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Aesthetic Plastic Surgery

A New Experimental Hypertrophic Scar Model in Guinea Pigs

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Abstract. Many aspects of the biology and effective therapy of proliferative scars remain undefined, in part due to a lack of an accurate, practical, reproducible, and economical animal model for systematically studying hypertrophic scars. This study was designed to investigate whether hypertrophic scar formation could be induced in guinea pigs by removal of the panniculus carnosus alone, and by a combination of the removal of the panniculus carnosus with application of coal tar afterwards. Whole thickness skin excision or deep partial thickness injury was used to create the lesions on intact skin. Different anatomic locations were tested in different groups. Scars thus developed were examined morphologically by light microscopy and electron microscopy (TEM and SEM) and biochemically by measuring the activity of glucose-6-phosphate dehydrogenase (G6PD) to check whether these scars had morphological and biochemical properties specific to hypertrophic scars. The albino guinea pigs used in this study were divided into three groups. Removal of the panniculus carnosus was performed from the ventral aspect of the torso in animals in groups I and II. On the skin overlying the area of panniculectomy, circular skin excision was performed in group I, and deep partial thickness burn injury was inflicted in group II, to see whether wounds would heal with hypertrophic scars. In group III, dorsal aspect of the torso were used and wounds were produced by circular skin excisions followed by panniculectomy on both sides but coal tar was applied to only one side. Tissue samples were taken from the scars that were hypertrophic in appearance, and from normal scars and normal skin for comparison. Light and electron microscopic examinations and G6PD activity measurements were performed on these samples. While hypertrophic scar development was not seen in group I and group II, scars with morphological and biochemical properties specific to hypertrophic scars developed in one third of animals in group III after healing of the wounds treated with coal tar.

In conclusion, it is shown that it is possible to develop experimental hypertrophic scars in guinea pigs with morphological and biochemical properties similar to those of human proliferative scars. Therefore this model is a new, practical, and economical experimental animal model to study proliferative scars, although improvements are needed to increase yield.

Key words: Panniculectomy—Coal tar—Light microscopy—Electron microscopy—Glucose-6-phosphate dehydrogenase

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Introduction

Hypertrophic scars and keloids resulting from excessive connective tissue formation to a pathological degree following the wound healing process are challenging problems facing the plastic surgeon especially in aesthetic plastic surgery, and the results of their treatment are not always satisfactory. Therefore, control of unsightly, excessive scar formation following wound healing is of great importance in plastic surgery.

Many aspects related to the biology and the effective therapy of proliferative scars remain undefined, in part due to a lack of an accurate, practical, reproducible, and economical animal model to systematically study proliferative scars. Although there are close similarities to porcine xenografts in donor swine, hypertrophic scars and keloids are not found in experimental animals [21]. Attempts to develop animal models for abnormal scar formation have always been difficult, and most of the time proved unsuccessful [3]. Despite many difficulties, various experimental animal models have been developed to study proliferative scars. A major difference between

humans and experimental animals is the presence of the panniculus carnosus in the latter. This fibromuscular layer enables the skin of the experimental animal to slide over the underlying fascia, allowing more rapid wound contraction than in human skin [17]. In pigs, removal of the panniculus carnosus, later followed by removal of a piece of skin, leads to hypertrophic scars with proper macro/microscopic and biochemical features, while wounds not deprived of panniculus carnosus heal normally. This has been defined as an experimental hypertrophic scar model [5].

Today there is a search for new animal models of proliferative scar progress with transplantation of human proliferative scar tissue to congenitally athymic mice and rats [11,18]. The development of scar hypertrophy in guinea pigs as a result of irritation caused by coal tar application to open wounds has been demonstrated morphologically by light and transmission electron microscopy, but without any biochemical measurement of metabolic properties specific to hypertrophic scarring [24].

Changes in the metabolism of proliferative scars are due to an increase in fibroblastic proliferation and extracellular matrix production. Changes in the activity of some enzymes in the carbohydrate metabolism have been reported. The most striking change was observed in the activity of glucose-6-phosphate dehydrogenase (G6PD) [7,20].

Studies with light and electron microscopes have shown certain morphological differences between normal scars and proliferative scars [15,16].

Guinea pigs are cheaper to obtain than pigs, athymic mice, or athymic rats. The care of guinea pigs is cheaper and easier as well. This study was performed to demonstrate if panniculectomy alone or in combination with coal tar application in guinea pigs results in morphologically and biochemically verified hypertrophic scars, and to define an experimental proliferative scar model.

