non-specific eruptions usually appear in the form of hemorrhagic manifestations. The specific eruptions are papular or nodular in nature, resembling those of lymphatic leukemia, from which they can be differentiated histologically as well as by study of the blood.

Reticulo-Endotheliosis

Followers of Downey's theories of white blood cell development regard reticulo-endotheliosis as an aleukemic manifestation of the Schilling type of monocytic leukemia. There is by no means universal acceptance of this concept. It was our good fortune in this clinic to have the opportunity for careful study of cutaneous lesions associated with a group of cases of the Schilling and Naegeli types of monocytic leukemia and the acute and chronic forms of reticulo-endotheliosis. The clinical and histologic changes were of a nature to conform with Downey's classification of these relatively uncommon diseases.

The cutaneous lesions of reticulo-endotheliosis do not differ greatly from those seen in leukemia. In the acute forms one may observe macular or papular eruptions which seldom lead to the development of deeper nodules. There is a tendency to hemorrhage or necrosis in these lesions and distinctly pustular eruptions may be observed.

Chronic aleukemic reticulo-endotheliosis with cutaneous changes has been reported by a number of observers. There seems to be nothing characteristic about the macular, papular and nodular eruptions which have been described; the hemorrhagic tendency is not so evident as in the acute cases.

We also observed in two cases a necrotic ulcerative tendency which seems to have a few definite characteristics. There may be a history of preceding lesions such as hemorrhagic bullae, or the ulceration may be the first change noted. These ulcers are tender but not extremely painful. The base is flat and necrotic, the borders are sharp and the edges undermined. The purulent discharge subsides in a few days but the lesions persist unchanged for many weeks. There is very little surrounding inflammation. In the earlier months of the disease the lesions may heal with scarring. Later lesions persist with no evidence of any tendency toward granulation or epithelization. Early the microscopic changes are inflammatory with perivascular cellular infiltration,

giant cells and necrosis.

Hodgkin's Disease

The nature of the cutaneous lesions associated with Hodgkin's disease is similar to those of lymphatic leukemia though the hemorrhagic tendency is much less pronounced than in leukemia. Cutaneous purpura is rare and the specific lesions are less likely to have the blue or brown tints suggesting hemorrhages. Pruritus and pruritic non-specific eruptions are more common than in leukemia; specific lesions are much less frequently observed.

Cutaneous nodules (single and multiple) and larger tumors have been observed in our clinic. Disseminated papular eruptions of a specific nature have not been seen here. A large ulcerating mass involving the female breast developed late in the course of one patient's disease.

The microscopic findings in cutaneous Hodgkin's disease are comparable with those observed in the lymph nodes. There are usually numerous lymphocytes (large as well as small) and considerable connective tissue reaction. Eosinophiles are noticeably increased in number. Sternberg (Dorothy Reed) cells are usually present. Although the pathologic changes are sufficiently characteristic to make a diagnosis, it is seldom that the diagnosis has not been made long before the patient gets to a dermatologist. Specific lesions seldom precede the lymphadenopathy. In the case of the non-specific eruptions the diagnosis of Hodgkin's disease may be suggested by the persistence and intractability of the lesions but in most cases the diagnosis is known before these eruptions appear.

Mycosis Fungoides

Mycosis fungoides enjoys a peculiar position in medicine. Known for more than a hundred years its existence is still challenged. Some deny its very existence; others consider it only as a clinical concept; still others regard it as a pathologic entity.

The clinical features of this disease are quite well known and are divided in three stages: 1, the premycotic, 2, the infiltrative, and 3, the fungoid or tumor stage. It is a progressive condition varying from months to years in its course. In some instances the first and second stages are passed through rapidly, in a few cases the tumors appear as early manifestations (tumeurs d'emblée). The tumor stage results in prostration, anemia, cachexia and finally sepsis.

Having a general resemblance to the leukemias and Hodgkin's disease, mycosis fungoides usually remains limited to the skin until the terminal phases and occasionally throughout its entire course. Lymphadenopathy and enlargement of the abdominal viscera are seldom seen until the tumor change. Changes in the blood are usually limited to a moderate leukocytosis with relative monocytosis.

In its earliest stages the eruption simulates psoriasis, eczema or mycotic dermatitis. In the infiltrative stage the dark color and the diffuse thickening should suggest the serious nature of the eruption, and in the final stages its malignant progress is evident.

