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TALCUM POWDER GRANULOMA

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Only one article dealing with talcum powder granuloma could be found in the literature. This was an article by Antopol,[1] devoted mainly to lycopodium granuloma. A short description of one case was given, in which a foreign body reaction was found in the presence of anisotropic crystals which morphologically resembled talc crystals (magnesium silicate—3 $MgO.4SiO_2.H_2O$).[1a]

My interest was aroused by a patient who entered the hospital with a diagnosis of tumor of the abdominal wall.

REPORT OF CASES

CASE 1.—A 44 year old woman had had an appendectomy and a herniorrhaphy in another hospital seven years prior to examination in the present instance. Six years later she had a slightly tender mass in the region of the old appendectomy scar. There was no diarrhea, constipation or loss in weight. Examination showed a small firm mass at the upper end of the scar, apparently in the subcutaneous tissues.

An exploratory laparotomy was made, with excision of the scar. It was observed that an unusual gray translucent nodular tissue occupied much of the fascia. On account of this extensive infiltration, the abdomen was opened. Over the entire cecum were slightly raised grayish translucent nodular plaques. In the omentum were several small translucent nodules and a generalized scattering of thin translucent granular tissue. Enlarged firm lymph nodes lay above the stomach in the preaortic region. On the lateral wall of the gallbladder were three small grayish translucent nodules. The appendix was absent. The scar in the abdominal wall was excised, with section of the anterior fascia, rectus muscle and peritoneum about the tumor.

The patient was discharged shortly before this paper was written, so that the ultimate course is unknown.

The specimen consisted of a piece of skin, subcutaneous fat and muscle, 12 by 6 by 3 cm. The skin measured 9.5 by 3.5 cm. and contained a scar 7 cm. long. The tissue between the muscle and the subcutaneous fat was dense, gray and translucent, with opaque grayish white trabeculae. This tissue extended into the subcutaneous fat and corium in an irregularly radiating manner. Also, there was a piece of muscle and connective tissue, 6.5 by 3 by 1.5 cm. The connective tissue was firm, translucent, slightly granular and pinkish gray.

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1. Antopol, W.: Arch. Path. **16**:326, 1933.

1a. Recently a case of glove powder granuloma has been described (Owen, M.: Texas State J. Med. **32**:482, 1936).

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Microscopic Examination.—Sections were prepared with eosin-methylene blue stain. An extensive lesion was seen, consisting of dense hyaline connective tissue in which numerous pseudotubercles were present. The lesion involved the



Talcum powder granuloma (case 1); eosin-methylene blue stain; × 48. Pseudotubercles containing numerous multinucleated foreign body giant cells invade the subcutaneous fat of the abdominal wall.

corium, subcutaneous fat and muscle. The more well defined nodules consisted of rounded collections of fibroblasts and endothelial cells with numerous large foreign body giant cells. In addition, lymphocytes were noted within the pseudotubercles, as well as a few infrequent polymorphonuclear leukocytes. Flattened,

elongated fibroblasts occurred at the periphery. Here and there one or two giant cells were present, surrounded in some instances by a few endothelial cells. The giant cells contained numerous oval nuclei with small chromatin masses. These nuclei were at times arranged in a semicircle at the periphery and at other times were scattered throughout the cell. The cytoplasm of the giant cells was abundant, and often small spaces were visible within it, apparently containing crystals. In some regions coalescence of the nodules had occurred.

Under crossed Nicol prisms, numerous anisotropic crystals were visible within the giant cells.

The diagnosis was a foreign body reaction.

CASE 2.—A 67 year old woman five years previously had been given a diagnosis of primary hyperthyroidism, and had a subtotal thyroidectomy in two stages. The pathologic diagnosis was primary hyperplasia of the thyroid gland with moderate involution. In the present instance she was admitted for a swelling which had been present in the region of the thyroid gland during the past three years. The left lobe of the gland was easily felt; the isthmus was partly substernal. There was no evidence of hyperthyroidism. The basal metabolic rate was + 4. It was felt that the remnants of the thyroid gland were a potential source of trouble and should be removed.

An excision of the thyroid remnants was made. Following the operation, the basal metabolic rate was + 11.

The specimen consisted of four irregular firm scraps of thyroid tissue, the total weight of which was 20 Gm. A small amount of muscle was attached. There was much increase in fibrous tissue. The thyroid tissue was translucent and pink.

Microscopic Examination.—The sections were prepared with the hematoxylin and eosin stain. An extensive lesion was seen, consisting of fibrosis and well developed pseudotubercles. Material staining with hematoxylin was present about some collections of crystals within giant cells.

Under crossed Nicol prisms, numerous anisotropic crystals were found within the giant cells.

The diagnosis was primary hyperplasia with late involution and hyperinvolution, recurrent, and a foreign body reaction.