Materials and Methods

Animals and Anesthesia

Thirty-five albino male guinea pigs weighing between 500 and 750 g were used in this study, carried out with the approval of the Hacettepe University Ethics Committee. All surgical interventions were performed under ketamin/xylazine anaesthesia (40/5 mg/kg IM).

Surgical Procedures and Wound Care

The animals used in this study were divided into three groups, with 10 animals in the first group, 10 animals in the second group, and 15 animals in the third group. Different interventions and wound care practices were employed in each group. All surgical manipulations were performed under sterile conditions with surgical instruments sterilized with hot steam. Antibiotic solutions were used to irrigate the surgical wounds to help prevent postoperative wound sepsis.

Group I. A linear skin incision 8 cm long was made longitudinally 4 cm from the ventral midline and a skin flap measuring 8×4 cm was raised on the ventral aspect of torso on the right side. Removal of the panniculus carnosus of the same size as the skin flap was performed and the incision was closed with sutures. The same incision was made on the left side and a skin flap measuring 8×4 cm together with the panniculus carnosus was dissected from the musculature of the ventral torso and the incision was closed. After three weeks, circular skin islands 2 cm in diameter were removed from the central part of the skin flaps on the right and the left sides. Wounds created in this way were left for secondary healing. Topical antimicrobial treatment was not applied to the wounds in order to promote hypertrophic scar formation, as the presence of microorganisms in the wound increases the likelihood of hypertrophic scar development by delaying wound healing [23].

Group II. Heavier animals were chosen to be in this group (700–750 g) to better withstand burn trauma. Heavier animals have higher total body surface area, which results in a smaller percentage of burned surface area, as the diameter of the aluminium plate to inflict burn injury was standard. All of the surgical procedures were the same as those in group I, except that wounds were created by a deep partial thickness burn injury circular in shape and 3.5 cm in diameter instead of circular skin excisions [9]. Aluminium plates, weighing 500 g, with a handle and a circular contact surface 3.5 cm in diameter was used for inflicting burn injury. Aluminium plates were left in hot water at 75°C for two hours and then applied to the skin of the animal for five seconds in such a way that only weight of the plate was responsible for the magnitude of the pressure of contact between the plate and skin [9]. Blanching of the skin was observed as a sign of burn injury. Topical antimicrobial treatment was not applied to the wounds in order to promote hypertrophic scar formation.

Group III. Circles of skin ranging 1.7–2.0 cm in diameter, depending on the weight of the animals, were removed from the dorsal part of the the thorax. The nearest distance between the circles and the dorsal midline was 2.0 cm (Fig. 1). The thoracic region was chosen since resting skin tension was higher and wound contraction was more difficult than in the muscular ventral abdominal wall. Additionally, when coal tar is applied to the dorsal region, it is not

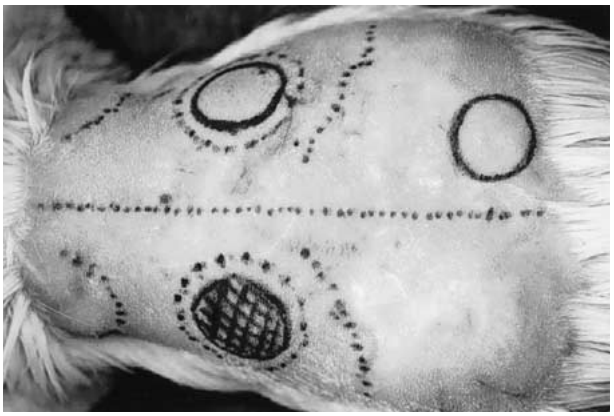

Fig. 1. Planning of the circular skin incisions, ranging 1.7–2.0 cm on the dorsal parts of the guinea pigs. The smallest distance between the skin incisions and dorsal midline was 2 cm. Circles of panniculus carnosus, 1 cm greater in diameter than those from the skin, were excised from both sides, but not from the caudal part. Coal tar was applied to the wound on the left (shaded area).

