Tissue Reactions to Injected Silicone Liquids

A Report of Three Cases

Three cases of siliconomas, two developing in the breast and one in the skin of the face, are reported. All occurred several months after liquid silicone injections for cosmetic and prosthetic purposes. Histopathological evidence is presented to show these reactions to be typical of a foreign body granuloma. Utilizing the polarized microscope the location of the crystals in tissue was determined and compared with similar preparations in the ape. One of the cases is presented with mammographic evidence of the silicone in the breast tissue. The evidence in respect to incidence and types of reactivity following silicone injections will not be known for many years. Because of this, the indiscriminate use of silicones should be avoided.

In a previous publication by Sternberg, Ashley, Winer, and Lehman \(^1\) two cases of tumors following injection of silicone mixtures were reported along with the response to subcutaneous injections of silicone liquid in an ape. It is our purpose in the present article to review briefly the cases referred to above and to report an additional case of multiple tumors in the breast following injections of a silicone liquid mixture.

Through the years there has been a continuous and exhaustive search for cosmetic materials and methods to delay or correct the changes associated with aging. Many substances, such as paraffin, petrolatum, vegetable oils, liquid petrolatum (mineral oil), hydrous wool fat (lanolin), sesame oil, and beeswax have been injected subcutaneously to remove facial wrinkles or improve the appearance of the ptotic breast. All of these materials were found to produce reactions in tissue of a common pathologic picture, namely, that of a foreign body granuloma. They were usually named according to the material which produced the tumor, such as oleoma, paraffinoma, lipid granuloma, and sclerosing lipogranuloma. These tumors occurred with such frequency as to force discontinuance of the use of these materials.\(^2\)

During recent years, a new group of substances, the liquid silicones have been used extensively in Japan, United States, Germany, and elsewhere for the correction of cosmetic defects. Some of these silicones have been pure preparations such as Medical Fluid 360 (formerly Dow Corning 200),\(^*\) while others have been “secret” mixtures containing a basic silicone liquid with the addition of other substances, such as vegetable or animal oils.

Silicones are the long-chained polymers of dimethyl siloxane and may be liquid, resin,

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or solid depending upon the length of their chain. The most commonly used of these, Medical Fluid 360, is a clear, colorless silicone fluid characterized by these properties: chemical inertness, high water repellancy, low volatility, resistance to decomposition by heat, and low surface tension. According to Kagan, some of the silicons when injected or implanted subcutaneously stimulate a local cellular hyperplasia including a mild proliferation of fibrous tissue, thereby giving the dermis and fatty layer more substance. Their present use includes reconstruction of deformities which may be congenital or secondary to surgery or trauma, removal of facial wrinkles, and breast augmentation.

**Case Reports**

**Case 1.**—A 32-year-old female was first seen in September, 1963, at which time she noted a mass in the right breast which was slowly enlarging. She stated that in March, 1961, she received silicone injections in Japan for augmentation of her breasts. The exact formula used in this patient could not be determined other than an assurance that it was a silicone liquid. On examination, there was diffuse nodularity of the right breast with a conspicuous 4 cm firm movable mass in the lower inner quadrant. The left breast was diffusely nodular, but no discrete masses were palpable.

**Histopathology.**—A section from the right breast, stained with hematoxylin and eosin, on low power examination (Fig 1) shows a degenerated anuclear stroma resembling necrobiosis of fibrous connective tissue surrounded by many irregular, oval, clear spaces or cavities. In other areas, this intervening stroma is invaded by a dense infiltrate consisting of lymphocytes, plasma cells, and histiocytes. Some of the clear spaces are lined by a single layer of nucleated cells, which are syncytial giant cells. Other clear spaces contain foreign body giant cells. The cellular infiltrate and foreign body cells surrounding clear spaces are similar to the reaction seen in a granuloma following paraffin injection.

The polarized light (Fig 2) examination reveals bright shining crystals at the site of the brownish amorphous masses within the cells lining the cavities and in the tissue stroma.

On increased magnification examination of the hematoxylin and eosin stained section (Fig 3) shows the large, brownish, dark masses within the thin cytoplasm of distorted phagocytic giant cells which surround the irregular spaces. Giant cells are seen within some of the spaces. The infiltrate in the stroma between these spaces consists of lymphocytes, plasma cells, and histiocytes.