A mineralogical analysis revealed that the crystals in the giant cells in both the foregoing cases possessed the following physical characteristics:

1. The extinction angle varied from 10 to 15 degrees.

2. Some crystals were in the orthorhombic and some in the monoclinic system.

3. The crystals had a higher refractive index than Canada balsam (1.54). Talc crystals possess an index of refraction of 1.589 along two axes.

4. The crystals were anisotropic.

5. The crystals were roughly of the same magnitude and morphologic appearance as those in talcum powder.

Further evidence of a mineralogical nature was obtained by incineration. Paraffin sections, unstained, were incinerated at about 400 C.

for five hours on two successive days. Examination revealed no alteration in the crystals.

The significant results obtained in the study of these two cases led to an investigation of all the records of foreign body reactions in the files of this laboratory. During a period of nine years only three other cases had occurred in which crystals resembling those in talcum powder were apparently responsible for clinically important lesions. Several other cases were discovered in which a reaction to crystals was present, but it was overshadowed by that due to suture material.

CASE 3.—A 50 year old woman had had a blue spot on the mucocutaneous border of the lower lip for a number of years. There had been a slight increase in the size of the lesion during a few months previous to an operation on the lip at another hospital four weeks prior to examination in the present instance. The pathologic diagnosis was basal cell carcinoma.

Examination showed on the left of the median line of the lower lip, a healed surgical scar 1 cm. in length. One portion of the scar, 0.4 cm. in diameter, was firm and nodular. In the left side of the neck there were from two to five enlarged palpable lymph nodes. The submaxillary gland on the left side was slightly larger than that on the right. The clinical diagnosis was recurrent carcinoma.

A V-shaped excision of the lesion was made, with later dissection of the submaxillary triangle.

Microscopic Examination.—A segment of the lip containing a small indurated area of mucosa was sectioned, and the sections were treated with the hematoxylin-eosin stain. Dense scar tissue extended into the muscle from the corium, with fairly numerous foreign body giant cells present. Laterally, whorl-like arrangements of fibroblasts surrounded the foreign body giant cells. The pseudotubercle formation was not well advanced. Numerous anisotropic crystals were surrounded by and contained within the foreign body giant cells.

The diagnosis was a foreign body reaction. The diagnosis of the lesion in tissue obtained in the submaxillary dissection was hyperplasia of the lymph nodes and slight chronic inflammation of the submaxillary gland. (No anisotropic crystals occurred within the lymph nodes.)

CASE 4.—A 54 year old man had had, fifteen years previously, a furuncle on the left side of the lower lip about 2 cm. from the mucocutaneous line. Two years prior to examination in the present instance, a small nonulcerated crater formed in the center of the old cicatricial tissue. This was treated with radium at that time. About one month before examination, an excision of scar tissue was made at another hospital. The pathologic diagnosis was carcinoma.

An excision of recurrent carcinoma and plastic repair were made. The specimen consisted of a small triangular piece of lip covered by skin and mucous membrane. The skin showed a small depressed area with some thickening and induration beneath it.

Microscopic Examination.—Sections were prepared with the hematoxylin-eosin stain. Dense scar tissue extended from the corium to the muscle. Within the scar tissue were small groups of foreign body giant cells surrounding and containing anisotropic crystals. Scattered lymphocytes were present.

In one section a small focus of tumor was surrounded by dense fibrous tissue in which numerous anisotropic crystals were present within foreign body

giant cells. The tumor tissue was arranged in the form of hair follicles, occupying about three quarters of a low power field. Invasion was fairly active. The cells were small, with oval nuclei containing fine chromatin granules. The cytoplasm was scanty; the cell outlines, indistinct. Mitotic figures were not numerous. There was palisading of cells at the edges.

The diagnosis was chronic inflammation, scar tissue, a foreign body reaction and a small focus of basal cell carcinoma, apparently of the hair matrix type. (This focus was found only after many sections had been examined.)

CASE 5.—A 23 year old man had a swelling on the right side of the perineum, which appeared three weeks prior to his first admission to the hospital. This steadily increased in size and became tender. Examination disclosed that in the right anterior perineal region there was an egg-sized indurated tender swelling with fluctuation at the center. There was no induration along the wall of the rectum. Incision and drainage were carried out.

The patient was again admitted two weeks later. An opening was made in the fistula seen at the site of the previous incision for drainage in the right anterior perineal region. A probe was passed along the left wall of the rectum, but no internal opening could be demonstrated. The condition was diagnosed as blind external fistula in ano.

Radical excision was performed.

The specimen consisted of a piece of skin and subcutaneous fat, 4 by 2.5 by 1.5 cm. The skin, 2.5 by 1 cm., was traversed by an incision which led into a sinus 1.2 by 0.2 cm. in diameter, running the length of the specimen. There was blue discoloration about the incision. The surrounding tissue was fibrotic.