removed or dissipated by the movement of the animal within the cage. A circle with a diameter 1 cm greater than that from the skin panniculus carnosus was excised, on both the right and left sides. Any latissimus dorsi muscular layer left interposed between the skin and thoracic wall after panniculectomy was removed to allow direct contact between the skin and the thoracic wall. For the control, a circule of skin, 1.5 cm in diameter, was excised on the right side, 4 cm from the caudal part on the back, leaving the panniculus carnosus intact. Since skin excision alone and with coal tar application were investigated in a previous study on 30 guinea pigs, a fourth circular skin excision was not performed, with the hope of decreasing mortality due to wound sepsis and coal tar toxicity. Four days after the wounds were made, coal tar was applied to the wound on the left side once every 48 hours. Just enough coal tar to cover the wound and a narrow rim of surrounding skin was used in order to decrease coal tar toxicity due to excessive absorption. The coal tar used in this study is semisolid at room temperature and was obtained from Kardemir Karabük Steel Plant, located in the Karabük province of Turkey. Guinea pigs were kept in cages in groups not exceeding three animals per cage in order to minimize dispersion of coal tar from the wounds. Coal tar application was continued for one month. No topical antimicrobial treatment was applied to the wounds, so as to promote hypertrophic scar formation.

Three weeks after the wounds had all healed completely on the guinea pigs, scars that were hypertrophic in appearance (erythematous and elevated) were observed on some of the animals in the group III, and tissue sampling and microscopic morphological studies were performed only on these animals. Sampling from normal skin, from scars of normal appearance, and from scars of hypertrophic appearance was performed with a punch biopsy instrument 0.5 cm in diameter.

Biochemical Studies

The tissue specimens taken for biochemical studies were immediately frozen and kept in liquid nitrogen until enzyme activity was assayed. For G6PD measurements, the fresh tissue weight of each specimen (varying between 19 and 68 mg) was recorded. Each specimen was homogenized with a glass homogenizer in 55 mM Tris. HCl buffer (pH 7.8) at 4°C and centrifuged at 1000×g for 10 minutes. Enzyme activity and protein concentrations were performed on the clear supernatant [1,2]. Enzymatic activities are expressed as μmoles per minute per mg of protein (μmol/min/mg protein).

Morphological Studies

Samples obtained from 10 animals with scars that were hypertrophic in appearance were preserved in formaldehyde for light microscopic studies and were fixed in 2.5% glutaraldehyde solution for 24 hours for transmission electron microscopic (TEM) studies.

Tissue samples from an animal with prominent hypertrophic scar formation were fixed in 4% formaldehyde and embedded in paraffin blocks for more detailed light microscopic examination. Slices 5 μm in thickness were obtained and stained with hemotoxylene-eosin and Masson's trichrome, and light microscopic examinations were performed.

After irrigation of tissues with Sorenson's phosphate buffer solution tissues were subjected to post-fixation treatment with 1% Osmium tetroxide solution for two hours. Tissues were irrigated again with Sorenson's phosphate buffer solution after post-fixation treatment and dehydrated in alcohol solutions of increasing concentration. Tissues were then irrigated with propylene oxide and adapted to epoxy resin embedding material. Then tissues were embedded in epoxy resin material and kept in an autoclave for 48 hours. Slices 2 μm in thickness were cut by ultramicrotome after tissues were taken out of the autoclave. These slices were stained with methylene blue, light microscopic studies were performed, and photographs were taken.

For TEM studies, thin slices of tissues (60 nm in thickness) were taken onto copper grids by ultramicrotome. These slices were stained with uranyl acetate and lead citrate, TEM studies were carried out, and photographs were taken.

LKB-Nova ultramicrotome (Sweden), Jeol JEM 1200 EX transmission electron microscope (Japan), and Nikon Optiphot (Japan) were used for light and TEM studies.

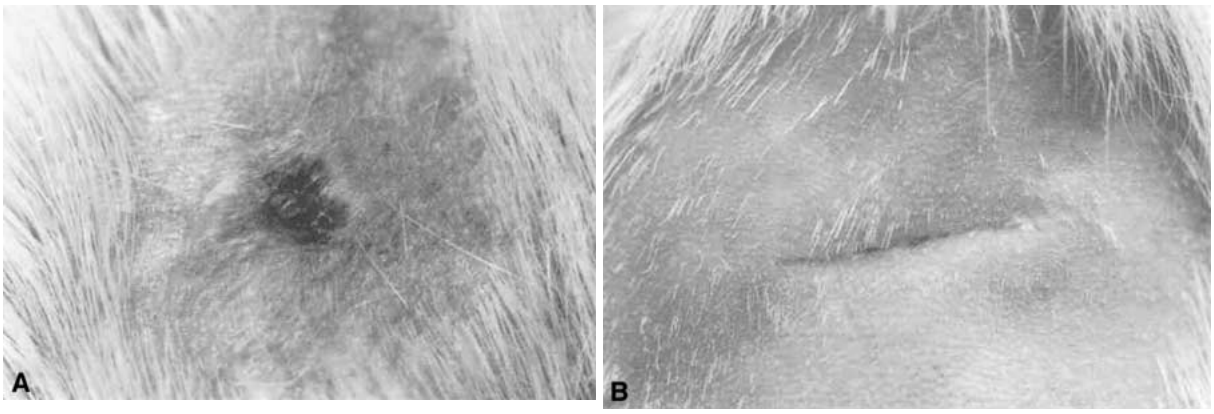

Fig. 2. **A** Healing of caudal control skin excision wound, two to three weeks postoperatively. **B** Healing of skin and panniculectomy wounds, four weeks postoperatively.