Although the cutaneous lesions resemble leukemia cutis they differ in several essential features. The eruption is usually constant and progressive though the individual lesions may be transitory. Even in the early stages clinically resembling the non-specific leukemides, the microscopic structure is usually specific or at least highly suggestive. Finally, in the late stages, the individual lesions are not relatively inactive nodules but more often actively progressing, fungating tumor masses.

Although in the various stages of this disease the extent of the pathology varies, its general nature remains constant. The multiformity of the cells is in striking contrast with the uniformity observed in lymphatic leukemia cutis. The connective tissue cells are usually proliferative, all the types of

leukocytes are represented, monocytes are numerous and giant cells are often present. Though a specific diagnosis may not always be possible one can easily see that he is not dealing with a simple and banal inflammation. Syphilis and tuberculosis can be excluded. Lymphatic leukemia is clearly differentiated but myelogenous and monocytic leukemia, Hodgkin's disease and reticulo-endotheliosis may have to be considered. Mycosis fungoides is usually diagnosed by exclusion of these latter conditions.

With reference to the identity of mycosis fungoides, one reason for confusion has been the tendency of many dermatologists to offer it as a diagnostic suggestion when none of the more common conditions can be identified. If, in confusing cases, one withholds this diagnosis until better evidence is available, fewer so-called cases of mycosis fungoides will terminate as leukemia or Hodgkin's disease. It is our belief that mycosis fungoides does exist, though it is rarely observed.

Many of the staff will recall a case of this condition reported before the Inter-departmental Seminar several years ago in association with the Pathology Department. In this case the disease had been present for a period of six years. At one time a diagnosis of "splenic anemia" was made and splenectomy performed. Although visceral involvement was present throughout the course of the disease, the cutaneous involvement was typical for mycosis fungoides. Complete study at autopsy confirmed the diagnosis.

Erythroderma

Generalized exfoliative dermatitis (erythroderma) is so closely related to the group of diseases under discussion that it deserves special consideration at this time. Such cases are not uncommon and always require the most careful study in order to determine their etiology.

Erythroderma can develop on the basis of chronic dermatoses (eczema, psoriasis, pityriasis rubra pilaris, lichen planus). In its mildest form it can be associated with generalized infectious processes (scarlet fever, streptococcic septicemia). It can be caused by intolerance to certain drugs, especially arsenic in the form of the arsphenamines. Finally it may be an accompaniment of systemic disease of the hemopoietic organs.

Some observers (Montgomery) believe that chronic extensive cutaneous disease may result in such prolonged cutaneous stimulation that a leukemic process will originate in the skin. Specifically, psoriasis in its erythrodermic form has been credited with this power. The majority of dermatologists are not in agreement with this theory.

When associated with Hodgkin's disease erythroderma is non-specific in nature. As a manifestation of leukemia it may be either non-specific or specific in its histopathology.

The diagnostic procedures indicated in the study of cases of erythroderma are:

1. Complete cutaneous examination and history to identify any pre-existing dermatoses.
2. Complete physical examination with particular note of lymphadenopathy, spleno- and hepatomegaly.
3. Complete study of the blood.
4. Roentgen study of the thorax to demonstrate any mediastinal changes.
5. Cutaneous biopsy.
6. Lymph node biopsy (adenopathy is nearly a constant finding).
7. Prolonged observation and repeated study if immediate diagnosis is impossible.

Summary

1. It seems unwise to use the term lymphoblastoma with application to all the conditions herein discussed. Separate classification is advantageous.

2. Cutaneous lesions associated with the leukemias may be specific (leukemia cutis) or non-specific (leukemides).

3. The specific lesions have distinctive clinical features (especially in lymphatic leukemia) usually allowing clinical diagnosis. The histopathology is diagnostic. These lesions are usually papules, nodules or tumors.

4. The non-specific eruptions are multiform and their pathology is banal.

5. Lymphatic leukemia results in the greatest number of cases of leukemia cutis; myelogenous leukemia provides the least examples.

6. Leukemia cutis is probably observed in a greater proportion of cases of monocytic leukemia than in the other leukemias.

7. Non-specific eruptions occasionally attract one's attention to the underlying disease before a diagnosis has been established.

8. Leukemia cutis is quite frequently the first presenting sign of the disease. It is often observed in the aleukemic phase of lymphatic leukemia.

9. In Hodgkin's disease one also observes non-specific and specific cutaneous lesions. The latter are uncommon.

10. Mycosis fungoides is chiefly and perhaps primarily a cutaneous disease. It has many features in common with the leukemias, Hodgkin's disease and reticuloendotheliosis.

