POST-TRAUMATIC SUBCUTANEOUS GRANULOMAS ASSOCIATED WITH A CRYSTALLINE MATERIAL *

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The purpose of this paper is to report 7 cases in which granulomatous lesions were found associated with traumatically introduced crystalline material. In all of these cases there was a definite history of trauma with laceration of the skin, healing *per primam,* a latent interval of 10 to 35 years, then the development of a subcutaneous nodule. Microscopically, all of these lesions were characterized by non-caseating tubercles, anisotropic crystalline material, and giant cells of the foreign body type. In most of these cases, according to the history, the foreign material contained silica. These lesions probably represent traumatic silicosis of the skin. The diagnosis is difficult, since a history of trauma may not be elicited. Also, these lesions may be readily mistaken for Boeck's sarcoid to which they have a strikingly similar histologic appearance.

Similar cases of granulomas of the skin have been described by King,[1] who reported "sarcoid-like" lesions, secondary to trauma. Three of his patients had been cut by glass, and in a fourth case the foreign material was considered silica. German [2] has described a "lupoid-sarcoid" lesion in the skin and subcutaneous tissue of the scalp, which was associated with crystalline material and occurred many years following the initial laceration. He believed this crystalline material to be silica. Grier, Nash, and Freiman [3] have described subcutaneous granulomas, following laceration of the skin by fragments of broken fluorescent lamp bulbs. They considered the granulomatous tissue response to be due to zinc manganese beryllium silicate which is contained in the fluorescent lamp bulbs.

In this paper, in addition to presenting the case reports, we shall discuss the spectroscopic analysis of the tissue, the differential diagnosis between these lesions and Boeck's sarcoid, the staining reactions of the lesions, and studies with the polarizing microscope.

REPORT OF CASES

The essential data on these cases are shown in Table I.

* The opinions or conclusions contained in this report are those of the authors. They are not to be construed as necessarily reflecting the views or the endorsement of the Navy Department.

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TABLE I

Summary of Cases

Case	Age	Race	Sex	Latent period	Duration	Material producing trauma	Site of lesion	Roentgenologic findings	Original pathologic diagnosis	Crystallography
[1] (NMS 48–4471)	27 yrs.	W	F	15 yrs.	2 wks.	Coal	Forehead	Not done	Boeck's sarcoid	Anisotropic crystals and amorphous anthracite
[2] (NMS 24564)	28 yrs.	W	F	15 yrs.	6 wks.	Slate	Forehead	Bone erosion present	Boeck's sarcoid	Anisotropic crystals
[3] (NMS 48–4421) (NMS 49–521)	27 yrs.	W	F	17 yrs.	1 mo.	"Dirty wound" (struck forehead on tree)	Forehead	Negative	Silicosis, skin	Anisotropic crystals
[4] (NMS 48–3639)	27 yrs.	W	M	12 yrs.	6 mos.	"Dirty wound"	Elbow	Not done	Boeck's sarcoid	Anisotropic crystals and amorphous anthracite
[5] (NMS 49–3125)	41 yrs.	W	F	33 yrs.	1 yr.	Shovel covered with cement	Forehead	Not done	Boeck's sarcoid	Anisotropic crystals
[6] (A.F.I.P. Acc. 272784)	27 yrs.	W	F	17 yrs.	2 mos.	Gravel	Elbow	Negative	Foreign body granuloma	Anisotropic crystals
[7] (A.F.I.P. Acc. 269770)	19 yrs.	Negro	M	10 yrs.	1 yr.	Brick	Forehead	Bone erosion present	Granulomatous inflammation, foreign body?	Anisotropic crystals

Case 1

A. T., a white female, 27 years old, was struck on the forehead by a piece of coal 15 years prior to admission. Since that time she had noticed a small, black area at the site of injury. This lesion was asymptomatic until 2 weeks prior to admission when it became tender but did not increase in size. No roentgenograms were taken. The lesion was excised under local anesthesia.

The gross specimen (48–4471) consisted of a formalin-fixed piece of skin and subcutaneous tissue measuring 2.5 by 1.5 by 0.5 cm. The epidermis was not ulcerated. In the dermis was an ill-defined nodule, 0.3 cm. in diameter, the cut surface of which exhibited many small, black markings. The nodule was surrounded by dense yellow-white tissue.