Tissue samples taken for the scanning electron microscopic (SEM) study were fixed in 2.5% glutaraldehyde solution for 24 hours. After irrigation of tissues with Sorenson's phosphate buffer solution, tissues were subjected to post-fixation treatment with 1% Osmium tetroxide solution for two hours. Tissues were irrigated again with Sorenson's phosphate buffer solution after post-fixation treatment and dehydrated in alcohol solutions of increasing concentration. Tissues underwent critical point drying, and samples were taken and adhered onto metal stubs and coated with gold 100 A in thickness. These tissue samples were then examined by SEM at 80 kV acceleration voltage and photographs were taken.

A Bio-RAD sputter apparatus (England) and Jeol scanning electron microscope ASID-10 (Japan) were used for SEM studies.

Results

In group I, wounds located on the control side without panniculectomy healed two weeks with scars of normal appearance. Wounds on the panniculectomy side healed within three weeks with distorted and larger scars.

In group II, eschar tissue was formed on the wounds of the control side and wounds healed within four weeks with normal appearing scars. Eschar tissue formed on the panniculectomy side and wounds healed in 5–5.5 weeks with scars of normal appearance. The appearance of scars on the panniculectomy side was more distorted, and scars were larger than those on the control side.

Three animals were lost in group III, and therefore the number of animals in this group was reduced to 12. The control wound created by skin excision alone healed with an atrophic scar in two to three weeks (Fig. 2A). Wounds created by skin and excision of the panniculus carnosus but not treated with coal tar healed within four weeks with normal looking scars (Fig. 2B). Wounds created by excision of the skin and panniculus carnosus and treated with coal tar healed within five weeks (Figs. 3A,B). In 10 animals out of 12, scars that had some erythema and were elevated from the surrounding skin, thus resembling hypertrophic scars, were observed at both ends of a linear scar (Fig. 3C). Scars were larger, and erythema and elevation were more prominent in six animals than in the other four animals.

Morphological Findings

The wounds of six of the ten animals healed with gross morphological findings specific to hypertrophic scars, which developed some erythema and elevation from the surrounding skin after wound healing in the third group were evaluated morphologically.

Normal Skin

On light microscopic examination, mild acantosis and a large number of hair follicles were observed in the dermis and other adnexal elements in hemotoxyleneeosin staining. In Masson's trichrome staining, fine collagen fibrils were interspersed between adnexal elements such as the sebaceous glands.

TEM and SEM studies revealed normal cellular elements without any morphological anomaly.

Normal Scar

On light microscopic examination, epithelization was almost normal. As far as the epidermis layer was concerned there was no difference between normal skin and the normal scar. There was blunting at the epidermo-dermal junction but no significant change in epidermis. Loss of skin appendages, fibroblastic activity, capillary proliferation, and mild mononuclear cell infiltration were observed in the dermis.

