SENILE OSTEOPOROSIS AND COLLAGEN LOSS IN SKIN

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SYNOPSIS

Skin biopsies were taken from the dorsum of the hand of patients with osteoporosis. The area of the amount of dermal collagen present was assessed by a histological method and compared with that of non-osteoporotic controls. Distinct morphological abnormalities of the dermal collagen fibres could be observed in some patients with severe grades of osteoporosis. Similar changes were not seen in the controls. A positive correlation was established between collagen loss in skin and osteoporosis, although a linear correlation was not found.

INTRODUCTION

McConkey, et al (1963) found that people with transparent skin were more likely to have osteoporosis. By measurement of the hydroxyproline content of skin, Black and associates (1970) showed that total skin collagen was decreased in patients with untreated osteoporosis.

The present study was undertaken to determine if a correlation exists between the degree of osteoporosis and the extent of collagen loss in skin.

MATERIAL AND METHODS

Forty-five patients of both sexes were studied. Their ages ranged from 55 to 81 years. Twenty-three patients had clinical "senile" osteoporosis. The diagnosis was based on radiological changes and the findings of a normal serum concentration of calcium, inorganic phosphate and alkaline phosphatase. These patients were admitted to hospital with fracture of the neck of femur following minor trauma or with severe backache due to osteoporosis. The other twenty-two patients formed the control group. Their ages ranged from 45 to 78 years. They had no radiological evidence of osteoporosis and were admitted with unrelated orthopaedic complaints.

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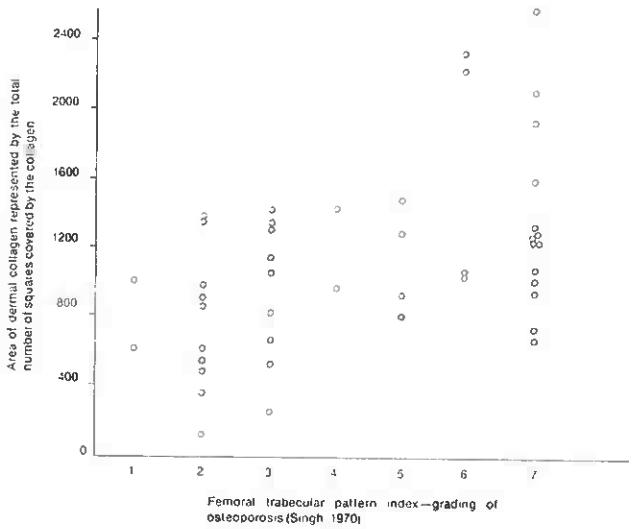

Fig. 1. Shows the relationship of the area of dermal skin collagen to the radiological grade of the femoral trabecular pattern of forty-five patients.

Fig. 2. Photomicrograph of the skin of an 80 year old female, osteoporotic patient who presented with fracture of the femoral neck and a radiological femoral pattern index of grade 2 osteoporosis (van Gieson stain, magnification X125).

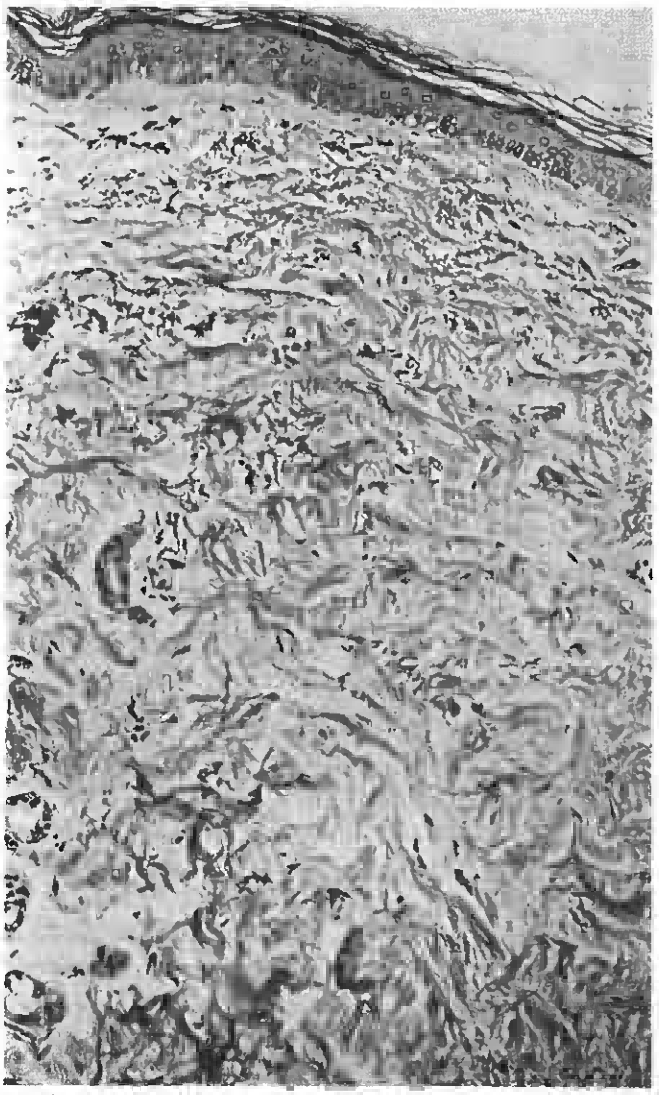

Fig. 3. Photomicrograph of normal skin from a 79 year old female who presented with spondylosis. She had a radiological femoral trabecular pattern index of grade 6, no osteoporosis (van Gieson stain, magnification X125).

