

AN EXOGENOUS VARIETY OF PSEUDOXANTHOMA ELASTICUM IN OLD FARMERS

Ole B. Christensen

Department of Dermatology, General Hospital, University of Lund, Malmö, Sweden

Abstract. Cutaneous lesions clinically similar to and histopathologically indistinguishable from pseudoxanthoma elasticum have been observed in the cubital folds of nine elderly farmers. In all cases the skin lesions were ascribed to exposure to salpeter during fertilization on a single occasion decades previously. Signs of systemic pseudoxanthoma elasticum were absent.

Key words: Pseudoxanthoma elasticum; Salpeter; Fertilizer; Elastica degeneration; Calcinosis cutis

Pseudoxanthoma elasticum (PXE) is known to be a genetically determined disorder of connective tissue, involving the cardiovascular system, the eyes and the skin. The disease usually makes its début before the age of 30. The clinical skin findings include yellowish papules and often confluent plaques located in the flexural folds. The histopathological picture is typical, with degenerate, fragmented and swollen elastic fibres with calcium deposition located in the mid-dermis. The pathogenesis of PXE is unknown. This paper described cutaneous lesions clinically similar and histopathologically indistinguishable from PXE, but apparently of exogenous origin.

MATERIAL AND METHODS

During 1975 nine male patients with similar skin lesions in the cubital folds were observed. The patients were referred to the surgical and internal medicine departments at the hospital in Trelleborg, Sweden, with the following diseases: hernia, hemorrhoids, cholecystitis, asthma bronchiale, diabetes mellitus, hypertension, arthrosis. All patients were or had been farmers. Mean age was 69 years (52-87). A clinical examination, with special reference to skin lesions in other flexural folds, was carried out. Five patients were examined by an ophthalmologist. Sections from punch biopsies were stained with hematoxylin-eosin, orcein and according to von Kossa's method in 6 patients. The patient submitted to the hospital with arthrosis died 3 weeks later, of metastatic osteosarcoma. At the autopsy arcus aortae was secured for histopathological investigation. P-cholesterol and P-triglycerides were estimated in 7 patients.

RESULTS

All patients ascribed their skin lesions to exposure to salpeter in the same way. Here is an example of the history: "Many years ago while fertilizing, I spread Norwegian hydrous salpeter with my hands. The weather was slightly rainy or foggy. My shirt sleeves were rolled up over the elbow. After spreading for some hours I felt a burning skin sensation on the forearm and soon a superficial ulcer was formed. The ulcers were healed after 2-3 weeks, and after healing the skin lesions have been unchanged." The skin lesions were provoked on a single occasion only, decades before the present study. For 7 patients the exposure took place in the 1930's, for one patient in the late 1920's, and for the last patient, in the 1940's. Thus, the skin lesions had been stationary for 30-50 years.

In 7 patients the lesions were located in the right cubital fold, in 2 patients the lesions were symmetrical. The lesions consisted of yellow-white plaques measuring 0.5-1.5 cm² and pinhead-size papules (Fig. 1). Mostly, the margin of the plaques was thread-like, but sometimes the margin crossed the plaque in different directions, giving the surface a reticulate pattern. The centre of the plaque was slightly atrophic. The number of plaques varied from a single one in one patient to seven plaques in another patient, but most frequently 4-5 plaques were seen in each patient. In 7 patients a more or less pronounced actinic elastosis of the face and neck was observed. Otherwise no skin lesions were observed, certainly no PXE-like lesions in the flexural folds. No signs of angioid streaks were seen. Clinically, the lesions were similar to PXE or flat xanthoma plaques. The patient with diabetes mellitus had a moderately elevated P-cholesterol level; otherwise P-lipids were normal.

The same histopathological picture was seen in all cases studied. The epidermis was slightly atrophic. Orcein-stained biopsies showed numerous



Fig. 1. Sharply demarcated plaques and small papules in the cubital folds.



Fig. 2. Short, swollen, fragmented elastic fibres in the mid-dermis (orcein stain, $\times 260$).

short, swollen, fragmented, ravelled elastic fibres in the mid-dermis (Fig. 2). Von Kossa's stain showed uptake of dense, black-coloured material inside the degenerated elastic fibres (Fig. 3). Light microscopic examination of arcus aortae (from the patient who died) showed slight arteriosclerotic changes, but no sign of elastic fibre degeneration as in PXE.

Norwegian hydrous salpeter is a composition of $\text{Ca}(\text{NO}_3)_2 \cdot 2\text{H}_2\text{O}$, $\text{Ca}(\text{NO}_3)_2$ and the double salt $5\text{Ca}(\text{NO}_3)_2 \cdot \text{NH}_4\text{NO}_3 \cdot 10\text{H}_2\text{O}$ with 78% $\text{Ca}(\text{NO}_3)_2$, 6% NH_4NO_3 and 15% H_2O . The chemical composition 30–50 years ago is principally the same today (4).