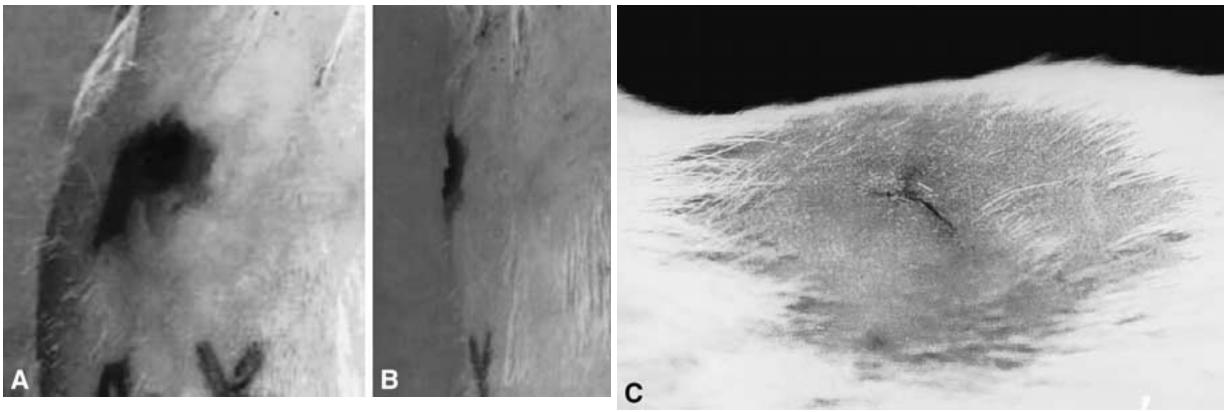

Fig. 3. **A,B** Development of an elevated erythematous hypertrophic scar around an incompletely contracted and open wound on the left side four weeks after application of coal tar to skin excision and panniculectomy wounds. **C** Appearance of the hypertrophic scar three weeks after the complete healing of panniculectomized wounds treated with coal tar in group III.

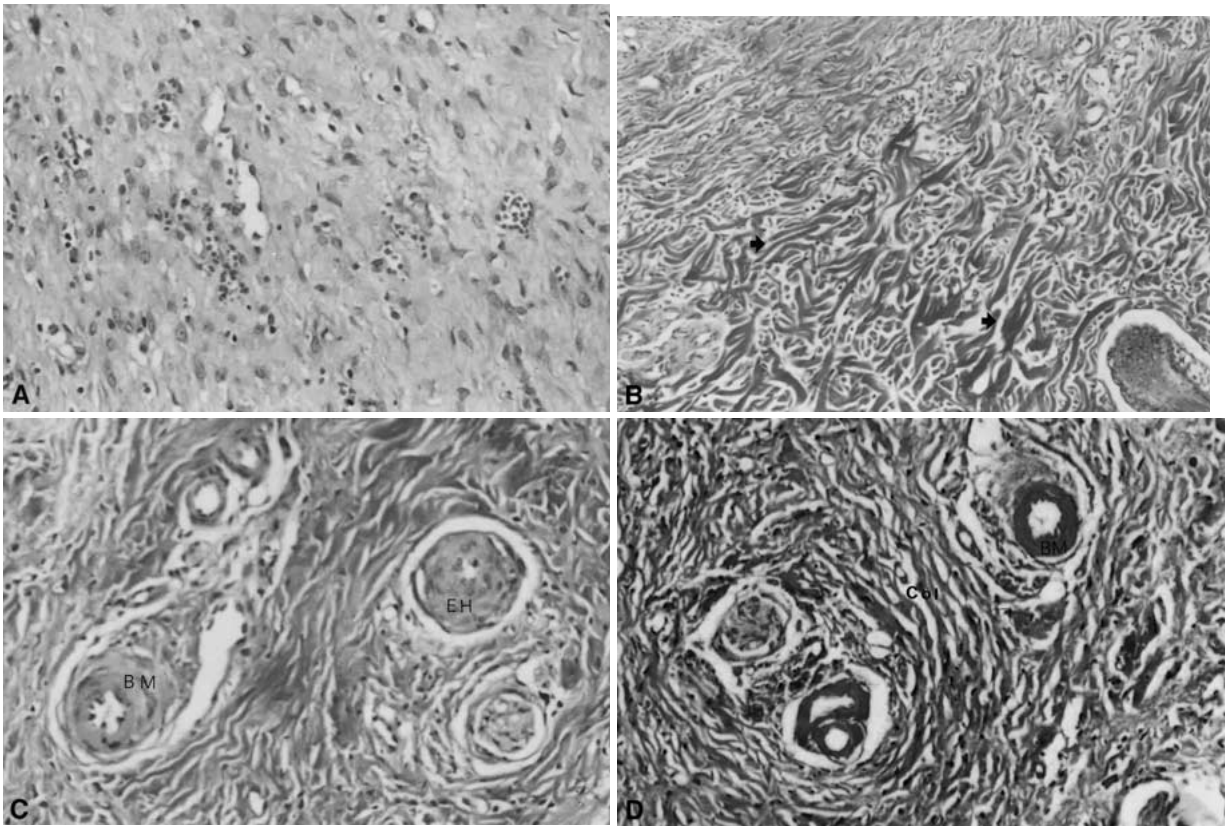

Fig. 4. **A** Hematoxylene-eosine-stained sections of a normal scar with fine, regularly oriented collagen bundles (×200). **B** Hematoxylene-eosine-stained sections of a hypertrophic scar with coarse, irregularly oriented collagen bundles with more intense staining, indicated with arrows (×200). **C** Hematoxylene-eosine-stained sections of a hypertrophic scar demonstrating the endothelial hyperplasia (EH) in the lumen of the blood vessels (glomeriloidal appearance) and the thickening of the basement membrane (BM) of the blood vessels. **D** Masson's trichrome-stained sections of hypertrophic scar emphasizing the irregularity of the collagen bundles (Col) and the thickening of the basement membrane (BM) of the blood vessels.