Case 2

A. B. was a white female, 28 years of age, who sustained a laceration of the forehead by a piece of slate roofing 15 years prior to admission. The wound was deep and was not thoroughly cleaned. About 6 weeks before admission a swelling was noted beneath the scar. Examination revealed an ill-defined, firm, non-tender, subcutaneous mass. Roentgenograms of the skull failed to reveal radio-opaque foreign material, but a small defect in the outer table of the skull beneath the mass was noted. Under local anesthesia a discrete, firm, subcutaneous nodule was excised from beneath the scar. The underlying galea aponeurotica was not seen to be involved.

The gross specimen (24564) consisted of a piece of skin and subcutaneous tissue measuring 2.5 by 2.5 by 1.5 cm. In the dermis was an ill-defined, firm, fibrous mass. A few fibers of skeletal muscle were adherent to the under surface of the specimen.

Case 3

M. D., a white female, 27 years old, sustained a 1 inch laceration to her forehead when she ran into a tree while skiing 17 years before admission. The wound healed *per primam*, leaving a barely noticeable, non-pigmented scar. One month before entry the patient noted a slightly tender swelling beneath the scar. This lesion was excised. The surgical incision healed, but shortly thereafter the swelling recurred. Three months after the first operation a firm, slightly movable mass, 2 cm. in diameter, was found on the forehead beneath the operative scar. Roentgenograms of the skull revealed no lesions in the bone. The clinical diagnosis was retention cyst. The nodule was excised together with a portion of the periosteum to which the mass was firmly attached. Healing was uneventful, and the patient has been free from symptoms for 1 year.

The specimen from the first operation (48-4421) consisted of an irregular piece of tissue, 0.3 cm. in greatest dimension.

The gross specimen from the second operation (49–521) consisted of two pieces of tissue. One was comprised of skin and subcutaneous tissue; it measured 1.6 by 1.0 by 0.8 cm. The cut surface was firm and yellow-gray. The overlying epidermis was intact. The other piece of tissue, representing an extension to the periosteum, consisted of an irregular fragment of brownish gray tissue, 0.5 cm. in greatest dimension.

Case 4

R. W. H. was a white male, 27 years of age, who received a laceration contaminated with dirt just below the right elbow which healed *per primam* after being cleaned. Twelve years later, he noted a slowly enlarging, non-tender mass at the site of injury. Six months later examination revealed a flat, well healed scar, 1 cm. in diameter, in the center of which was a blue, mottled area of pigmentation. Beneath the scar there was a soft, apparently encapsulated mass measuring approximately 4 by 3 by 3 cm. The scar and mass were removed under local anesthesia. The clinical diagnosis was chronic olecranon bursitis. The mass was described by the surgeon as "a scarred granulomatous mass of great density with small dirt particles scattered throughout."

The gross specimen (48–3639) consisted of a formalin-fixed piece of very firm, grayish brown tissue measuring 3.0 by 2.5 by 1.5 cm., which cut with a cartilaginous consistency. The sectioned surface was gray and homogeneous.

Case 5

M. A. W., a white female, 41 years old, was admitted to the U.S. Naval Hospital, Bethesda, Maryland, complaining of swelling underlying a scar over the left eye. She had been struck there 34 years prior to admission by a shovel covered with wet cement. The wound had bled freely and healed *per primam*, leaving a small scar. One year prior to admission the scar became slightly tender and more prominent. It continued to increase slowly in size until it was removed under local anesthesia.

The gross specimen (49–3125) consisted of an elliptic piece of skin measuring 1.7 by 0.8 by 0.5 cm. The epidermis was not ulcerated, but the faint outline of an old healed scar was seen. The cut surface revealed the dermis to be replaced by dense, white scar tissue.

Case 6

L. J. was a white female, 27 years old, who sustained a deep laceration on the right elbow as a result of a fall on a gravel walk at the age of 10 years. Seventeen years later a painless, non-tender swelling developed at the site of trauma; 2 months later she was admitted to the Army Station Hospital, Fairfield, California, where the lesion was excised. A roentgenogram of the skull did not show calcification or foreign body.

