REPORT OF TWO CASES OF IDIOPATHIC HEMORRHAGIC SARCOMA (KAPOSI), THE FIRST COMPLICATED WITH LYMPHATIC LEUKEMIA *

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The subject of idiopathic hemorrhagic sarcoma of Kaposi has already been written about from many standpoints, and to date quite a large number of cases have been reported. They have been reviewed so thoroughly in the articles of Gilchrist and Ketron,[1] and in that of Hazen,[2] that we feel that it would be superfluous to mention these reviews except in connection with the cases relevant to conditions in the patients we wish to report.

CASE REPORTS

CASE 1.—*History.*—William K., a Russian Hebrew, aged 63, was seen by one of the writers in 1913, in consultation with Dr. G. W. Crile, on whose service the patient was at that time and to whom we are indebted for these notes. His principal complaint was that he had some red spots on the bottom of his left foot (Fig. 1), which at first had caused him very little trouble; later they had increased in size and were very painful when he walked. A year or so later he told us that some reddish spots had begun to develop on the surface of his left leg, and also on his right leg (Fig. 2). About one year before the patient had entered the hospital, he told us, there had also developed some reddish spots on the arm, and a few on his face; otherwise he said his health was very good, and he had no other discomfort.

The patient's family history was negative. Four years ago he was operated for mastoid disease, which delayed healing for nine months. The patient denied infection with syphilis. He had been married forty-five years; there were six children, living and well. He drank very little and smoked in moderation.

Examination.—Physical examination of the internal organs proved to be entirely negative. The spleen and kidneys were not palpable, the liver was just palpable at the costal margin. The reflexes were present. There seemed to be general lymphatic enlargement, the glands in the axillae being large and freely movable; the ones in the groin were small.

The skin showed the following changes: Over the entire body were scattered numerous irregularly shaped areas of brownish-red pigmentation, these being especially marked on the lower limbs (Fig. 3). There was quite a little scar formation on the lower limbs. These brownish-red and bluish-red areas were usually more markedly pigmented at their periphery, and seemed lighter in the centers. The limbs showed plenty of evidence of old and new hemorrhages into the tissues, while the bluish-red areas were markedly infil-

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1. Gilchrist, T. A., and Ketron, Lloyd W.: Jour. Cutan Dis. **34**:429, 1916.
2. Hazen, H. A.: J. Cutan. Dis. **10**:521, 1911.

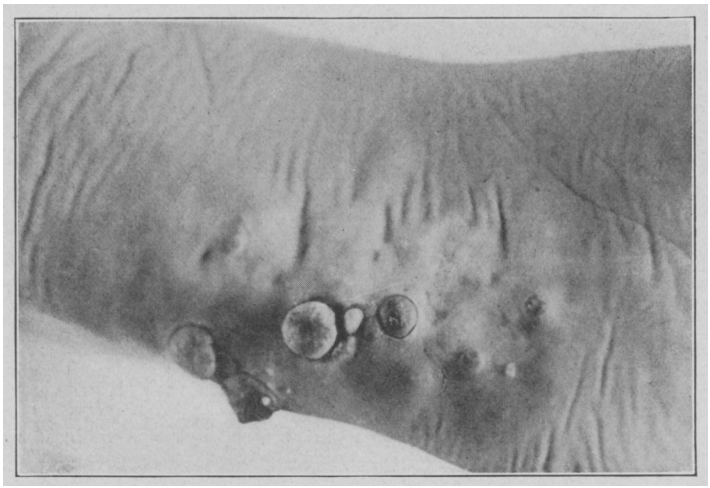

Fig. 1 (Case 1).—Wart-like lesions on bottom of foot.

