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

Mycosis Fungoides

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William A. O'Brien, M.D.

I. LAST WEEK

Date: February 2, 1940

Place: Recreation Room
Powell Hall

Time: 12:15 to 1:15 p.m.

Program: Movie: "Mental Poise"

Degenerations of the Macular Region
Karl Benkwitz

Discussion
Edward Burch

Present: 142

Gertrude Gunn
Record Librarian

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II. MOVIE

Title: "Donald's Cousin Gus"

Released by R-K-O

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III. ANNOUNCEMENTS

1. HONORED

Dean Diehl has been made a member of the National Advisory Health Committee for the Surgeon-General of the United States Public Health Service. Appointment is for three years, and the purpose of the committee is to study trends and to advise the Public Health Service on other programs. The other members are: H. A. Carlson, Chicago; Esmond Long, Philadelphia; W. A. Sawyer, Rockefeller Foundation; Hans Clark, Columbia; Carl Meyer, Hooper Foundation; E. L. Bishop, T.V.A.; Roger I. Lee, Boston; Paul O'Leary, Mayo Foundation; Lowell J. Reed, Johns Hopkins; and representatives from the army, navy, Bureau of Animal Industry, At their first meeting in Washington last month, preliminary steps toward organization were made and the activities of the health department were discussed.

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2. M. M. HAUGE

Clarkfield, Minnesota, died last week. He was the father of Cecilia H. Hauge, Superintendent of Nurses, University Hospitals; also of both Drs. Hauge, all graduates of the University of Minnesota. Their many friends sympathize with them in their loss.

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3. LECTURE

Sigma Xi - Friday, Feb. 9, 1940.

Dr. J. Charnley McKinley, head of the department of medicine, will give the second in the University's series of public scientific lectures, delivered annually by members of Sigma Xi society, at 8:15 p.m. today in Northrop auditorium.

"The Problems of Poliomyelitis" will be the subject of the lecture.

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IV. MYCOSIS (GRANULOMA) FUNGOIDES

Harry A. Cummings

Definition

In spite of the infrequent occurrence of mycosis fungoides, the excellent descriptions given of it since the time of its recognition by Alibert have made its various types familiar to dermatologists. Studies have been made of affections of this class during recent years, yet they are still involved in some obscurity and their pathology unsettled. Mycosis fungoides has been described by Oliver as being a chronic malignant disease developing gradually and characterized earliest by superficial inflammatory lesions of an erythematous, eczematoid or urticarial type, and later by irregular thickening and infiltrations of the skin with subsequent formation of nodular growths which frequently ulcerate and form mushroom like tumors.

Clinical Features

The onset of the disease is insidious, and there is nothing in the condition suggesting the initial stage of a grave and fatal disease. It may be met with in one of several ways. The patient may present himself with a polymorphic eruption resembling a dry eczema or seborrheic dermatitis, or some plaques which have a scaly surface resembling psoriasis, others may be lichenoid or of an oozing character similar to that of lichen planus or eczema respectively.

The trunk may be widely involved, and where the skin of the face is thickened a leonine appearance suggesting nodular leprosy may be produced. The skin surface in some of the infiltrated areas may be finely mammillated like the rind of an orange or in other places there may be characteristic tumors.

Another mode of onset is the primary development of an erythroderma. This may be the earliest manifestation of the disease, or may follow one of the stages previously described. Here one finds red or violet plaques chiefly in the flexures. The surface is dry, and they may spread until it is practically universal. Hair falls over the affected areas, and the nails may be involved. The skin becomes edematous, and there is enlargement of lymph nodes. In extreme cases the lips and buccal mucosa are involved, the lesions being white patches and superficial ulcers. After a variable time, the characteristic tumors and nodules appear. Rarely death may occur without the formation of these tumors.

The disease is divided into three stages. The pre-mycotic, which manifests lesions usually accompanied by intolerable itching. Infrequently, pruritus without any tegumentary change will usher in the disease, and this may remain as such for months or years before any further changes develop. The series of cutaneous phenomena noted in this pre-fungoid stage have been described as resembling various congestive, inflammatory skin affections. Tumors may develop when no such precedent eruptive symptoms have appeared, but cases where these signals of danger are wanting are rare. The other group shows tumor formation without any preceding surface disorder. In the latter the disease runs a more rapid and fatal course.

Crocker added a third type whose course is marked by recurrent attacks of lymphangitis. An elephantiasic type of thickening of the skin results and tumor formation completes the picture. The usual order of formation of the lesions in this disease is scaly erythematous patches, papules, nodules, and finally mushroom shaped tumors.