The gross specimen (A.F.I.P. Acc. 272784) consisted of an ellipse measuring 3 by 2 by 1 cm. In the center of the skin surface, a firm scar measuring 2 by 0.5 cm. was present, beneath which was an area of dense gray-white tissue. (This case is included through the courtesy of the Armed Forces Institute of Pathology.)

Case 7

B. W. S., a Negro male, 19 years old, was struck on the forehead by a brick at the age of 9, resulting in a transverse scar on the left frontal region. Ten years later and 1 year prior to admission, he noticed intermittent swelling of the scar, which persisted until he was admitted to Percy Jones General Hospital, Battle Creek, Michigan. Physical examination at that time revealed the scar on the forehead to be firm, non-tender, and fixed. A roentgenogram revealed bone erosion of the outer

table of the skull beneath the soft tissue mass. The scar and subcutaneous mass were removed under general anesthesia. Healing was uneventful, and the patient was returned to duty 2 weeks later.

The gross specimen (A.F.I.P. Acc. 269770) consisted of two portions, the first of which was bone chips representing an area of 1.5 to 2.0 cc. The second portion included several pieces of skin and subcutaneous tissue, the largest measuring 5.0 by 1.5 by 1.0 cm. (This case is included through the courtesy of the Armed Forces Institute of Pathology.)

Microscopic Examination of Cases 1 Through 7

Since the histologic appearance of the lesions of all 7 cases was similar, one description will suffice.

Sections stained with hematoxylin and eosin showed in the subcutaneous tissue and dermis many discrete, and occasionally confluent, non-caseating tubercles, composed of whorled epithelioid cells (Figs. 1, 2, and 3). These tubercles were separated by dense collagenous bundles and diffusely arranged epithelioid cells. In some of the tubercles were giant cells of the Langhans type (Fig. 2). Infiltration of the intervening stroma with lymphocytes and a few plasma cells was found regularly. The most striking feature was the presence of highly refractile, anisotropic, crystalline foreign bodies, often located within tubercles (Figs. 4, 5, 6, and 7). This crystalline material was irregular in shape and varied in size from being just visible under the high dry lens to approximately 100 μ in length. The larger crystals produced much scoring of the tissue where caught by the microtome knife (Figs. 4 and 6). Some of the crystals were found in the cytoplasm of giant cells of the Langhans type (Fig. 6). The overlying epidermis was not remarkable. In 2 of the cases (nos. 1 and 4), a mixture of crystalline material and black, amorphous material was present (Fig. 5). In one of these there was a history of having been struck with a piece of coal; in the other case the wound was described as dirty. In cases 2 and 7, the tubercles were not only present in the skin, but extended between skeletal muscle fibers down to the periosteum. In one case (no. 3), in some areas, there was no tubercle formation but only crystalline material embedded in dense fibrous tissue (Fig. 8). In another case (no. 7), the tubercles had undergone necrosis and were replaced by hyalinized connective tissue containing numerous crystals. About these areas was a rim of tubercles. Asteroid bodies similar to those found in Boeck's sarcoid and other granulomas were present in the cytoplasm of giant cells in 2 of the cases (Figs. 9 and 10). In none of the cases were Schaumann-Boeck bodies found. This negative finding is not of significance since only 7 cases are reported.

The sections were stained for phosphate with von Kossa's method, for calcium with alizarin, and for iron by Perls' reaction. None of the crystals in these cases showed iron, phosphate, or calcium. Sections of Boeck's sarcoid of the skin likewise were stained by these three methods and the anisotropic Schaumann-Boeck bodies showed calcium, phosphate, and iron. The Schaumann-Boeck body cannot be confused with the crystalline material in our cases because the Schaumann-Boeck body is laminated and stains blue with hematoxylin.

Special Studies

Special studies were undertaken in an attempt to characterize the crystals further.

Crystallographic Studies. Representative sections were studied under the polarizing microscope. Very little information was obtained. All of the crystals were strongly anisotropic, which serves to differentiate them from crystals of the cubic system, such as sodium chloride and other simple salts of inorganic acids, and from glass particles which are amorphous and isotropic. Due to the minute size of the crystals, it was impossible to obtain more specific identification by crystallographic technic. However, known crystals of talc (magnesium silicate) were compared, and they were likewise strongly anisotropic and similar in all respects to the crystals seen in the sections.