Examination of the section with polarized light (Fig 4) shows that the brown granular masses lying in the giant cells, and in the cellular infiltrate surrounding the nonstaining cavity are bright, shining, silvery, luminous crystals and bodies.

**Case 2.**—A 35-year-old female was first seen in May, 1960, at which time he had a left hemimandibulectomy for a fibrosarcoma. This procedure left him with a typical post-mandibulectomy deformity. An iliac crest bone graft was only partially successful in correcting the defect. In March, 1962, liquid silicone with a base of Medical Fluid 360 was injected into the area, and a very satisfactory cosmetic effect was achieved. However, in June of 1962, a tumor was noted near the ramus of the mandible, dependent to the area of original injection. In February, 1963, the tumor was removed and sent to the laboratory for pathologic study.

**Histopathology.**—A section from the tumor is stained with hematoxylin and eosin. Low power examination (Fig 5) shows irregular cavities lined by distorted histiocytic giant cells. The connective tissue adjacent to these irregular spaces is of loose texture and stains very faintly. The cells lining the spaces resemble the epithelioid foreign body giant cells seen in paraffinoma.

On polarization (Fig 6), the clear spaces fluoresce brilliantly and show many silvery white bodies, such as one sees in a foreign body granuloma due to minerals. A few of these fluorescent granules are seen in the cells which line the larger irregular spaces.

Since publication of the above cases an additional instance of tumor following injection of silicone has come to our attention. The pertinent history is as follows:

**Case 3.**—A 25-year-old showgirl had injections with liquid silicone over a period of one year for augmentation of the breasts. The last injection was in December, 1963. She developed painful breasts in February, 1964. On examination there was noted diffuse painful nodules within both breasts. Roentgen mammography was then performed.

**Bilateral Mammography (Fig 7 and 8).**—The film study consists of craniocaudal and mediolateral views of each breast. Both breasts are the same in appearance. The skin and nipple shadows are normal. No normal appearing breast parenchyma is visible, and in place of it, extending to the immediate skin surface, there are numerous opacities, many of which are confluent and many of which are discrete. The discrete opacities are well margined, have a somewhat lobulated margin.
Fig 1.—Photomicrograph of hematoxylin eosin stained section of breast tumor from case 1 shows cavities lined by histiocytes and abnormal giant cells, within which are dark irregularly granular substances. In the lower right corner is a vessel surrounded by an inflammatory cellular infiltrate of lymphocytes and histiocytes. The interspaces between the cavities consist of anuclear necrobiotic connective tissue fibers. × 60.

Fig 2.—Polarization of area shown in Fig 1. The brown amorphous granules within the cells lining the cavities fluoresce. Fluorescent granules are also seen in the amorphous necrobiotic connective tissue fibers in the interspaces between the cavities and within the cellular infiltrate at the lower right.

Fig 3.—Photomicrograph of hematoxylin and eosin stained section of another field from the breast tumor of case 1. In the upper left corner is a giant cell within one of the spaces. Abnormal giant cells line some spaces between which there is an infiltrate consisting of lymphocytes, histiocytes and capillaries. × 160.

Fig 4.—Polarization of area shown in Fig 3 shows the previously dark granules in the histiocytic giant cells fluorescing silvery white. Similar shining granules are seen in the cellular infiltrate. × 160.
Fig 5.—Photomicrograph of a hematoxylin and eosin stained section from case 2 shows spaces lined by abnormal giant cells. Adjacent to the spaces are histiocytes, lymphocytes, and edematous connective tissue. X 60.

Fig 6.—Polarization of area in Fig 5 shows silvery shining granules of irregular size and shape in interspaces between the connective tissue fibers. Giant cells contain fine small fluorescent granules.

Fig 7 and 8.—X-ray of breasts.
in some regions, and vary in shape from rounded to oval to triangular. The largest of these measures approximately 1.5-2 cm in diameter. The findings are quite consistent with the injection of radiopaque material into the breast tissue without uniformity of distribution. Where the opacities are confluent, the change due to them is more or less uniform, but where the opacities are nodular, there is lack of uniformity. No other changes are noted.

Conclusion.—Bilateral mammographic opacities are shown replacing the parenchymal tissue of the breast and extending from the immediate subcutaneous region to the chest wall.