Pruritus for several years previous to tumor formation is not at all uncommon, while in the rare type "mycosis fungoides d'emblee" new growths are the first sign of the disease. The tumors vary in size from that of a cherry to that of a half an orange. They frequently arise in one of the primary lesions, but they may start in apparently healthy skin. They are soft, dull red, hemispherical, or nodular on the surface and often constricted at the base. Extension is toward the periphery, and they often ulcerate and become gangrenous. They may form on any part of the body including

the face and scalp, and a remarkable feature is their mode of disappearance. Even large tumors sometimes vanish without the formation of any scar or pigmentation.

Rarely symptoms such as hemiplegia, anasarca, and epileptiform seizures, which may be due to metastases, have been reported. Intercurrent disease sometimes exerts a beneficial effect. Jamieson and others have reported the disappearance of tumors following erysipelas, influenza, and other diseases. In this connection I might add that hyperpyrexia was tried in the treatment of the disease without avail.

Laboratory Findings

The only laboratory finding consistently noted in these cases is the elevation of the monocyte count which averages around seven per cent. Most of the other findings are either within normal limits or those which are consistent with a disease of this nature.

Etiology

A review of the literature impresses one as to how little we really know of the cause of mycosis fungoides. Interpretations derived from the features of the disease vary tremendously. Most observers are inclined to view it as a form of chronic infection. Some classify it with the malignancies related to the sarcoma family. Opinions differ, however, regarding the true nature of the lesions.

Hyde and Montgomery concluded that the phenomena here exhibited differ in clinical type but have many characteristics in common and are varied expressions of a morbid process. They were of the opinion that the disease first declared itself with pruritic symptoms and that the skin eruption is quite as important as are the tumors.

This name (Mycosis fungoides is also known as granuloma fungoides) is confusing in that it gives the impression that it is an inflammatory disorder due to some variety of microorganism. No one can be sure that it is always inflammatory, and nothing is known of any causative agent. In discussing the problem we must necessarily think of the various malignant hyperplasias of lymphoid tissue which originate in different parts of the body. Tissue from which this can develop is found in various locations such as the reticular tissue of the skin, submucous lymphoid tissue, lymph nodes, and spleen. Until the present time there has been no satisfactory solution as to whether these hyperplasias are inflammatory or neoplastic. Webster believes that the essential nature of the process is inflammatory.

Dr. Symmers concluded, after a careful study, that the disease is a cutaneous expression of at least three different diseases of the lymphatic system--Hodgkins, lymphosarcoma, and round cell sarcoma. Fraser believes that there are three possible phases to the pathogenesis;--First, that the lesions are inflammatory in their essential nature from beginning to end; Secondly, that they are inflammatory in their early stages and are later transformed into a neoplastic process; and last, that they are neoplastic all the way through. Advocates of the first interpretation attempt to explain the presence of many mitotic figures as evidence of active proliferative inflammation. In regard to the second, namely, that the neoplastic features are overcome early by strong inflammatory reaction, one notes that this is similarly seen in certain scirrhus forms of carcinoma, Kaposi's sarcoma, and according to Mallory, in Hodgkin's disease.

It would seem from this that the inflammatory features which dominate the histopathologic picture early in the disease can be interpreted as a reaction to the development of tumor cells. Careful search, however, will reveal the presence of cells showing neoplastic features. Tryb believed the disease to be an inflammation which always began in the sub-papillary region.

Kaposi regarded it as a clinical type, a single disorder in a group of sarcoid diseases. Opposed to this is the spon-

taneous disappearance of many of the tumors, a species of involution rarely if ever observed in any other malignant tumors.

Many men believe, as pointed out by Wile and Stiles, Keim and others, that granuloma fungoides is one type of the large lymphoblastoma group of diseases, and that the clinical mutations that occur between these types is evidence favoring the view that they are genetically related neoplasms involving lymphoid tissue. They agree that the term lymphoblastoma is justified until more is learned concerning the cause of this disease.

Duration

Cases have been reported as lasting for as long as thirty-five years, several as long as twenty, and many from five to twelve years. In the less common d'emblee type, the duration is only a matter of months. Multiple and metastatic lesions with general toxemia predispose to the terminal stage of cachexia. Death occurs from toxemia and exhaustion or from some intercurrent infection.

Diagnosis

A case in the tumor state is diagnosed without difficulty. Syphilis, yaws, and leprosy are the affections for which it is commonly mistaken, but the history usually prevents error. More difficulty is encountered in the pre-tumor stages. The lesions then often resemble other diseases which is confusing. As stated by Besnier, "In all cases of ambiguous pruritic dermatoses which are prolonged and rebellious to treatment, the possibility of pre-mycotic mycosis fungoides should be born in mind."