Fibroblastic proliferation and thin-walled, narrow vascular structures with erythrocytes-filled lumens were observed at a higher magnification (Fig. 4A). Masson's trichrome stain confirmed the presence of collagen, which stained green.

TEM showed the presence of epithelial cells located in the epidermis. Dense aggregates of collagen fibrils were not observed around fibroblasts present in normal scar tissue (Fig. 5A). Myofibroblasts were not present in normal scar tissue.

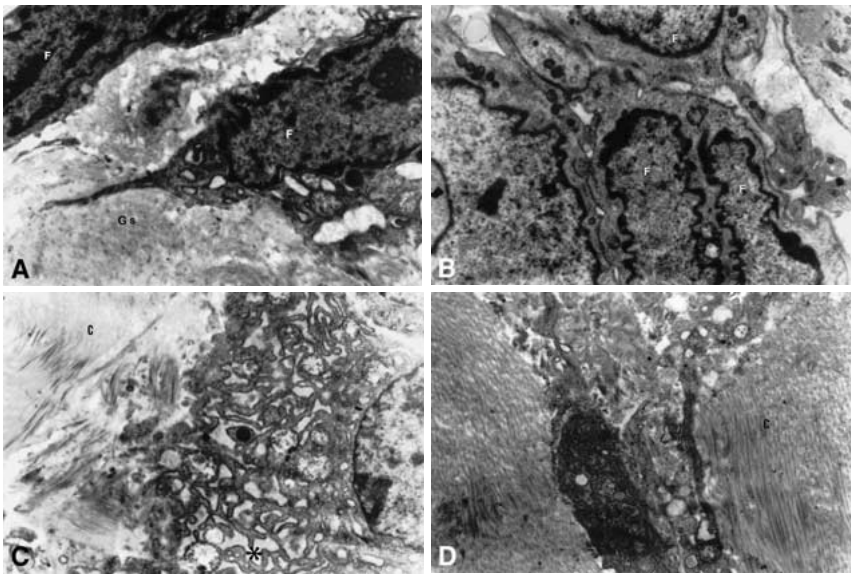

Fig. 5. **A** Appearance of a fibroblast (F) with the presence of the ground substance (Gs) around, demonstrated by transmission electron microscopy (original magnification ×6000). **B** An increase in number of fibroblasts (F) in hypertrophic scar demonstrated by transmission electron microscopic examination (original magnification ×6000). **C** Transmission electron microscopic appearance of collogen fibrils (C) and a myofibroblast with well-developed, rough endoplasmic reticulum (*). **D** Presence of dense collagen bundles (C) in a hypertrophic scar demonstrated by transmission electron microscopic examination (original magnification ×6000).

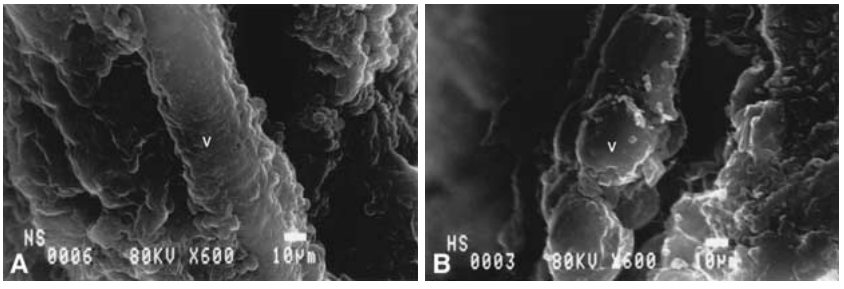

Fig. 6. **A** Scanning electron microscopic appearance of a normal vessel (V) in normal scar (original magnification ×800). **B** Scanning electron microscopic appearance of a vessel with endothelial hyperplasia (V) in hypertrophic scar (original magnification ×600).

Endothelial hyperplasia was not observed in the vessels within the normal scar tissue in SEM studies (Fig. 6A).