Spectroscopic Analysis. Tissue from cases 1, 2, and 3 was subjected to spectrographic analysis. In each case, primary and secondary lines of silicon were found at the following locations of the spectrum: primary lines at 2881.59 and 2516.12 angstroms; secondary lines at 2506.9, 2514.32, 2519.21, 2524.12, and 2528.52 angstroms.

The most dense silicon lines were found in case 2.

Semiquantitative estimation determined that silicon was a major inorganic constituent of the tissue examined. However, Brown [4] reported that silicon may be present in normal skin in amounts as high as 0.045 to 0.055 mg. per gm. of skin. Therefore, these determinations are not significant.

Micro-Incineration. Paraffin sections of the tissues from cases 1 through 5 were micro-incinerated and treated with 5 per cent HCl in an effort to identify the crystals as silica. However, due to the relatively small quantity of crystalline material present in the tissue, and the possible loss of the crystals during cutting and micro-incineration, the results were inconclusive.

Solubility Studies with Acids. Frozen sections of the tissue from case 5, which contained abundant crystalline material, were treated with 5 per cent and 38 per cent hydrochloric acid, and 48 per cent

hydrofluoric acid. Examination of these sections at varying intervals revealed the crystals to persist in the tissue sections following the addition of the hydrochloric acid; but they disappeared following the addition of hydrofluoric acid. This is further evidence that the crystalline material is siliceous in nature.

Discussion

We believe these 7 cases constitute a clinical and pathologic entity, which in the past has not been clearly defined. The lesions all occurred in young patients, who, many years prior to the onset of symptoms, sustained a laceration contaminated by foreign material. The foreign agents included coal, slate, cement, gravel, brick, and earth, all of which contain silica. The lacerations healed without difficulty, but the patient developed symptoms many years later. This latent interval varied from 10 to 33 years and averaged 17 years. Despite this long latent interval there was a rather acute onset of symptoms, varying from 2 weeks to 1 year, with an average of 5 months. The symptoms consisted of the development of a small, usually slightly tender, firm mass beneath an old scar. The only sites in our cases were over the forehead and elbow. Roentgenograms did not reveal the foreign material but showed erosion of the outer table of the skull in 2 of the cases. The surgeon was often in doubt as to diagnosis, and in a few cases found the operative procedure more difficult than contemplated since the granulomatous reactions extended through muscles to involve periosteum. The histologic appearance was strikingly similar in all cases. After complete excision, the patients have remained well. In one case, in which all of the crystalline material was not removed, there was prompt recurrence; after re-excision the patient has remained well.

These granulomatous responses to foreign crystalline material may be readily mistaken for Boeck's sarcoid of the skin, as attested by this erroneous diagnosis in 4 of the 7 cases. Although both Boeck's sarcoid and these granulomas contain non-caseating tubercles, giant cells of the Langhans type, anisotropic, intracellular, crystalline material, and occasional asteroid bodies, the differential diagnosis may be made with relative ease by study of the crystalline material. The crystalline material in these granulomas is often coarse, colorless, non-laminated, spiculated, and gives a negative reaction to stains for iron, calcium, and phosphate. In contrast, the anisotropic Schaumann-Boeck body is small, round, laminated, stains blue with hematoxylin and eosin and positively for iron, calcium, and phosphate. Schaumann-Boeck bodies are absent in many cases of Boeck's sarcoid. It is believed that the mistaken diagnoses have been the result of lack of awareness of this entity and the

belief that the foreign crystalline material represented artifact, or Schaumann-Boeck bodies.

Gardner[5] has demonstrated that silica is tubercle-producing both in animals and man.

Spectrographic, crystallographic, and micro-incineration technics furnished no specific or conclusive data, but gave results compatible with the *a priori* hypothesis that the material was either silica or a silica-containing substance. That these lesions represented a reaction to silica is supported by the history of trauma with diverse silica-containing materials and the similarity of the lesions to talc granulomas (first described by Antopol,[6] and later by German[7]), silicosis of the lungs,[8] and beryllium granulomas.[2] Some of the cases contained black, amorphous material in addition to crystalline material. When the amorphous substance was unassociated with crystalline material there was no epithelioid cell response. Additional support for the theory that these 7 cases represent a type of traumatic silicosis is that a long latent interval between introduction of the foreign material and the development of symptoms also obtains in silicosis of the lungs.

