Superficial Changes in Skin of Pressure Sores: Clinical and Experimental Study

Toshiaki Takeda

Department of Fundamental Nursing, Faculty of Nursing, Iwate Prefectural University

Abstract

The response of superficial skin to compression pressure is not yet fully understood. Histologic study of superficial changes is important for understanding the initial histogenesis of pressure sores (PS). Therefore, superficial changes in slight PS were investigated histologically in human cases as well as in experimental animals. The characteristic histologic changes in the epidermis of human PS at the early stage were hyperkeratosis, perinuclear vacuolization, and random arrangement of cells. Also, cell infiltrates as well as hydropic degeneration were occasionally seen in the epidermis. At a more advanced stage, necrosis of the epidermis was recognized, and thick collagen fibers were present in the dermis. Superficial changes in PS were produced experimentally in rabbits whose skin was exposed to a balloon-produced compressive force of 120±10 mmHg for 3 hours. Biopsies were taken at 24 hours after pressure application. The histologic changes in rabbits closely resembled those in humans, thus confirming that this experimental balloon-induced pressure model of PS is a useful one for studying the histogenesis of the early stages of PS.

Key Words: pressure sore; skin; histopathology

Running Title: Superficial Changes in Skin of Pressure Sores

要旨

加圧による皮膚表層の変化に関する研究は少なく、いまだその詳細は不明である。褥瘡は加圧に起因する皮膚病変であることから、初期変化を理解するためには、圧迫による皮膚表層の変化を組織病理学的に明らかにする必要がある。そこで本研究においては、ﾋﾄの軽度な褥瘡および実験動物に作製した軽度な褥瘡を用い、皮膚表層の変化について組織病理学的に検索した。その結果、ﾋﾄ褥瘡の表皮層に認められた特徴的な初期変化は、角質増生、表皮細胞の核周囲空胞化、表皮細胞配列の不規則化であった。またこの時期には、表皮層に炎症性細胞浸潤および表皮細胞の空胞変性も散見された。さらに障害の程度が進行した部位では、表皮細胞の壊死および真皮層における膠原線維の肥厚が認められた。実験的研究においては、新規に開発したﾊﾞﾙｰﾝ加圧装置を用い 120±10 mmHg の圧力をｳｻｷﾞの皮膚に 3 時間持続加圧することによって軽度な褥瘡を作製した。ｳｻｷﾞの加圧部皮膚に認められた病巣の組織変化は、ﾋﾄの軽度な褥瘡と類似していたことより、ﾊﾞﾙｰﾝ加圧による動物ﾓﾃﾞﾙは、褥瘡の初期発生機序の解明に有用であると考えられた。

Introduction

The skin necrosis that usually occurs over a bony prominence as a result of ischemia has long been known as pressure sores (PS), or decubitus ulcers. PS are a serious problem in elderly bedridden patients with chronic diseases or in patients with spinal cordinjury[1)-3)]. For investigation of the etiology of PS, experimental studies have been performed with several kinds of animals[4)-9)]. These studies focused mainly on the deep-tissue histologic changes, especially the muscle lesions induced by compression. Although 70-90% of PS are superficial [10)-11)], little is known about the superficial histologic changes. The response of superficial skin, especially the epidermis, to compression pressure is poorly understood. Destruction of the epidermis readily leads to bacterial infection of the PS, and bacterial invasion of ischemic tissues increases the destructive effect and rapidity with which an ulcer develops[12)]. Thus, histologic study of superficial changes is clearly important in order to gain a better understanding of the histogenesis of PS.

We have developed a system of balloon compression for studying the superficial changes in PS. Using this system we investigated in detail the histologic changes, especially those in epidermal cells, in PS produced in rabbits. These changes were then compared with those found in human cases.

Materials and Methods

1. Human cases

Thirty-seven samples of PS from 21 patients (14 males, 7 females) were obtained at autopsy. The ages at death ranged from 22 years to 82 years with an average age of 65 years. These lesions were macroscopically detected as slight erythema, erythema with edema, and erosion. The PS specimens including the surrounding normal skin were fixed in neutral 10% formalin, embedded in paraffin, and then sectioned with a microtome. Light microscopic investigation was carried out after hematoxylin and phloxin-tartrazine (H&P-T) staining.

