MISCELLANEA

Beryllium Granuloma of the Skin*

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Granulomatous lesions of the skin produced by beryllium compounds were first described by Grier, Nash, and Freiman (1948), but no case occurring in this country has yet been published. As interest in the effects of exposure to beryllium has grown with the increased use of this metal during the last decade, a case of multiple beryllium granulomatosis of the skin occurring in a girl of 20 years is described.

The patient was employed in a factory making fluorescent tubes. The makers of the tubes informed us that the fluorescent powder used at the time of the injury consisted of a mixture of zinc beryllium silicate with an average beryllium content of about 8%.

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Splinters from a broken tube penetrated the hands and feet. The small wounds healed with simple treatment and it was four years later when she attended as an out-patient complaining of lumps at the sites of injury. There was no pain.

On examination there were four granulomatous nodules at the sites of injury, two of which were slightly ulcerated (Figs. 1, 2, 3, and 4). The largest of the lesions on the plantar surface of the left foot measured about 2 cm. in diameter. There was no tenderness. Radiographs of the chest and small bones of the hands showed no abnormality. A Mantoux test was negative.

The lesions were excised and she made a complete recovery.

Histology of the Lesions

The lesions involved the skin and the underlying fat tissue and showed considerable structural variety. In some sections (Fig. 5) the nodule was made up of numbers of discrete or confluent granulomata, each consisting of compact collections of mononuclear epithelioid cells surrounded by scanty lymphocytes and

FIG. 1

FIG. 2

FIG. 3

FIG. 4

FIGS. 1-4.—Granulomatous nodules of the hand and feet, and ulceration (Figs. 2 and 3).

FIG. 5

FIG. 6

FIG. 7

FIG. 8

FIG. 5.—Lesion on the hand showing a sarcoid-like granuloma $\times 38$.

FIG. 6.—Sarcoid-like granuloma from lesion of foot $\times 70$.

FIG. 7.—Extensive caseation: one foreign body with adjacent giant cell is present in the outer rim of a granuloma, another near the centre of a caseous focus $\times 47$.

FIG. 8.—Same as Fig. 7, showing the granular foreign body lying in an empty space $\times 260$.

including a very few giant cells of either Langhans or the foreign-body cell type. There was considerable condensation of the areolar tissue separating single or groups of granulomata, a very few of which showed a mild degree of central caseation. This picture (Fig. 6) is indistinguishable from a typical sarcoid lesion. In other lesions, in addition to these changes, there was extensive caseation of confluent granulomata (Fig. 7). Conchoidal bodies were not found in any of the slides. The epidermis over the different nodules showed various degrees of atrophy, ulceration, or hyperkeratosis. Serial sections failed to show foreign bodies in most of the examined material, but in one of the lesions which had not ulcerated small granules of refractile but polariscopically inert material were found within the necrotic zone and also at the periphery of a granuloma (Figs. 7 and 8). Sections were stained by Denz's (1949) naphthochrome G method to detect beryllium histochemically. Negative results were obtained in material void of foreign bodies, but in sections containing the refractile granules there was a faint but diffuse positive histochemical reaction. In one area, where the granules had been lifted out in the cutting, a narrow, greenish rim surrounded the hole.

Spectrographic examination of the material for the presence of beryllium gave negative results. As cases have been reported in the literature of sarcoid-like lesions in the skin following road accidents which have been attributed to the presence of silica in the road dust, the biopsy specimens were also examined spectrographically for silica. All portions of the samples contained silica in low concentration but the silica content of normal and abnormal tissue did not vary appreciably.

Finally, in order to determine the nature of the granular material, sections were incinerated at 500° C. It was found that the material was still present after exposure to heat. Treatment with hydrochloric acid after incineration resulted in the particulate matter disappearing.