The lumbar spine and both the hips were examined radiologically and the serum levels of calcium, inorganic phosphate and alkaline phosphatase were done in all patients. Full thickness skin biopsies were taken from the dorsum of the right hand over the fourth metacarpal. Five to six micron sections were stained with the hematoxylin-oesin and the van Gieson stains. The following values were measured with a scaled eyepiece through a microscope:—

(i) thickness of the epidermis,
(ii) thickness of the dermis up to the level of the sweat glands,
(iii) thickness of the individual collagen fibres in the deep dermis.

These measurements were made at ten different points in each section of skin and the mean value determined.

Photomicrographs of the van Gieson stained sections of skin were taken at a magnification of X125. Their images were projected at a fixed magnification and traced out on graph paper. In a constant width of skin, the area of the amount of collagen present were represented by the total number of squares covered by the collagen fibres.

Radiological diagnosis of osteoporosis and grading was based on the trabecular pattern of the upper end of the femur according to the method established by Singh et al (1970). By their criteria of assessment, persons with a femoral trabecular pattern index of grade 4 or lower had a pathological degree of bone loss, whereas those with grades 5 to 7 were considered to be normal.

RESULTS

The relationship of the amount of collagen in a constant area of skin to the radiological grade of osteoporosis is shown in Fig. 1. The difference in the amount of collagen between the patients with clinically osteoporosis and the controls was statistically significant ($p = 0.010$). There was, however, no significant linear correlation between the collagen present in skin and the radiological grade of osteoporosis ($p = 0.05$). Skin sections which showed severe loss of collagen were easily identified by microscopic examination. Such loss of collagen in skin consistently came from patients with severe grades of osteoporosis. Many osteoporotic patients, however, had normal amounts of skin collagen.

In comparing the thickness of the dermis (up to the level of sweat glands) in the osteoporotic patients and the controls, no statistical difference was found. The mean thickness of dermis in the osteoporotic individuals was 529 microns (range 400 to 1,200 microns) and the value in the normal group was 656 microns (range 420 to 1,080 microns). Similarly, when the thickness of the deep dermal collagen fibres was compared, no significant difference could be found. The osteoporotic patients had collagen fibres with average thickness of 5.67 microns (range 1.8 to 9.8 microns) and in the controls the thickness was 5.84 microns (range 1.8 to 9.6 microns). None of the controls had evidence of osteoporosis and their radiological indices fell between grade 5 and 7.

HISTOLOGY

Severe collagen loss was readily identified microscopically. In these cases, the skin showed a thinning of the dermis, Fig. 2. The collagen fibres stained less intensely pink with the hematoxylin-eosin stain and had an orange-yellow colour with the van Gieson stain. The individual fibres were thin and fragmented, running in short and loose strands as opposed to the coarse, closely-packed fibres of normal skin which stained an intense pink with eosin and a bright red with the van Gieson stain, Fig. 3. It was, however, not possible to make out significant microscopic differences in specimens showing intermediate degrees of collagen loss; neither were consistent abnormalities noted in the epidermis of the osteoporotic patients. The epidermis showed a variable amount of keratinisation which did not differ from that of the control group.

DISCUSSION

Like bone, the primary structural protein of skin is collagen. It has been suggested that "studies of the absolute collagen content of skin may help to clarify our views on collagenolytic diseases such as osteoporosis" (Shuster and Bottoms, 1963); however, only a few reports are available on the subject. Based on their initial observations that the skin of osteoporotic patients was transparent, McConkey et al (1967) demonstrated that the collagen content of transparent skin was only about half that of normal skin. They also found that the rate of biosynthesis of protein, estimated by incorporation of ^{14}C-proline into skin in vitro was at least as active, if not more active, than in normal skin. They suggested that their observations could result from a failure of maturation of the collagen fibres. The abnormal fibres would be metabolically more active and subject to a greater turnover accounting for the increased rate of biosynthesis.

By measuring the hydroxyproline content of skin biopsies, Black and associates (1970) were able to demonstrate an actual decrease of the total skin collagen in untreated patients with osteoporosis. Our results lend further support to their findings.

It has been shown that skin collagen decreases with age (Shuster and Bottoms, 1963). The incidence of osteoporosis increases with age (Gitman and Kamholtz, 1965) suggesting that age may be a common denominator accounting for the positive correlation between loss of skin collagen and osteoporosis. All our patients with microscopically indentifiable collagen loss in skin had osteoporosis. However, not all patients who had clinical osteoporosis showed significant deple-

tion of dermal collagen by our method of assessment. Osteoporosis, representing collagen loss in bone appears therefore to precede collagen loss in skin. Although a positive correlation exists between collagen loss in skin and osteoporosis, the severity of loss does not run parallel.

REFERENCES

1. Black, M.M., Shuster, S. and Bottoms, E.: Osteoporosis, skin collagen and androgen. Brit. Med. J., 4: 773-774, 1970.
2. Gitman, L. and Kamholtz, T.: Incidence of radiographic osteoporosis in a large series of aged individuals. J. Gerontol., 20: 32-35, 1965.
3. McConkey, B., Fraser, G.M., Bligh, A.S. and Whiteley, H.: Transparent skin and osteoporosis. Lancet, 1: 693-695, 1963.
4. McConkey, B., Walton, K.W., Carley, S.A., Lawrence, J.C. and Ricketts, C.R.: Significance of the occurrence of transparent skin. A study of histological characteristics and biosynthesis of dermal collagen. Ann. Rheum. Dis., 26: 219-224, 1967.
5. Shuster, S. and Bottoms, E.: Senile degeneration of skin collagen. Clin. Sci., 25: 487-491, 1963.
6. Singh, M., Nagrath, A.R. and Maini, P.S.: Changes in trabecular pattern of the upper end of the femur as an index of osteoporosis. J. Bone Joint Surg. (Am)., 52: 457-467, 1970.