Evans and Zeit[8] have proposed the "piezo-electric theory" for explaining the production of silicosis. This is based on the principle that if a mechanical force is applied to two opposite faces of a silica crystal, an electric charge appears on the other two faces; conversely, an electric charge applied to two opposite faces will cause mechanical distortion of the crystal. They believe that the fibrosis provoked by silica particles represents a tissue response to a recurrent mechanical or electrical insult caused by the piezo-electric effect. It is of interest that the lesions in our cases occurred either on the forehead, or elbow, two sites subject to frequent motion, and thus subject to the piezo-electric effect.

Conclusions

In the tissues removed from 7 patients with post-traumatic subcutaneous granulomas a crystalline material was present. The foreign material was probably silica.

These cases present a clinical and pathologic entity characterized by trauma with silica-containing material, with laceration of the skin healing *per primam*, a latent interval of many years, and a rather acute onset of an often tender nodule beneath the scar, which on pathologic examination reveals non-caseating tubercles, giant cells of the Langhans type, and anisotropic crystalline material.

These granulomatous lesions have been mistaken for Boeck's sarcoid of the skin, but may be differentiated by the appearance of the crystalline material, and by special stains.

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[*Illustrations follow*]

DESCRIPTION OF PLATES

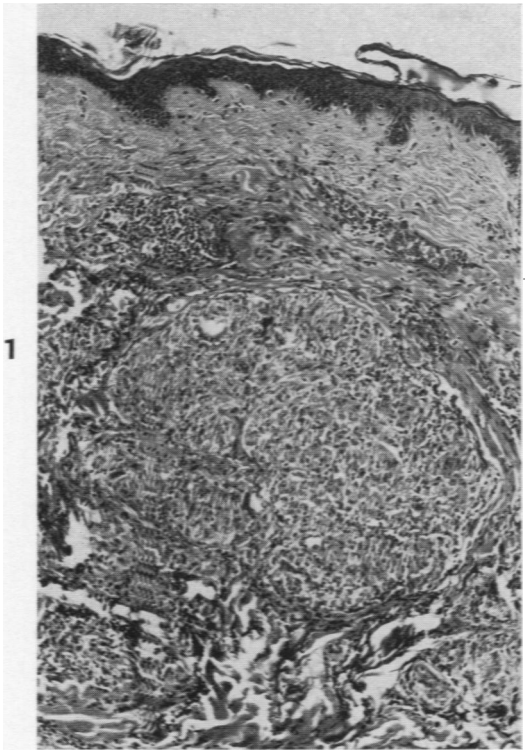
PLATE 52

FIG. 1. Case 5 (49–3125). Confluent subcutaneous tubercles composed of epithelioid cells. × 30.

FIG. 2. Case 5 (49–3125). Discrete tubercles containing giant cells of the Langhans type, surrounded by dense connective tissue. × 100.

FIG. 3. Case 4 (48–3639). Discrete tubercles in subcutaneous tissue. There is lymphocytic infiltration in intervening connective tissue. Resemblance to Boeck's sarcoid may be noted. × 100.

FIG. 4. Case 3 (49–521). Subcutaneous tubercles composed of epithelioid cells and a large crystalline fragment. Of note is the scored tissue where the crystal was caught by the microtome knife. × 200.