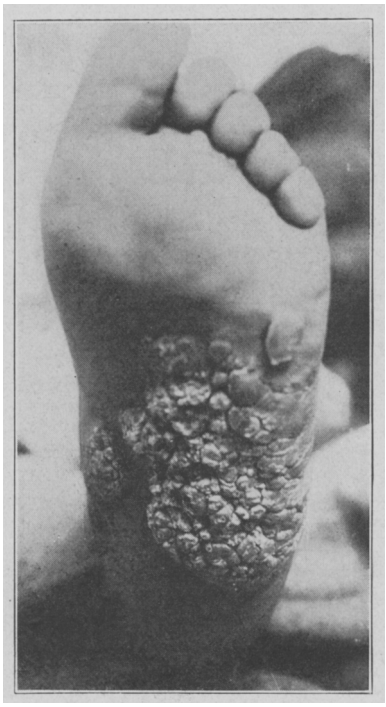

Fig. 2 (Case 1).—Later stage of condition shown in Figure 1.

trated down to the subcutaneous tissues. Both the lower limbs were edematous and pitted quite readily, while along the outer border of the left leg and on the bottom of the left foot, the skin was thickly studded with horny, very vascular nodes, bluish in color; they were quite painful to the touch. Scattered especially over the upper limbs were quarter to dollar size nodules, with deep bluish, infiltrated, raised areas (Fig. 3), while the ears (Fig. 4) showed numerous bluish, raised lesions, the size of a small finger nail. All the lesions on the upper extremities and on the ears were very vascular, and it was possible to squeeze out most of the blood by simple pressure with the fingers.

At this time the white blood count was 23,600 and the red blood count 4,780,000. A clinical diagnosis was made of hemorrhagic sarcoma of Kaposi, and was later substantiated by microscopic study of the tissues. Unfortunately a differential count of the blood was not made, and the patient was lost sight of by the writer, as he was not on his service.

Course and Treatment.—In June, 1916, the patient consulted one of us at his office, and showed much the same condition, except a marked exaggeration of the disease; he was then sent into the hospital for further observation and study. The papillomatous overgrowths on the lower limbs and on the bottom of the left foot had much increased in size, so that it was almost impossible for the patient to walk. He was also somewhat weaker, and unable to work. At this time a careful examination was made of the blood, and we were surprised to find the following condition:

Hemoglobin (Talqvist), 70 per cent.; white blood cells, 66,000 per cubic millimeter; red blood cells, 4,000,000 per cubic millimeter.

Differential count: Small mononuclears, 90 per cent.; large mononuclears, 2 per cent.; transitionals, 1 per cent.; polymorphonuclears, 7 per cent.; eosinophils, 2 per cent. Two hundred cells counted.

The red cells showed irregularity in size, and no nucleated red corpuscles were seen. Blood cultures were made at this time, but showed nothing of interest. The patient was put on injections of sodium cacodylate, 2 grains daily, for three weeks. Later the white blood count dropped to 40,000. He also had several roentgen-ray treatments on different areas of his body. He seemed to improve somewhat generally, but refused to stay longer in the hospital. Some specimens of tissue were removed from different areas for future study.

The patient thereafter called at the office of one of the writers, from time to time, and on May 2, 1917, once more entered the hospital. His condition at this time was much worse, the lesions had all increased in size, and the patient was quite feeble. He complained of gastric distress, and of inablity to walk. The skin of the legs felt hard and leathery, though there were occasional small patches of clear skin between lesions. Both feet had a "cauliflower," fungating, vascular growth on the plantar regions. There was no lymphatic enlargement. The spleen was not palpable with certainty, as the patient was very