Review of the Literature

VanOrdstrand, Hughes, DeNardi, and Carmody (1945) in describing toxic manifestations resulting from exposure to beryllium mentioned one patient who developed a chronic skin ulcer from traumatic implantation of beryllium. Chronic lesions in the skin, cut with broken fluorescent lamps coated with beryllium containing phosphor, are described by Grier and others (1948) and compared with identical cutaneous manifestations in two patients suffering from pulmonary beryllium granulomatosis. Beryllium was demonstrated spectrographically in one of these lesions. Coakley, Shapiro, and Robertson (1949) describe a beryllium granuloma of the skin occurring in a boy of 16 years, two years after injury to the face by a broken fluorescent bulb. Gerrie, Kennedy, and Richardson (1950) report a similar case after injury to the forehead, and Ormsby and Ebert (1950) a granulomatous lesion following an accidental cut of the finger by a broken fluorescent bulb. The other toxic manifestations of beryllium have been reviewed by Vorwald (1950) and Hardy (1951).

Experimental Beryllium Poisoning

Gardner and his successor Vorwald (1950) at the Trudeau Foundation tested various beryllium compounds on a number of animal species by intravenous, intraperitoneal, subcutaneous, and intratracheal injections and obtained tissue reactions in no way comparable to the human lesion. Neither did inhalation experiments with fluorescent powders reproduce the type of human tissue reactions. It was found, however, that some of the injected beryllium compounds proved highly toxic even in small amounts. Aldridge, Barnes, and Denz (1949) studied the effects of a large number of beryllium compounds injected intravenously and subcutaneously into rats and mice. They concluded that beryllium ions have the property of reacting rapidly with tissue protein to form a stable beryllium protein complex which still retains the toxicity of the beryllium. This would explain the localized tissue reaction following implantation or inhalation of beryllium salts. Stokinger, Ashenburg, DeVoldre, Scott, and Smith (1950) using beryllium sulphate mist in inhalation experiments were able to produce pulmonary lesions resembling those of acute pneumonitis of beryllium workers, but did not obtain tissue reactions comparable with the granulomatous type. They further showed by alternating daily exposures to beryllium sulphate mist and hydrogen fluoride vapour that fluoride enhanced the toxicity of the inhaled beryllium. The same group of workers, Hall, Scott, Laskin, Stroud, and Stokinger (1950) investigated by inhalation experiments the action by four grades of beryllium oxide dust varying in particle size and state of aggregation. They found that the smaller the particle size and the lesser the degree of aggregation the greater was the injury to the lungs. On the basis of these findings Dutra (1951) produced granulomata in pigs after implantation into the cutis and the subcutaneous fat tissue of fluorescent powders containing zinc oxide, beryllium oxide, and silica in equal molecular ratio and of average particle size of 1.5 and 3.0 microns respectively. The author failed, however, to produce granulomata with metallic beryllium or beryllium oxide alone. It is interesting to compare these results with the experiments of Lloyd Davies and Harding (1950) who produced cellular pulmonary granulomata after intratracheal injection into rats of a mixture of beryllium oxide and manganese dioxide. Davies and Harding concluded that granulomata may form only when the action of the beryllium is reinforced by some other agent or agents provoking histiocytic proliferation.

Conclusion

Sarcoid-like skin lesions following implantation into the skin of fragments of broken fluorescent bulbs, histologically identical or similar to pulmonary changes found in chronic pneumonitis of workers engaged in the beryllium industry, have been attributed to the beryllium in the coating of these lamps. In our case multiple injuries caused by particles from a broken tube, coated with a fluorescent powder containing zinc beryllium silicate, resulted in the formation of typical granulomatous lesions. Histochemical examination of the

affected tissue indicated beryllium as present in traces. Spectrographic analysis by a method capable of detecting one part of beryllium in one hundred million (10^8) parts of tissue failed to demonstrate it. Results of incineration were inconclusive. Silicon was present in identically low concentrations in normal and granulomatous portions of the skin and it is thought that this amount could easily be due to pick-up from storage of the specimens in glass containers.

The negative results of chemical analysis are inconclusive since it is probable that the chemical substance implanted into the skin has disappeared in the interval of four years following the trauma.

Summary

A case is described of multiple granulomatous skin lesions resembling Boeck's sarcoid following traumatic implantation of fragments of a broken fluorescent bulb coated with zinc beryllium silicate.

Histochemical and spectrographic examination failed to prove that beryllium was the causative agent.

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