2. Experimental animals

Male Japanese white rabbits (Kitayama Labes Co., Ltd., Nagano) weighing 2800～3700 g were used. Prior to the application of pressure, the back of each animal was closely clipped, depilated with a depilatory agent (DIVELE®, Shiseido Co., Ltd., Osaka), rinsed very carefully with water, and dried. Twenty-four hours later, each rabbit was given an intraperitoneal injection of pentobarbital sodium (Nembutal® Abbott Lab, USA) at an initial dose of 100 mg per animal. Additional pentobarbital sodium was given intravenously as needed for the duration of the experiment. Immediately thereafter, a metal cylinder containing a Latex balloon (20 mm in diameter, 0.4 mm thick) was attached gently to the surface of the skin over the flat portion of the ilium (ala ossis ilium) after the animal had been placed in lateral recumbency (Fig.1). A pressure of 120±10 mmHg was applied for a period 3 hours to the iliac skin of seven rabbits by a compressor (OFP-02B, Anest Iwata Co., Ltd., Tokyo). The animals were anesthetized

during the application of pressure. The intensity of pressure on the skin was measured by a pressure sensor (MR-05k, Showa Measuring Instruments Co., Ltd., Tokyo), and pressure in the balloon was monitored during compression by a recording system (SP-K4V, Riken Denshi Co., Ltd., Tokyo). Twenty-four hours after the release of pressure, the skin of the lesion was biopsied so that the specimen contained both normal skin and affected skin. The specimens were fixed in neutral 10% formalin, embedded in paraffin, and then sectioned with a microtome. Light microscopic examination was conducted after H&P-T staining. The animals used in this study were maintained and used in accordance with recommendations in the Guidelines for Animal Experimentation (prepared by the Japanese Association for Laboratory Animal Science,1987).

Results

1. Human cases

The initial changes seen in the human epidermis were hyperkeratosis, perinuclear vacuolization, and random arrangement of cells (Fig.2a). Also, cell infiltrates and hydropic degeneration were occasionally seen in the epidermis at this stage. Following these changes, necrosis of granular cells as well as severe hydropic degeneration of prickle cells was noted(Fig.2b). Also, a few sections revealed detachment of part of the epidermis from the lower epidermal layer. However, the deep parts of the epidermis, particularly the basal cells, remained viable. At a more advanced stage, necrosis of the epidermis was recognized. Thick

collagen fibers were present in the dermis (Fig.2c).

2. Experimental animals

Immediately after the release of pressure, the skin in the compressed area appeared paler than the surrounding skin. A few minutes later, a slightly red area was seen at the compression site; however, by 24 hours, the site was indistingishable from the intact areas.

Histologically, perinuclear vacuolization, a random cell arrangement, and cell infiltrates were recognized in the epidermis (Fig.3a). Polymorphonuclear leukocyte (PMN) infiltration under the epidermis was evident in a wide area. Also, hydropic degeneration in the epidermis was evident (Fig.3b). A crust containing PMNs was occasionally recognized on the epidermis. In more advanced lesions, disruption or necrosis of prickle cells was recognized in animals of lower body weight (Fig.3c). As in the human specimens, thick collagen fibers were also evident in the dermis.

Discussion

As the skin of rabbits is covered with long hair, the superficial changes in PS cannot be detected macroscopically unless the hair is removed. In this experimental study, therefore, prior to the application of pressure, the back of each animal was closely clipped and then depilated with a depilatory agent. The surface of rabbit skin closely resembles that of human skin. Accordingly, superficial changes in skin such as ischemic skin reactions were easily recognizable grossly, as in human cases. In a preliminary study, we ascertained that there were no

inflammatory changes in the depilated skin at 24 hours after depilation.

Up to now, the skin over bony prominences has been used for the site of application of pressure in experimental studies of PS. As examples, the following studies may be cited: Kosiak[5] applied constant pressure to the trochanter as well as the ischial tuberosity in dogs. Dinsdale[13] used the posterior superior iliac spines as the site of application of pressure to pigs. Daniel et al.[8] employed the greater femoral trochanter of pigs. In these studies, hard materials were used for application of pressure to the skin surface. Consequently, deep-tissue histologic changes, especially muscle lesions, were easily produced. Thus histologic changes in muscle and the duration of pressure time needed to produce muscle lesions have been well investigated. However, little is known about changes in the superficial skin of PS, especially epidermal lesions.