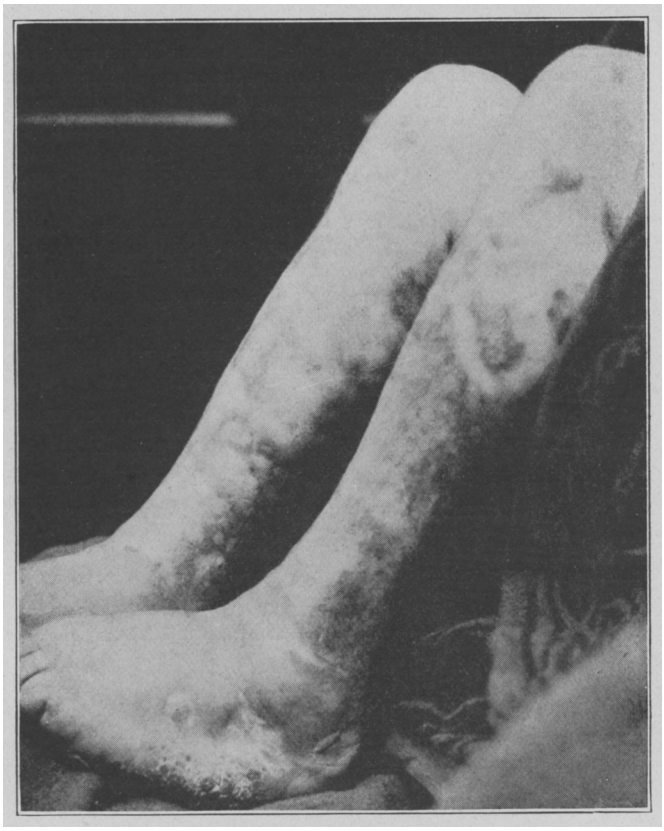

Fig. 3 (Case 1).—Side view of foot.

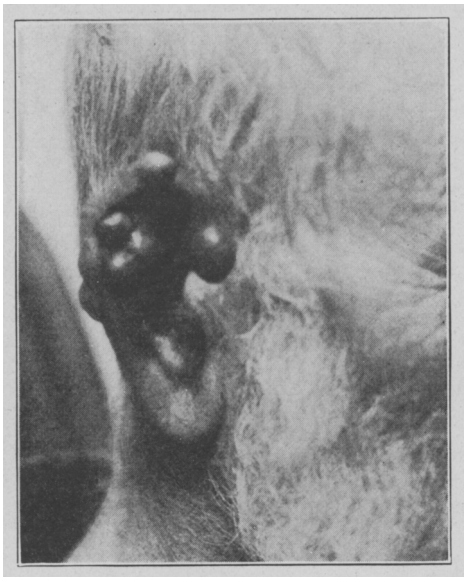

Fig. 4 (Case 1).—Vascular lesions of ear.

rigid; the liver just palpable. At this time there was general enlargement of the glands, which were discrete and firm. His blood findings were as follows:

Hemoglobin (Talqvist), 70 per cent.; white blood cells, 68,000; red blood cells, 3,600,000.

Differential: Small mononuclears, 89.6 per cent.; large mononuclears, 1.1 per cent.; polymorphonuclears, 7.2 per cent.; transitionals, 0.8 per cent.; mast cells, 1.2 per cent.

The red blood cells showed nothing remarkable. The patient was treated with roentgen rays on the plantar surfaces of the feet and on his hands and ears. The feet improved quite remarkably. However, as his general condition did not seem to improve, he refused further treatment and was discharged June 19, 1917, his white blood

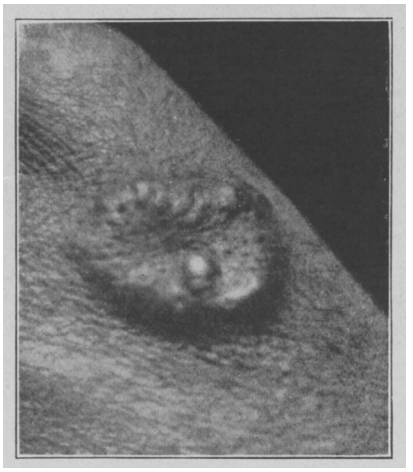

Fig. 5 (Case 1).—Hard indurated vascular lesion at base of thumb.

count rising to over 200,000 before leaving the hospital. A few days later one of the writers was summoned, but before he could get to him the patient died. Necropsy was refused because of religious convictions. Specimens of tissue were removed from the patient on this visit, from a large circular, vascular area on the back of the left hand.

HISTOPATHOLOGY

A very striking characteristic of all the tissues, on examination, was the very marked vascularity. Throughout all of the involved tissue, there was a great increase in newly formed blood vessels. Here and there throughout the entire tissue there was a line of endothelial cells indicating newly formed vessels. There was a marked increase in blood pigment throughout the tissues, especially around these vessels. The neoplastic growth was especially pronounced

around the coil glands. This lesion appeared as a very early one, and the lesions were characterized by cellular infiltration of lymphocytes and occasional plasma cells. The neoplasm itself was made up of spindle cells that appeared to arise from the vessels, which placed it in the sarcoma group. The tissues were quite edematous and swollen. The epidermis was not especially thickened. In several areas there was noted an infiltration of cells which were practically homogeneous in character, and apparently of the small round cell type, though not of the type seen in leukemia.