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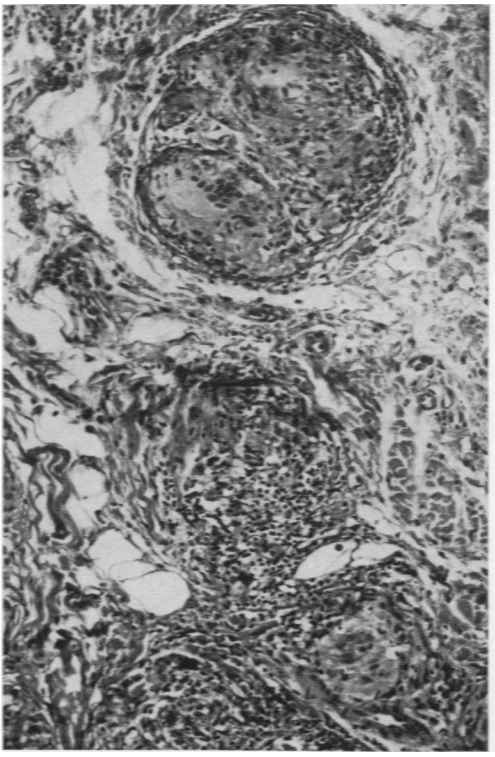

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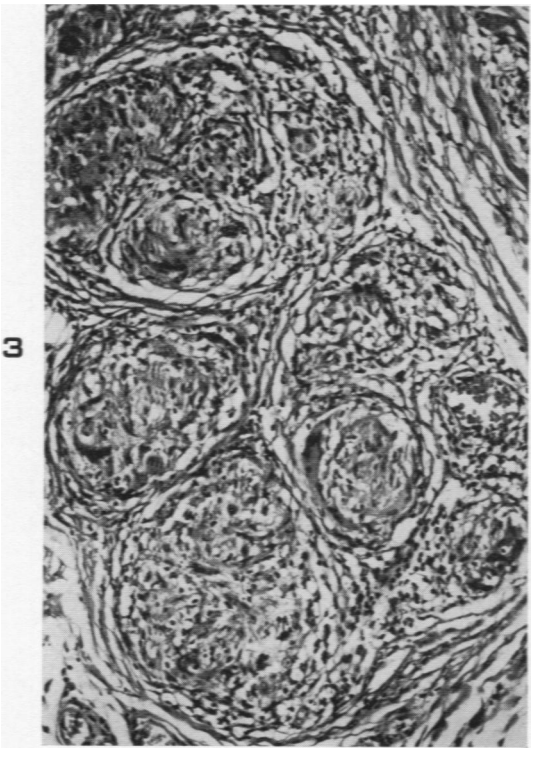

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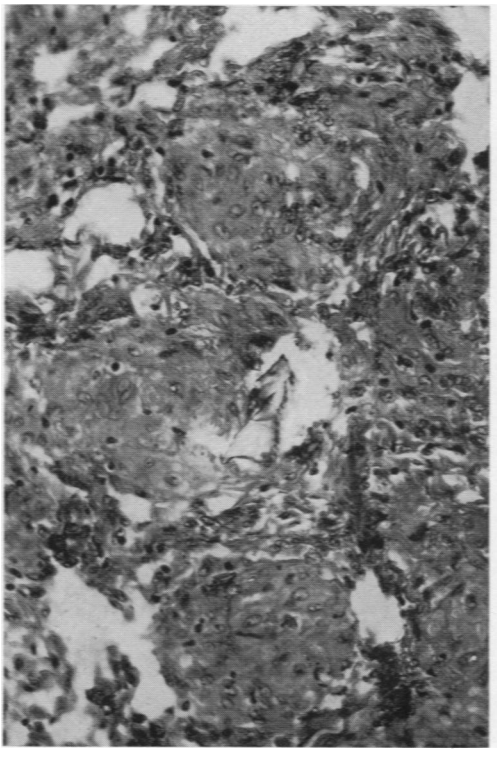

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PLATE 53

FIG. 5. Case 1 (48–4471). Amorphous black material and crystalline material within a tubercle. × 200.

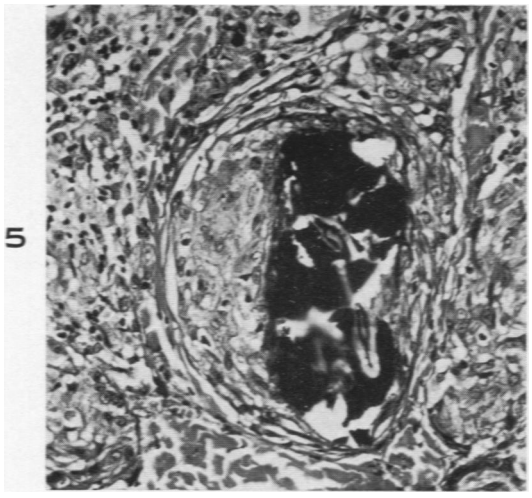
FIG. 6. Case 2 (24564). Crystalline material in the cytoplasm of a giant cell of the Langhans type. × 200.