Hypertrophic Scar

On light microscopy, keratinization and mild, irregular acantosis were observed in the epidermis, and irregularly dispersed coarse collagen bundles and collagen nodules were observed in the dermis. A significant decrease in the number of skin appendages was observed when compared with normal skin. Under greater magnification, coarse and irregular collagen bundles were more obvious and vascular proliferation was present (Fig. 4B). Masson's trichrome stain confirmed the presence of collagen, which stained green, in the dermis (Fig. 4D). Under greater magnification vascular proliferation, thickening of the basal membranes and endothelial proliferation (glomeruloid appearance) were noted (Fig. 4C). The thickened basal membrane was more pronounced with Masson's trichrome stain (Fig. 4D).

Fibroblasts present in collagen nodules were observed in TEM studies (Fig. 5B). There were myofibroblasts in the dermis with dense aggregates of collagen fibrils present around them (Figs. 5C,D).

Endothelial hyperplasia was observed in the vessels of hypertrophic scar in SEM studies (Fig. 6B).

Biochemical Findings

G6PD enzyme activity measurements was measured in three different samples (normal skin, normal scar, and hypertrophic scar) from the same animal in 10 group III guinea pigs (raised and erythematous scars suggesting the presence of hypertrophic scar indicated in Table 1). The presence of hypertrophic scar was supported by morphological studies in only six of these ten animals (numbers 1, 2, 4, 5, 9, and 10). G6PD enzyme activity measurements in 1, 2, 4, 5, 9, and 10 were compared statistically among each group by Wilcoxon Signed Rank Test. The difference between normal skin and normal scarring was not statistically significant ($p > 0.1$). The difference between normal skin and hypertrophic scarring was statistically significant ($p < 0.10$). The difference between normal scarring and hypertrophic scarring was statistically significant ($p < 0.05$) and greater than the difference between normal skin and hypertrophic scarring.

Table 1. G6PD activity in six group III guinea pigs.

	Normal skin	Normal scar	Hypertrophic scar
1	0.0656211	0.04255722	0.04255722
2	0.04255722	0.05586135	0.08842444
4	0.02275071	0.011375356	0.03152386
5	0.02527857	0.0598618	0.07382374
9	0.01837391	0.0445214	0.07168837
10	0.0739705	0.04908425	0.0757109

In short, in group III, scars with erythma and elevated edges developed in 10 out of the 12 animals. The presence of hypertrophic scarring was supported by morphological studies in only six of these ten animals. Increased G6PD enzyme activity was observed in four of these six animals.

Discussion

Various experimental models have been described for the study of proliferative scars. Although there are close similarities with porcine xenografts in donor swine, hypertrophic scars and keloids are not found in experimental animals. Therefore, studies have been undertaken to produce experimental animal models for hypertrophic scars [21].

In pigs, the removal of the panniculus carnosus from under a skin flap, followed by elliptical excision of skin, leads to hypertrophic scarring with macro/microscopic and biochemical features similar to human hypertrophic scars. In our study, panniculectomy followed by circular skin excision failed to produce hypertrophic scars in guinea pigs. This could be explained by the fact that the anatomical relation of the panniculus carnosus to the overlying skin in pigs is different from that in guinea pigs, and that guinea pigs belong to the order Rodentia while pigs do not [4].

The timing and method of creating wounds after panniculectomy may affect the development of hypertrophic scars. It is known from clinical observations in humans that wounds produced by burn injury heal with hypertrophic scarring more frequently than other types of wounds [8]. However, panniculectomy followed by burn injury to the overlying skin did not result in hypertrophic scar formation. Panniculectomy caused a delay in the healing of wounds created by both circular skin excision and burn injury in guinea pigs. Moreover, the scars on the side where panniculectomy had been performed were larger, their borders and appearance were more irregular. Thus, panniculus carnosus causes the rapid contraction and healing of open wounds and faster healing of burn wounds. The appearance and quality of the resulting scars were better when the panniculus carnosus layer was present. Scar hypertrophy has been observed in guinea pigs as a result of irritation caused by coal tar application to open wounds [24]. In that study, scar hypertrophy was shown by light microscopy and transmission electron microscopy, but there was no biochemical confirmation of these morphological findings [24]. Coal tar may lead to scar hypertrophy by either chemical irritation or its toxic effect in biological systems [23,24]. In our study, 10 animals out of 12 in which panniculectomy combined with coal tar application were developed scar hypertrophy when scars were evaluated macroscopically, although only approximately one-third of these animals developed a hypertrophic scar with morphological (both macroscopic and microscopic evaluation) and biochemical features similar to those of human hypertrophic scars. Thus, scar hypertrophy does not always indicate hypertrophic scarring. This can be explained by the fact that genetic predisposition of the individuals and the location of the lesion are important factors in genesis of hypertrophic scar. Since isogenetic animal model was not used in this study, development of hypertrophic scars cannot be expected in all animals treated with panniculectomy combined with coal tar application.