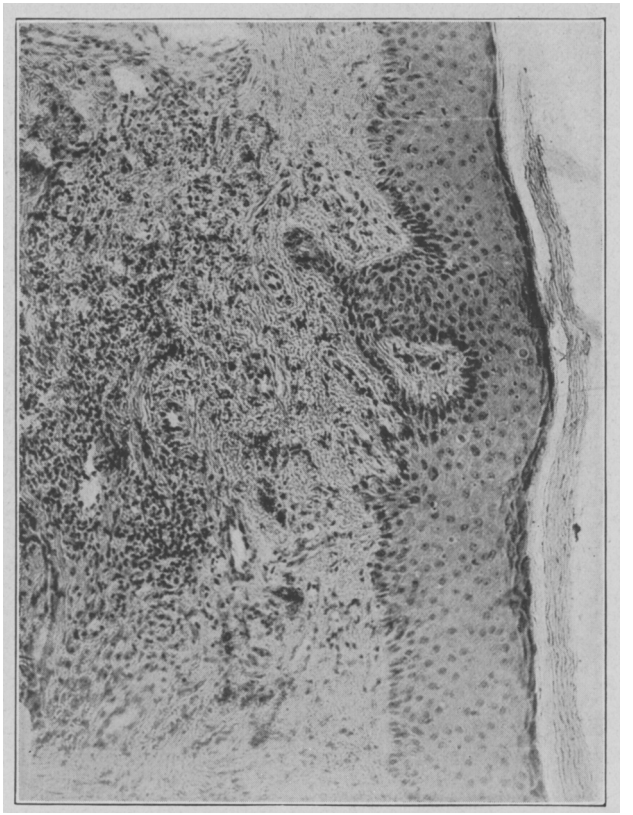

Fig. 6.—An early stage of sarcoma showing new-formed vessels lined with endothelial cells, edema of the tissues and pigment formation.

CASE 2.—*History.*—Gust R., aged 56, was seen through the courtesy of Dr. D. G. Tanno, by one of the writers. He complained of a tumor on the hand, causing inability to work. He said that some twenty years before, he at first had a swelling of the second finger of the left hand, which was bluish in color. This bluish discoloration and swelling had gradually spread to the third and little fingers, and about seven years ago it had spread back to the dorsum of the hand, up the wrist, and some lesions had begun on his lower limbs. Of late the swelling of his hand had become quite painful, the skin of the second finger was breaking down, and discharged more or less

serum; it was almost stiff, so that the patient was unable to work. He gave no history of having had this hand injured or frozen. The family history and physical examination were negative. With the exception of the condition above mentioned, the patient had always been well, and denied any venereal infection. General physical examination revealed nothing extraordinary. The glands showed no especial enlargement, except the left axillary glands, which were somewhat enlarged and discrete. Neither the liver nor spleen were palpable. Examination of the patient's blood showed nothing abnormal, and is therefore not reported in detail. The Wassermann test of the blood was negative.

Physical Examination.—There was symmetrical involvement of both lower limbs, though the lesions were not of the same character entirely on each limb. The left one was, if anything, more involved, and in each case the eruption