DISCUSSION

The clinical picture, with yellow-white papules and plaques located in the cubital folds, was very similar to PXE. Also, the histopathological picture was identical with PXE. However, the thread-like margin seen in several patients does not occur in PXE, and this may be an important differential diagnostic detail. Furthermore, skin lesions in other flexural folds or angioid streaks, as existing in PXE, were not observed in the patients. Seven patients had actinic elastosis in sun-exposed areas but not, however, in the cubital folds. Actinic elastosis is often seen in elderly farmers and is not connected with PXE. The story told by all 9 patients convincingly speaks in favour of a causal relationship between the lesions and exposure to salpeter.

Apparently, this is the first description of a variety of PXE, that should be classified as an exogenous PXE. Dermatologists probably have not

seen these patients with exogenous PXE, as the patients are very well aware of the cause of the eruptions. A farmer would not even think of turning to a dermatologist on account of such harmless eruptions. On the other hand, internists may have observed the eruptions when testing the blood pressure of their patients, but have not recognized the similarity to PXE. In fact, I observed the first patient when testing the blood pressure.

Seven patients had skin lesions only in their right cubital fold, but 2 patients had symmetrical lesions. These 2 patients were able to spread salpeter with both hands, which fact seems to explain how the lesions were induced. Mechanical friction of a wet, stiff shirt edge induces stratum corneum injury and traumatic inflammation. The hygroscopic and thus adhesive quality of salpeter makes the salpeter grains react more intensely on injured skin. The salpeter has a mordant effect, and this is probably

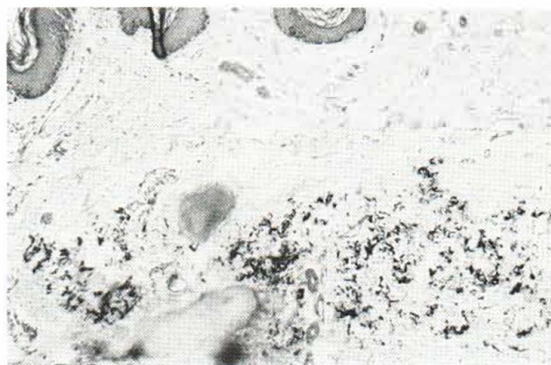


Fig. 3. Short, black coloured fragmented material in the dermis (von Kossa's stain, $\times 42$).

much stronger on an injured skin. When a superficial ulcer is formed an osmotic effect of the salpeter ions may be involved in provoking the clinical and histopathological picture described.

However, it is suprising that an industrially produced fertilizer such as Norwegian hydrous salpeter can induce eruptions clinically very similar and light microscopically indistinguishable from PXE. The strongly positive von Kossa's staining observed in all 6 patients so studied is probably an expression of the presence of calcium salts. The salts are obviously located inside the elastic fibres. Theoretically, it would be interesting to know whether the calcium salts derive from the salpeter, or from an endogenous calcium deposition. Seley (5), Bridges (1) and Gabbiani (2) have been able to induce cutaneous calcinosis in different species, either by subcutaneous injection of "direct challengers" or after sensitization by a systemic calcifying factor (Vitamin D compounds, parathyroid hormones) followed by subcutaneous injections of "indirect challengers". A variety of organic and inorganic chemical compositions have been tested, but not calcium nitrate or ammonium nitrate, which are present in the salpeter spread by the patients. Histologically, cutaneous calcinosis in different species affects all connective tissue fibres, and not merely the elastic fibres, as in PXE and the present disease. Seley (5) assumes that the challenging agents act somewhat like mordants in preparing tissues for the uptake of calcium. Hass (3) states that calcium has a stronger affinity to injured elastic fibres than to normal ones.

One question to be raised is whether all human beings are able to develop "exogenous PXE" on contact with salpeter ($\text{Ca}(\text{NO}_3)_2\text{NH}_4\text{NO}_3$), or whether some latent PXE may need to exist before the lesions can develop. To differentiate the present disease from true PXE further investigations (ultramicroscopical, histochemical, etc.) are needed. If such investigations cannot differentiate the two cutaneous disorders, induction with calcium nitrate and ammonium nitrate may be a possible model for pathogenetic studies on PXE.

REFERENCES

1. Bridges, J. B. & McClure, J.: Experimental calcification in a number of species. *Calc Tiss Res* 10: 136, 1972.
2. Gabbiani, G., Badonnel, M. C. & Baud, C. A.: Relationship between iron, calcium and phosphate during experimental cutaneous calcinosis. *Calc Tiss Res* 4: 224, 1969.
3. Hass, G. M.: General reviews, elastic tissue. *Arch Pathol* 27: 33, 1939.
4. Norsk Hydro A. S., Oslo, Norway: Personal communication, 1976.
5. Seley, H.: *Calciphylaxis*. Chicago University Press, Chicago, 1962.

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O. B. Christensen, M.D.
Department of Dermatology
General Hospital
S-21401 Malmö
Sweden