Scars with morphological and biochemical features specific to hypertrophic scars were larger and more erythematous, and the elevation of the scar tissue was more prominent than in the control groups. Thus, in this model it is appropriate to use scars with prominent erythema and elevation as a hypertrophic scar. In addition, the amount of hypertrophic scar tissue is adequate for therapeutic studies. On the other hand, scars showing minimal hypertrophy with regard to external appearance have morphological and biochemical properties specific to hypertrophic scars infrequently and should not be used as a model.

Since coal tar is both toxic and carcinogenic, it should be used cautiously and male animals should be used whenever possible to minimize animal loss [19,22]. Cancer development was not observed in our study, but three animals were lost due to the toxic effects of coal tar. Mortality due to the toxic effects of coal tar appears to be a disadvantage of this model, which could be minimized by limiting the amount of coal tar applied to the wound to an amount just adequate to cover the wound and a rim of normal skin, and waiting for a few days to allow the wound edges to adhere to the thoracic wall, which will prevent the tar from disseminating into the dead space between the panniculus carnosus and thoracic wall musculature.

Combining panniculectomy with coal tar application results in the development of hypertrophic scars in a greater number of animals, as a preliminary experiment employing coal tar application without panniculectomy with the same wound size and location resulted in a lower number of scars with erythema and lower elevation (4/30) even when compared with the number of morphologically and biochemi-

cally proven hypertrophic scars (4/12) in our experiment. The scar hypertrophies observed in the preliminary experiment were not examined morphologically or biochemically. Panniculectomy delays wound healing, thus increasing the duration of the action of coal tar on the wound. Moreover, panniculectomy has adverse effects on the quality of wound healing [5,6]. Hypertrophic scars produced by panniculectomy and coal tar application are morphologically larger and more prominent, and the measured biochemical parameters from these scars are compatible with those of hypertrophic scars. The use of different methods to inflict wounds at the same anatomical location after panniculectomy and daily application of coal tar to the wounds has the potential to increase the number of animals developing hypertrophic scars with proper morphological and biochemical features.

Hypertrophic scars produced in guinea pigs were shown by both light and electron microscope (TEM and SEM) to have morphological features similar to those of human proliferative scars. The presence of coarse and irregular bundles of collagen, and vascular and fibroblastic proliferation were observed in light microscopic studies. The presence of myofibroblasts is an important electron microscopic finding in human hypertrophic scars [10,12,14,16]. Endothelial hyperplasia, found in guinea pig hypertrophic scarring, is an important finding in SEM studies of human hypertrophic scars [13].

Enzyme activity measurements showed that G6PD enzyme activity was higher in guinea pig hypertrophic scars than the G6PD enzyme activity of normal scars and normal skin of guinea pigs. This finding demonstrates a biochemical similarity between guinea pig hypertrophic scars and human hypertrophic scars [7,20].

This experimental hypertrophic scar model will be useful in studying the pathophysiology of hypertrophic scars. The results of these studies could lead to the development of therapeutic interventions to prevent or limit the occurrence of hypertrophic scars and keloids. In addition, the effectiveness of new therapeutic modalities for the treatment of hypertrophic scars and keloids once they occur could be tested on this model.

Since this hypertrophic scar model has been developed in guinea pigs, it is cheaper and more practical than the model developed in pigs [5], as guinea pigs are cheaper and easier to obtain and to care for. It is possible to keep large numbers of guinea pigs in a single cage. It is also easier to conduct an experiment animals smaller than pigs.

In animal models of proliferative scars developed by the transplantation of human proliferative scar tissue to congenitally athymic mice and rats, it is difficult and expensive to obtain and care for these immunocompromised experimental animals [11,18]. Cages equipped with laminar flow systems and specific feeding protocols make the maintenance of these immuncompromised animals expensive. It is also known that the aggressiveness of scars transplanted to experimental animals is less that that of the original scar [18].

In conclusion, experimental hypertrophic scars produced in guinea pigs have morphological and biochemical properties similar to those of human proliferative scars. This experimental scar model is a new, practical, and economical model to study both the pathophysiology and the effectiveness of the new therapeutic modalities of the proliferative scars, despite the fact that improvements are needed to increase the number of the animals developing hypertrophic scars.

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