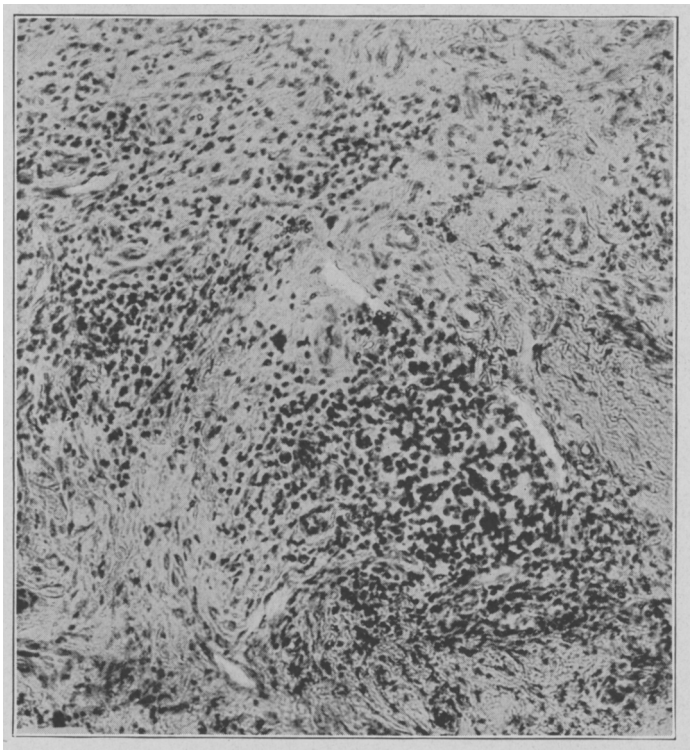

Fig. 7.—New-formed vessels, clumps of pigment and cellular infiltration of the tissues.

was below the knees. The lesions consisted of irregular, deep reddish-blue areas varying in size from the head of a nail to irregular areas, some of them many centimeters in diameter. On the left limb there were numerous small, light bluish spots. Over the tibia there was a long lesion about 5 by 2 cm., deep blue, fairly well defined and markedly indurated; on the lower portion of this limb, extending from a spot 6 cm. above the outer malleolus, to a spot 3 cm. below the same landmark, anterior to the base of the third toe, and posteriorly around to the inner malleolus, the skin was raised, verrucose, and of deep bluish tint, also markedly indurated; a like area was

found on the outer border of the right foot, though this was not so marked in extent, pigmentation or verrucosity. On the right limb, however, was a very extensive, indurated deep bluish lesion, extending posteriorly from the heel half way to the calf. Its outlines were irregular, but with very distinct borders. On the inner surface of the right knee, there was an area about the size of a nickel, containing several bluish striae. These lesions as yet showed no induration. There was one small bluish area on the left buttock. The most notable change was seen on the left hand and wrist. The entire skin from the wrist down was markedly swollen, so that the three middle fingers were about twice their normal size, and on the posterior surface of the hand was a large, deeply pigmented area extending from the wrist distally to the second joint of the second and third fingers, to the nail of the

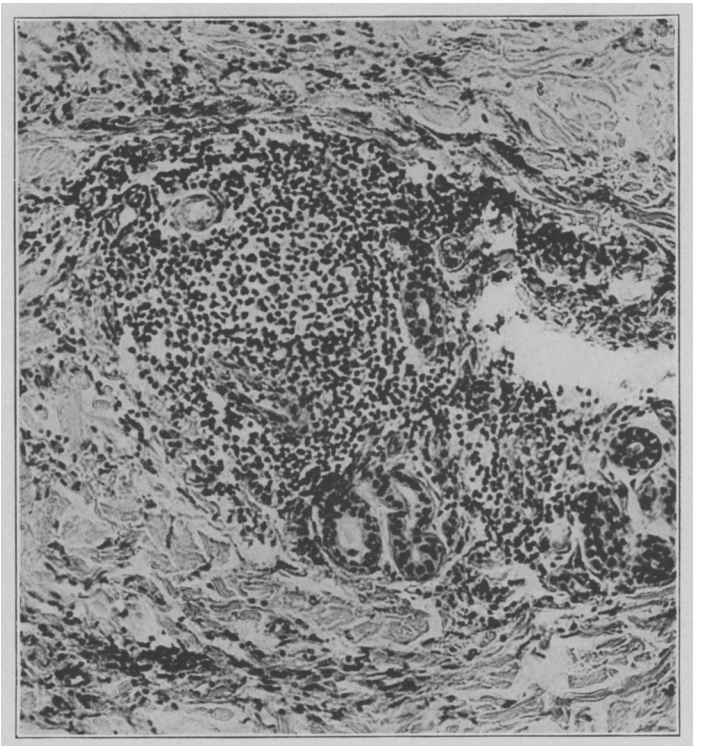

Fig. 8.—An infiltration with homogeneous small round cells around the coil glands.

middle finger, and on each side to the palmar border, while the palmar borders of the middle and second fingers were deeply pigmented. This area was much swollen, edematous and indurated, while the skin on the three fingers was broken and showed some exudation. There were some pustules on the surface of the large lesions from secondary infection. Just above the wrist was another area of deep pigmentation about 6 cm. in length and 3 cm. in width at its widest portion. The borders of this lesion were irregular, and over the surface of the same, as over the surface of the back of the hand, were scattered numerous nodules varying in size from a split pea to that of a castor bean.