Animal Study
In a previous study by Ashley, the effect of liquid silicones on animal tissue was evaluated. Ten milliliters of Medical Fluid 360 was injected subcutaneously in an ape in eight different locations. The areas were excised at varying intervals for laboratory examination. A biopsy specimen, taken from the abdomen eight weeks after the injection, is presented for comparison with the two clinical cases studied histologically and reported above.

Histopathology.—A hematoxylin and eosin stained section shows cavities of variable size (Fig 9). Some of the cavities are lined by band-like foreign body giant cells. The stroma contains many phagocytic histiocytes and irregular masses of degenerative connective tissue. On polarization (Fig 10), shining silvery crystals are demonstrated which appear identical to those shown in Fig 2 and 4 above.

Comment
Because of previous experience, dermatologists and plastic surgeons would be the first to predict that almost any substance or combination of substances injected into the skin could, in certain prone individuals, produce tissue reactions which might progress to a true foreign body granuloma. The three cases presented in this report seem to support this premise. All three patients received silicone injections, and all three subsequently developed tumors as demonstrated by clinical, histopathological, and radiological examination. In the first two instances, study of the histological sections by polarized light revealed luminous crystals to be present in giant cells and in the cellular infiltrate surrounding nonstaining cavities.

It is of obvious importance that the mixtures used in the three human cases be identified with as great a degree of certainty as possible. In the first case, the exact content of the injected solution could not be determined other than that “a silicone liquid” was used. However, in the second and third cases the exact formula was known and was based on Medical Fluid 360 with the addition of 1% animal and vegetable fatty acids of an unknown type. In the ape, only Medical Fluid 360 was used. In the ape and in the two subjects studied histologically, the tissue reaction was similar. Using polarized light, the appearance and location of the crystals were also similar.

† Sakauri formula.
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At the present time, it is quite impossible to even hazard a guess as to the incidence of tumor formation which will result from the introduction of liquid silicone into the skin. The present three cases appeared in 18, 4, and 3 months after injection, and it is not certain whether these were due to the silicone, the additive, or the combination. In the ape the reaction was due to silicone alone. There is evidence in animals that a considerable latent period exists between implantation and tumor formation, although a shift of the injected fluid due to gravity may occur almost immediately. Oppenheimer embedded various plastic films, including silicone, into the subcutaneous tissue of rats. He found that the initial reaction was the formation of a cellular granulation tissue around the implanted material with a generalized fibroblastic activity. This reaction decreased about the fourth month after implantation. About the sixth month an increased fibroblastic proliferation was again noted adjacent to the embedded material, and this progressed to true fibrous tumor formation during the next two years. If this latent period in rats is transposable, it might be 10 to 20 years before the true incidence of tumors in humans will be determined.

Because of Oppenheimer's research and that of others, some consideration must be given to the potential occurrence of malignancies after silicone implantation. In rats Russell and Oppenheimer have observed fibrosarcomas developing in 1.7% to 40% of the test animals. These occurred from 7 months to 2.5 years after implantation. Ben-Hur and Neuman injected 3 ml of Medical Fluid 360 subcutaneously into each of 36 white mice. Two of the mice developed malignant epithelial tumors, probably of sweat gland origin. It has been demonstrated that the fibroblasts of the mesenchyme play a major role on epidermal differentiation and are also observed to proliferate after injection of silicones. One may speculate that possible alteration of the dermis by silicone and its stimulation of fibroblastic proliferation may have played some part in the production of these epithelial tumors.

While the evidence in respect to incidence and types of reactivity following injections of silicone into the subcutaneous tissues will not be completely known for many years, there seems to be sufficient evidence at this time that complications of this nature are to be expected. One of us, Ashley, has recently pointed out the many problems involved with the use of silicones and stated that at least another five years of controlled study will be necessary for even partial answers. He added that in the meantime, the indiscriminate use of silicones in plastic surgery should be avoided. While awaiting the accumulation of research data, the best advice relative to this new therapeutic procedure is from Cronin, which we quote as follows:

We regard injectable fluid silicones as still a highly experimental technique and we cannot recommend its use.

Case 3: courtesy John Pangman, MD.

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REFERENCES


Winer et al