Histopathology

The histopathologic picture found here is one composed of a number of features which, if enough of them are present in any one section, makes a definite diagnosis possible. In the clinical cases of the pre-mycotic stage where the inflammatory process predominates, one can see that the diagnosis is not proven. Here the upper cutis is mainly involved, the process being perivascular, but it soon becomes more diffuse. Generally, acute reaction is minimal, consisting of some dilatation of blood vessels with varying degrees of edema. Infiltrating cells may even permeate the epidermis which is considered by some to be pathognomonic of the disease.

The characteristic finding is a polymorphous cellular infiltration arranged in groups or nests within spaces of connective tissue reticulum. Some clumping and granular degeneration of nuclei with varying numbers of mitotic figures is also found. Predominant among the many cell types found here are epithelioid cells, small round cells, fibroblasts, giant cells, plasma cells, and eosinophiles. They are all markedly irregular in outline, a typical feature being the breaking up of the cell bodies resulting in many free nuclei.

To make a histopathologic diagnosis, therefore, a polymorphic infiltration in the connective tissue reticulum is absolutely essential.

Prognosis

It is true that this is a serious and uniformly fatal disease. Its duration, however, depends on the stage in which the disease is recognized. Incipient cases frequently go on for some years, while those seen in the tumor stage terminate in several months. The prognosis is obviously poor, but in some cases we can render the disease less severe, and treatment gives some measure of relief.

Treatment

The history of the treatment of this disease dates from Jamieson's paper in 1904. Previous to that time arsenic and mercury had proved of little avail. More recently, established dermatologic

principles have been applied to each case depending on the pertinent indications.

In the early stages baths, moist dressings, ointments, and pastes containing keratolytic and anti-pruritic drugs are used with occasional small amounts of arsenic and mercury. When infiltration, node and tumor formation becomes prominent, our only means of giving the patient relief and prolonging life is roentgen therapy. All patients so treated will improve remarkably, but recurrence is the rule. The relief from itching, healing of foul discharging ulcers, and the removal of fungating masses by this method is worthwhile even though it is only temporary.

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CASE REPORTS

Case I. A white male aged 60 was admitted to the dermatology service at the University of Minnesota Hospitals on March 24, 1939. At the time of admission, he stated that he had suffered from a skin eruption for one and a half years. It was eczematoid in nature and began as dusky red scaly plaques over the right side of the chest. The eruption soon spread over the body. Many forms of local therapy were used without avail.

Several weeks after admission to the hospital, the plaques became thickened and several eroded areas developed over the chest. Not long after this, nodules and tumors developed, some of which became ulcerated from which there drained a foul smelling bloody serous discharge.

The tumors disappeared when treated with roentgen rays only to reappear in new areas. This sequence of events continued until the patient became emaciated and exhausted. He died on August 13, 1939, 142 days after his admission to the hospital.

On April 16, 1939 a biopsy specimen taken from the skin of the chest showed findings consistent with a diagnosis of lymphoblastoma. Microscopic examination of lymph nodes on several occasions showed only hyperplastic changes.

Blood studies throughout the course of hospitalization showed a steadily declining hemoglobin and a white blood count ranging from 17,500 to 36,000. The differential count, however, was always normal. The urine and serology were negative.

The positive autopsy findings were: 1. hyperplastic axillary, mesenteric, and inguinal lymph nodes, 2. acute pericarditis, 3. fibrous pleural adhesions, 4. polymorphous infiltrate of the skin, suggestive of mycosis fungoides. The pathologic diagnosis was lymphoblastoma of the skin which was clinically mucosis fungoides.

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Case II. A white female, aged 58 years, was admitted to the dermatology service of the University of Minnesota Hospitals on January 12, 1939. Because of numerous fungating, draining skin tumors and the apparent cachexia, the admitting diagnosis was mycosis fungoides.

The patient had been seen previously at the Mayo Clinic, where she was given a course of roentgen ray treatments over the cervical axillary and inguinal regions. The anterior chest and epigastric regions were also treated at that time.

For three years previous to the hospital admission the patient had suffered from a generalized erythematous scaling eruption. Local therapy for this dermatosis gave little or no benefit. One year previous to admission to the hospital fungating masses developed in scattered locations over the body.

Examination reveals an elderly white female with a scaly uniformly pigmented skin eruption. On the face, neck, chest, and arms are numerous raised fungating masses varying in size from 1 - 6 cm. in diameter and from which exudes a bloody serous discharge.

Microscopic examination of a section made from one of these tumor masses was consistent with a diagnosis of mycosis fungoides. The lesions responded well

to roentgen ray therapy but soon recurred in new areas. The patient became progressively worse and died on April 12, 1939.