Course and Treatment.—The patient was put on local applications of 1 per cent. of aluminum acetate solution for the hands, and given daily injections of sodium cacodylate, 2 grains; the fingers, back of the hand and lower limbs were also treated with roentgen rays. There seemed to be marked improvement, and the patient was discharged from the hospital, March 8, 1919, with quite good use of his left hand; the lesions on the lower limbs were very much improved. A large area of the bluish infiltrated mass on one calf was removed under aseptic precautions, for future study. Likewise a small beginning lesion over the right knee, and a small lesion on the back of the left hand.

HISTOPATHOLOGY

All these tissues presented a picture quite similar to that seen in Case 1. There was a marked formation of new blood vessels with accumulation of pigment, especially around the coil glands. There was

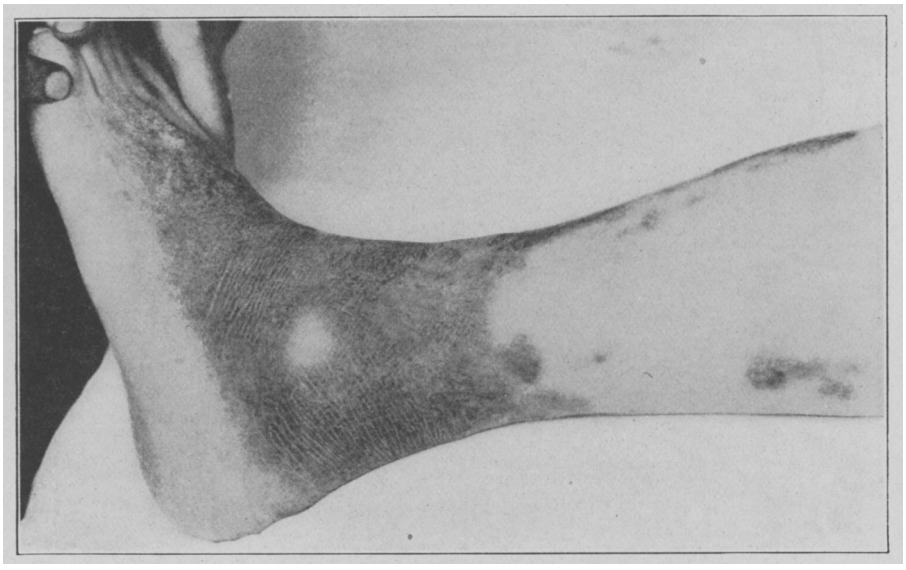

Fig. 9 (Case 2).—Eruption on feet.

similarly an infiltration of round cells, some plasma cells and later, spindle cells. In this patient likewise were noted, though not so frequently, isolated areas made up of a homogeneous mass of small, round cells. Pigment granules were found in the tissue spaces apparently having no relation to blood vessels, and not confined to phagocytes.

ETIOLOGY

There has been much discussion in the past as to the etiology of hemorrhagic sarcoma of Kaposi. Clinically, the disease looks much like a granuloma, infectious in origin. It usually begins on one of the

extremities and spreads slowly, and gradually involves other portions of the body. Ewing[3] feels that it is a granuloma, which in certain predisposed subjects begins taking on a neoplastic property. The new growths in the viscera he thinks are probably not metastases, but arise from multiple foci which were originally inflammatory. The final tumor product is a spindle cell sarcoma. We are all familiar with the fact that it is seen more in Italians and Russian Jews. Lieberthal has already mentioned freezing as one of its predisposing causes, the disease always beginning on one of the extremities. We agree with him that trauma may predispose to its origin. If it is actually an infectious granuloma, the histologic picture is a terminal event, and puts it in the angiosarcoma group.