Microscopic Examination.—Sections were prepared with the hematoxylin-eosin stain. The sinus tract was lined by granulation tissue, which was infiltrated with numerous lymphocytes. About the sinus tract was dense scar tissue, also heavily infiltrated with lymphocytes. This fibrosis extended into the fat. Within the fibrous tissue were numerous anisotropic crystals, many of which were within numerous foreign body giant cells. Crystals and giant cells were close to the sinus.

The diagnosis was a fistula with chronic inflammation and a foreign body giant cell reaction.

All of the crystals in the last three cases resembled those found in the first two. Furthermore, in morphologic character they were strikingly similar to talc crystals which were mounted in glycerin and examined under the microscope.

EXPERIMENTAL STUDY

Three adult mice were used. In each mouse 1 cc. of a sterilized 10 per cent suspension of talcum powder in distilled water was injected subcutaneously into the abdominal wall, as well as intraperitoneally. At the end of seven weeks the mice were chloroformed and examined. The findings were more or less similar in all. Firm opaque white nodules about 0.3 cm. in diameter were found in the subcutaneous tissues of the anterior abdominal wall at the point of injection. Within the peritoneal cavity, similar nodules, covered by smooth serosa, were found on the serosal surfaces of the spleen, liver and small and large intestines, as well as within the mesentery of the small intestine and omentum. These nodules measured from 0.1 to 0.3 cm. in diameter. Some of the larger nodules, both

in the anterior abdominal wall and within the peritoneal cavity, possessed centers of unaltered dry powder.

Microscopic Examination.—Sections were prepared with the hematoxylin-eosin stain. The nodules described in the macroscopic examination were composed of granulomatous tissue, with numerous foreign body giant cells surrounding and containing anisotropic crystals similar to those found in the surgical specimens described. There was much fibroblastic proliferation about the crystals. At times a rather thick fibrous capsule formed at the periphery. In addition, scattered endothelial cells, lymphocytes and a few polymorphonuclear leukocytes were visible. There was invasion of the fat of the mesentery of the small intestine and of the omentum by the granulomatous tissue.

There was localized compression of the spleen and liver by large nodules but no invasion of parenchyma. In some of the larger nodules, crystals were present centrally, with a few necrotic phagocytic cells visible. Fibroblasts and foreign body giant cells were present at the periphery. No tubercle formation was seen, but this was probably due to the fact that the time during which the crystals remained in the animals had been comparatively short.

COMMENT

In the first two cases, the results obtained following incineration showed that the crystals were mineral. This, together with their physical characteristics, makes it practically certain that talc crystals were present. In the last three cases, the crystals were found to be morphologically identical with those in the first two cases and with talc crystals examined under the microscope. That talc crystals may produce lesions similar to those found in the cases studied is brought out by the results obtained in animal experimentation.

It is of great interest that in the first two cases the length of time necessary to produce clinically perceptible masses ranged from five to seven years. This long period of time might be the cause of clinical error in that the possibility of the introduction of a foreign body like talc during the previous operation might be forgotten.

An analysis of the cases affords much instruction. One is struck by the varied character of the cases in which talc crystals introduced a cause of diagnostic error. In the first case, an exploratory laparotomy was done for a suspected tumor of the abdomen. Even examination during the operation did not reveal the error, which was further masked by the diagnosis of tuberculosis suggested by the frozen section. It was only after the section was examined under crossed Nicol prisms that the true nature of the lesion was suspected.

In the second case, the patient had suffered from hyperthyroidism, and it was natural that the nodules palpable in the neck were thought to be dangerous, although no symptoms of hyperthyroidism were present. Here, too, the presence of a foreign body was unsuspected.

In the next two cases lesions were presented in still another region, the lip. In the first of these, recurrent carcinoma was suspected, but the

nodule was found to be caused by a foreign body reaction to crystals. On the other hand, the presence of crystals in the second case caused a lesion to be suspected which alone would probably have been missed for some time and in this way proved to be a boon to the patient.

While the last case, one of a fistula in ano, presented no difficulty in diagnosis, it offered evidence that talc crystals in some instances may be responsible for keeping sinuses open.

Although cases of the type described are admittedly rare (5 in 30,000) the surgical lesions suggest that the indiscriminate use of talcum powder on gloves is to be avoided. Washing the gloves before entering the operative field tends to prevent such granulomas. In view of the extensive use of the dry technic, the rarity of such a complication suggests the possibility of individual variation in the reactions of patients.

The cases offer another example of the harmfulness of silicates in the human body. While rare, the lesions may be a cause of diagnostic error.

SUMMARY

Two cases have been presented of granuloma caused by anisotropic crystals shown to be talc (magnesium silicate—$3\,MgO.4SiO_2.H_2O$). Three cases have been described of similar lesions in which the crystals were morphologically similar to talc crystals. Lesions similar to those found in the foregoing cases were produced by talc in mice.

An analysis of the cases revealed the diagnostic errors caused by talc crystal granuloma under varied circumstances.

The value of examination of suspicious sections under crossed Nicol prisms is stressed.

The indiscriminate use of talcum powder in the operating room may produce granulomatous lesions.