The epidermis is the tissue that protects the body from the effects of external agents, and its destruction is clearly a serious problem with respect to bacterial invasion into the body. One region where PS often occur is the ischial tuberosity and sacral area[14)-17)], and infection can arise there due to contact of damaged skin with feces and/or urine. Infecting bacteria tend to become localized in ischemic tissues, which provide a good medium for their growth. Bacterial invasion of ischemic tissues increases the destructive effect and rapidity with which an ulcer develops, and also inhibits the healing process[18)-19)]. As a patient's defense mechanism against infection is usually weakened, an infection can affect the body's general condition even when it is localized.

Therefore, it is very important to understand the mechanism of destruction of the epidermis that operates during the formation of infected PS lesions.

In this experimental study, the flat portion of the iliac bone (ala ossis ilium) of rabbits was chosen as the site of pressure application instead of a bony prominence. Consequently, we were able to maintain a constant pressure on the skin. It was also possible to apply a low pressure to the skin surface in our animal model, and a soft material (latex balloon) was used to make contact with the skin surface. With the use of this technique, several types of epidermal lesions were produced successfully. The experimental study revealed that the superficial histologic changes in skin at the early stage were perinuclear vacuolization and random arrangement of epidermal cells, as well as cell infiltration into the epidermis. Also, hydropic degeneration of epidermis and PMN infiltration under the epidermis were evident. In the more advanced lesions, disruption or necrosis of prickle cells was recognized. Thick collagen fibers were also present in the dermis. The severity of these lesions appeared to depend on the body weight of the animals: more severe lesions were occasionally recognized in animals of lower body weight. This tendency supports the findings of Williams' clinical study that thin individuals are more likely to develop PS[20]. Comparison between humans and experimental animals with PS showed that the histologic changes were quite similar in the two groups. Therefore, this experimental model is a useful one for the study of human epidermal

cell lesions induced by compression.

The migration of inflammatory cells into the epidermis was called “exocytosis” by Wolff [21]. He reported that increased invasion of foreign cells results in metabolic disturbances of the epidermal cells that are recognizable electron microscopically by the accumulation of glycogen and lipid droplets, intracellular edema, an increase in the number of lysosomal elements, and/or focal cytoplasmic degradation. Also, it is known that epidermal cells are able to withstand a prolonged absence of oxygen both *in vivo* and *in vitro* [22]. Considering these facts, therefore, we consider that the initial epidermal cell degeneration occurs not only through ischemia but also exocytosis.

It is known that any damage to the skin is associated with activation and possibly the release of epidermal enzymes. Among the enzymes that may contribute to inflammation are neutral proteinase and cathepsin B [23]. The neutral proteinase could be released as a consequence of epidermal cell damage, and the enzyme might generate chemotactic factors [24]. In PS specimens showing initial changes, cell infiltration was recognized in the epidermis. Diffuse eosinophilia of the epidermis was also noted as an initial sign in another study of human cases[25], as well as in another experimental study[7]. The cell infiltration within the epidermis may be induced by the above chemotactic factors. To substantiate this possibility, we are now conducting on immunohistochemical investigation of the mechanism of PMN infiltration at the early stage of PS.

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Fig.1. a: Metal holder containing the pressure sensor and balloon for compression of rabbit skin. b: Schema of experimental apparatus:
A, pressure sensor; B, latex balloon; C, balloon holder; D, ilium of rabbit; E, regulator.

Fig.2. Human cases. (a) Hyperkeratosis, perinuclear vacuolization, and random arrangement of epidermal cells are evident. Arrow points to infiltrating cells. (b) Necrosis of granular cells and hydropic degeneration of prickle cells. (c) Necrosis of the epidermis. Thick collagen fibers are also evident in the dermis (H&P-T).

Fig.3. Animal cases. (a) Perinuclear vacuolization and random arrangement of epidermal cells. PMN infiltration is also evident in the epidermis. (b) Hydropic degeneration of the epidermis. (c) Necrosis of prickle cells (H&P-T).