We are disposed to report our cases inasmuch as one of them is the first on record, at any rate to our knowledge, in which a lymphatic leukemia developed. Whether there was any connection between the

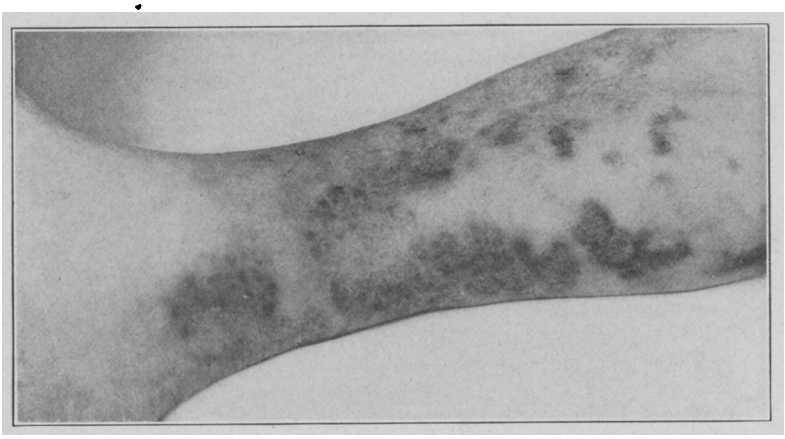

Fig. 10.—Eruption on leg.

lymphatic leukemia and the hemorrhagic sarcoma of Kaposi, we are unable to state. Unfortunately we could not obtain a necropsy. Certainly as the patient's clinical lesions became worse, his leukemia increased in severity and before his death he had a white blood count of over 200,000, yet the cutaneous lesions showed nothing especially characteristic of a leukemia, but were always distinctive of hemorrhagic sarcoma of Kaposi.

We are all familiar with the case of Pardee and Zeit,[4] in which the patient with a typical mycosis fungoides, was found also to be affected with leukemia. Wende[5] has also reported a case of probable

3. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Co., 1919.
4. Pardee, L. C., and Zeit, F. R.: J. Cutan. Dis. **29**:7, 1911.
5. Wende, G. W.: J. Cutan. Dis. **16**:205, 1898.

Hodgkin's disease transformed into a leukemia before death. There are many cases on record[6] of Hodgkin's disease being complicated with leukemia, and vice versa. One of us[6] has recently reported transformation of a lymphosarcoma before death into a leukosarcoma, with a white blood count of 152,000. This has already been discussed by one of us[6] in connection with lymphogranulomatosis. As we have said before, we are unable to say whether there is any connection between the lymphatic leukemia and the hemorrhagic sarcoma in the first of our cases. It is certainly an unusual occurrence, and we record it in the hopes that perhaps later some one may find it of use in correlation of diseases. It was unfortunate in our case that because of the patient's religious point of view, a more careful study of conditions was not possible.

Justus[7] has recently reported having injected in the back of a white mouse, some emulsion of a rapidly growing area from a case of hemorrhagic sarcoma of Kaposi. Later on, in the lungs, heart and liver, he observed collections of new formed cells, especially around the arteries. He succeeded through emulsifying the kidneys of the injected animal, in transmitting this disease down through five generations, and areas injected always showed the lesions characteristic of sarcoma of Kaposi. We regret to say that in our experiments this has not been possible, as we have injected white rats, guinea-pigs, young cats and rabbits with pieces of tissue emulsions intraperitoneally, subcutaneously and intratesticularly, from Case 2, yet we have no result, so we are able to add nothing to the mooted question of etiology in this disease.

TECHNIC

Our technic was as follows: Tissue was excised under aseptic precautions, and placed immediately in saline with ice around it. It was then emulsified by grinding with sand, and injected, as before mentioned, into the animals. We also made transplants of tissue pieces subcutaneously, intraperitoneally and intratesticularly. After two months the animals showed nothing. We then killed them and careful postmortem examination showed no evidence of disease. Emulsions were made of the organs and injected into another generation of white rats. They remained alive and are still well at the end of one month.