Laboratory findings were as follows: Hemoglobin 27%, erythrocytes 1,410,000, leukocytes 10,200, neutrophiles 22%, lymphocytes 76%, monocytes 2%. X-ray of the chest was negative.

An autopsy was done on the day of death, and the positive findings were as follows:

1. Sections from the skin showed a typical lymphoblastoma picture.

2. There was a polymorphous cellular infiltration in the kidneys, axillary lymph nodes, and liver.

3. A proliferative endarteritis of the vessels in the brain.

The pathologic diagnosis was "Leukemic reticulo-endotheliosis with a clinical picture of mycosis fungoides."

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Summary

1. Mycosis fungoides is a grave disease which is characterized early by superficial inflammatory lesions and later by neoplastic growths.

2. Early lesions often simulate other common dermatoses and late lesions appear to be neoplasms of the skin.

3. The cause of the disease is unknown.

4. The prognosis is uniformly poor.

5. The treatment is palliative and symptomatic.

6. Two typical cases, studied at the University of Minnesota Hospitals are reported.

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V. GOSSIP

Recent reports indicate that the maternal death rate in Minneapolis in 1939 was 2.1 deaths per 1000 births, and the infant death rate was around 33. Also of interest is the fact that 97% of Minneapolis babies were delivered in hospitals. Public health authorities insist that with our ideal hospital set-up our maternal death rate could be 1 and our infant rate could be at least half of what it is. Two-thirds of all infant deaths in Minneapolis last year occurred during the first month of life and one-third in the following eleven months.... ..The Center for Continuation Study is host this week to a group of 54 Minnesota physicians representing all the medical societies in Minnesota except Ramsey and Hennepin. These men are studying ways and means of reducing still births and neonatal deaths. When they return to their respective societies, they will act as chairmen of discussion groups and will make every effort to change local practices to coincide with modern pediatric public health practice. Although the men are regularly enrolled students at the Center, all of their expenses are being paid by the Minnesota Department of Health. Ten representatives from other states are also present. The reason that Minneapolis and St. Paul are not included is because these cities have independent health units (metropolitan districts)... ..In Cleveland, private obstetric patients are instructed in groups by representatives of the Academy of Medicine. Physician members of hospital staffs have established uniform obstetric and pediatric practices in their institutions with the result that they enjoy a low morbidity and mortality rate. One unusual by-product is a substantial saving in purchasing layettes (after the nurses have explained what is essential)....Although Minnesota as a whole enjoys a favorable infant and maternal death rate, there is a great deal which remains to be done. Unique is the work of Miss Carlsrud who is touring the state instructing hospital nurses on modern methods of premature and newborn care.....William Henry Schmidt, Assistant Professor of Physical Therapy, Jefferson Medical College of Philadelphia, will be a guest member of the faculty for the course in Physical Therapy Technology at the Center for Continuation Study, March 4, 5, and 6. On March 7 he will address the Midwestern Section of the American Congress of Physical Therapy at the Center. For further information see Dr. Milan Knapp.....Margaret Culkin Banning, noted author from Duluth and convocation speaker this week, used the word "allergic" in reference to education and propaganda in the same way that we use it for hypersensitivity to antigens. Another reference had to do with the time that Oscar Firkins went to Duluth to make an address and found himself marooned at the high table between solicitous ladies and a creamed luncheon (soup, chicken, fruit salad, ice cream). He stood it as long as he could and finally got up and walked out, saying that he came to speak, not to watch them eat.....One of our faculty members recently made a remark that Minnesota differed from other schools in that she had free convocations, a General College, a Center for Continuation Study, and Student Health Service. In every instance, the item mentioned was not only unique but was also a superior approach to the question....Another impression by a New York visitor was about the number of blondes and trailers attached to cars. (No connection between the two)....Thomas T. Mackie, Assistant Clinical Professor of Medicine, Columbia University, and attending Physician at Roosevelt Hospital will be our guest next Friday. He will address the medical students following the meeting. Dr. Mackie is well-known for his work in gastrointestinal diseases especially ulcerative colitis and amebic dysentery.....Dr. Edith Potter, one time Minnesotan, now pathologist at Lying-in Hospital, Chicago, reports that over 80% of still births and newborn infant deaths in her city are being examined at necropsy. This is an all-time high for any city (part of a general campaign to reduce the death rate). Few pathologists have had as much experience as Dr. Potter in studying this question, and many this week have enjoyed hearing her discuss her observations....Carl Melancton Peterson, Minnesota 1927, now secretary of the Council on Industrial Health of the American Medical Association will be our guest February 24. He will be here to attend the meeting of Medical Secretaries in St. Paul and will also discuss with us the new program for Industrial Medicine.

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