FIG. 7. Case 3 (49–521). Photograph made with the polarizing microscope to exhibit many large and small anisotropic crystals. × 150.

FIG. 8. Case 3 (49–521). Crystalline material embedded in dense connective tissue. Tubercles are absent. × 200.

FIG. 9. Case 1 (48–4471). Giant cells of the Langhans type containing an asteroid body in the cytoplasm. There is also tubercle formation and an infiltration with lymphocytes. × 200.

FIG. 10. Detail of Figure 7. × 400.



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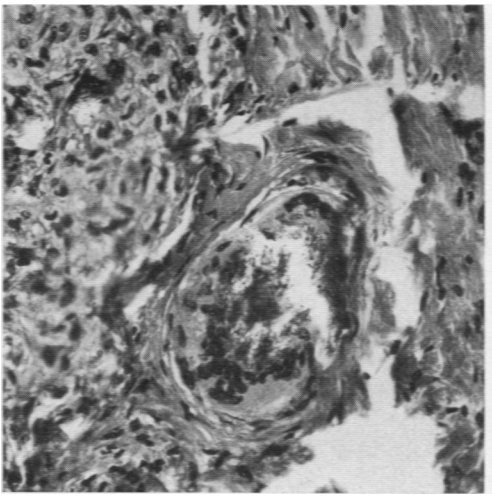

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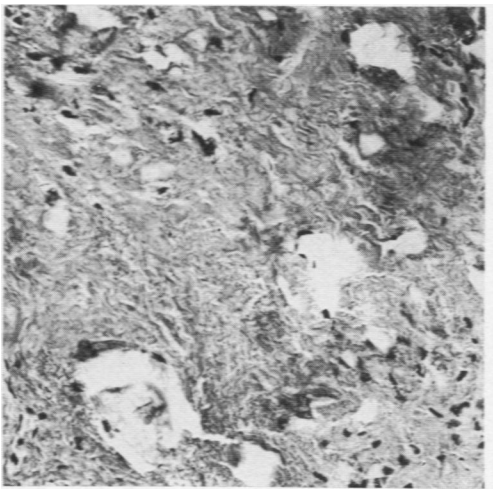

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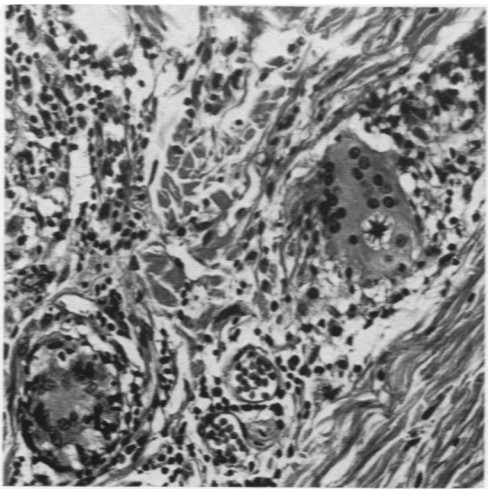

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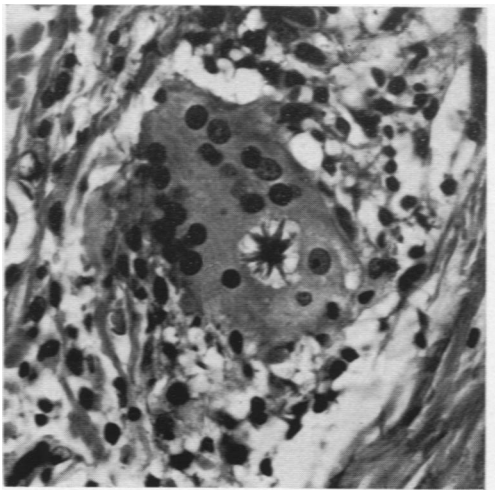

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