PIGMENTATION

The blood pigment does not appear in phagocytes, but is free in the spaces, and especially around the vessels and coil glands. It appears very early — being seen before there is much inflammatory change and

6. Cole, H. N.: J. A. M. A. **69**:341, 1917.
7. Justus: Arch. f. Dermat. u. Syph. **99**:446, 1912.

typical proliferation of the cells, characteristic of this disease. We proved this pigment to be hemosiderin by the iron reaction of Nishimura,[8] a modification of Perl's method. It gives excellent results, the iron is well differentiated against the tissues. It may be used with a secondary stain of eosin-hematoxylin without interfering with the pigment stain.

RÉSUMÉ

We report two cases of idiopathic hemorrhagic sarcoma of Kaposi in a Russian Hebrew, aged 66, and in an Italian, aged 56. In the first case the disease being of five or six years' duration; in the other case, of twenty years' duration. In Case 1, the patient developed a lymphatic leukemia in the course of his disease, but throughout the course his cutaneous lesions showed the histologic characteristics of hemorrhagic sarcoma of Kaposi; i. e., the formation of new blood vessels in the corium, perivascular infiltration with small, round cells, plasma cells and spindle cells, and with a marked infiltration of the tissue with blood pigment, consisting of hemosiderin. Experimentally, we were unable to transmit the disease to cats, white rats, to guinea-pigs and to rabbits.

We wish to thank Dr. H. T. Karsner for suggestions and for reviewing our work.

DISCUSSION

DR. LANE asked about the appearance of the lesions on the feet. In the illustrations some of them very much resembled granuloma pyogenicum. This was interesting in view of the fact that occasionally lesions which at first sight appeared to be those of granuloma pyogenicum proved to be sarcoma.

DR. WISE said it was so long since he had had an opportunity to read up on Kaposi's sarcoma that he wished to know how Dr. Cole distinguished his cases from ordinary nodular multiple sarcoma of the skin. Kaposi's disease occurred almost exclusively in immigrants; he had never seen it in an American-born citizen, which might be an unimportant observation. How did Dr. Cole distinguish the cases of which he presented the pictures from the ordinary relatively benign type? The classical form of Kaposi's sarcoma was a plaque disease which occurred ordinarily on the backs of the hands and feet and legs, slightly elevated and indurated, violaceous in color; and he wished to know how the differentiation between the ordinary disseminated type of sarcoma and the typical Kaposi type was made.

DR. LIEBERTHAL said that he looked over the illustrations and agreed with the diagnosis. In reference to the remark by Dr. Wise regarding the disease in Americans he stated that of four cases reported by him one was that of an American. The striking feature was that the majority of these cases occurred in foreigners in lowly walks of life. He had found that injury preceded the development of the lesions in some cases. In the beginning the lesions were bluish and soft, gradually becoming quite firm, those on the feet even showing cornification and cup shape. In his own specimens it was shown that the infiltration commenced in the adventitia and gradually penetrated the whole wall of the blood vessels. The speaker had performed a necropsy on one of his cases which disclosed metastases in all organs.

8. Nishimura: Centralbl. f. allg. Path. **22**:10, 1910.

DR. LITTLE said that four cases had been shown in the English race quite recently in London, but they were not at all convinced that the condition was at all related to sarcomatosis. The name was probably a misnomer. In his opinion the tumor formation in Dr. Cole's case was very exceptional indeed.

DR. COLE stated that neither of his cases had occurred in Americans; one patient was a Russian Jew and the other an Italian, and these were the people who were usually affected with this disease. He agreed that it was not a sarcoma. When they were differentiated it was readily found that in Kaposi's disease there was the early hemorrhage and not the homogeneous character of cell infiltration that occurred in sarcoma. Without the condition of hemorrhage it might be hard to differentiate, but this made it possible to do so readily.

In the early lesions there was no resemblance to granuloma pyogenicum. A little later some of them had that appearance but this was not the case histologically.

He said that he had quoted Dr. Lieberthal in regard to the treatment, but had not read that part of his paper. In one patient the disease had lasted for about twenty-five years and seemed almost like melanotic sarcoma, but of course it was not, for had it been, the man would not have lived that length of time.