11. Erythroderma (generalized exfoliative dermatitis) is not uncommonly a manifestation of disease of the lymph nodes and other hemopoietic tissues. It may be specific or non-specific in its pathology. The diagnostic procedures indicated in such cases are enumerated.

Case Report

History: , 56 years old, first noticed a nodule over the left eyebrow eight years ago. This lesion disappeared spontaneously but new nodules appeared on the arms and persisted for one year. The eruption has become generalized and has persisted for four years but the individual lesions occasionally disappear spontaneously.

Joint pains and some bony tenderness were noted several years ago but have since disappeared. There has been a progressive weight loss of forty pounds in two years, associated with some general weakness.

Examination: Repeated examinations in the past have failed to demonstrate any abnormal physical findings with the exception of the aforementioned eruption. Very numerous deep and superficial nodules and large plaques have been observed. They have been reddish brown or dusky colored, firm and only slightly tender.

Splenomegaly and generalized lymphadenopathy were noted several months before admission to the hospital. Slight enlargement of the liver was first observed in medical consultation here.

Treatment: Superficial roentgen radiation to the individual lesions has been successful in controlling them for the past several years. Radiation to the node bearing areas was carried out in February, 1938.

Laboratory: Since January, 1935, the blood has been studied at six-month intervals by Dr. Downey with the following results. The white cell counts have ranged from 7,000 to 10,000 with one exception. Differential counts have been essentially normal. No immature cells have been seen. On one occasion some peculiar, large lymphoid cells were present but could not be identified.

Biopsy: Repeated sections of the cutaneous lesions have shown pathologic changes characteristic for lymphatic leukemia.

Recent sections from an enlarged lymph node were regarded as highly suggestive but not diagnostic of lymphatic leukemia.

Smears from sternal bone marrow, from puncture of a cutaneous nodule and directly from a nodule freshly removed were regarded as compatible with a diagnosis of lymphatic leukemia.

VII. GOSSIP

Change in meeting date. Next week the meeting of the general staff of the University of Minnesota Hospitals will be held on Thursday, March 10, to hear Dr. Alfred W. Adson, Professor of Neurosurgery, Mayo Foundation, discuss Radiologist Harold Peterson's report on the Radiological Diagnosis of Brain Tumors. This change is for next week only. The meeting will start and close at the usual time..... The Lynches have a brand new baby boy who arrived Friday, February 25. Long expected, he weighed over 9 lbs. on arrival. This is their second boy. Congratulations!.....A former Fellow in the Department of Pathology, who was foreign born, made the mistake of going into one of our department stores to make a purchase during a sale. He carried the familiar metal box which contained, among other things, some very choice material for further study. In attempting to go through the crowds, he struck a lady's limb with his bag. Its sharp edge gave her the impression that he had pinched her, and she turned around and slapped him. Many of the women joined in denouncing him for his freshness. Before long the store detective arrived. He insisted on knowing more about the box. The Fellow refused to open it. The crowd grew larger and still he insisted that he did not want to open the box. Finally he did and as the box was very crowded, its contents were scattered into the crowd. I leave the rest to your imagination.....Ancker Hospital continues its remodeling with governmental aid. Many who have not seen it for some time will be agreeably surprised by the many alterations, which include a landscaping project.....At the Bankers' Institute at the Center for Continuation Study now in progress, one of our prominent bankers sent in an unsigned check for his registration. He was written the usual polite note which we all get on these occasions.....At the County Secretaries' Conference of the Minnesota State Medical Association held in St. Paul last Saturday, many interesting reports were read. One of the most interesting was the contribution of Herman Ertresvaag Hilleboe, who told of the plan in which the waiting list for crippled children has been reduced by sending the children to private hospitals and paying for their hospital and medical care. As soon as the list is down to normal, they will be sent to the State Institution under the old plan.. ....And speaking of names, Ejvind Palmer Kirketerp Fenger presided at the founders' dinner of the Phi Chi's last Saturday. The address was made by Eben James Carey, Dean of the Marquette University Medical School of Milwaukee. Dr. Carey is American Medicine's number one exhibit man.

He planned the Century of Progress exhibit in Chicago and was responsible for the very successful exhibit in connection with the last meeting of the Wisconsin State Medical Association in Milwaukee.....The "Birth of a Baby" has proved to be a most attractive picture for the good citizens of Minneapolis. Everyone is frank in praising it. There is a large sprinkling of men in every audience. Strange to relate, most of the fainters have been of the stronger sex. The part which disturbs them is the venipuncture for blood for a Wassermann test. A few cranks have called by 'phone to pay their respects but refused to give their names.