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MORPHOLOGICAL ALTERATIONS IN THE NASAL MUCOSA IN HEAT STROKE

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A preliminary histomorphological examination of the nasal mucosa of 8 heatstroke patients who presented without epistaxis, showed stromal vascular damage and degenerative changes in the basal lamina of the overlying epithelium, severe enough in two cases to indicate impending epistaxis, even in the absence of disseminated intravascular coagulation (DIC). It is suggested that direct damage by the extreme heat to mucosal structures, especially the prominent, thin-walled blood vessels, plays an important role in the genesis of epistaxis in heatstroke even in the absence of DIC.

INTRODUCTION

Heat stroke is a health problem when the annual Makkah Pilgrimage falls in the hot summer months of Saudi Arabia (1,2). During this period ambient temperatures in excess of 50 degrees Celsius in combination with physical exertion, results in progressive rise in body temperature leading to various degrees of heat illnesses in the pilgrims, especially the aged (3,4). The pathological alterations in heatstroke are mostly biochemical with attendant functional deficits. Very few morphological alterations, both gross and microscopic, have been documented; largely because the biochemical changes evolve so rapidly and patients present as medical emergencies that must be treated with despatch.

The few morphological changes described in the syndrome of heat illness usually accompany the most severe form of the condition - heatstroke (5,6). These include, cardiovascular complications resulting from haemodynamic alterations (7,8), rhabdomyolysis and renal injury (9-13), central nervous system manifestations (14), Gastrointestinal manifestations (15-17), pulmonary injury (18,19), dermatological and sweat gland injury (20); and haematological abnormalities (21-23). These haematological abnormalities usually take the form of disseminated intravascular coagulation, which has been implicated in the epistaxis commonly complicating heat stroke (22,23). The complication of heatstroke by epistaxis or hemorrhage in other parts of the body usually signals a poor prognosis. There is little information available on morphological changes in the upper respiratory tract; specifically the nose, that occur in heat stroke; changes that lead to or accompany epistaxis.

This paper is a preliminary report on some histopathological changes occurring in the nasal mucosa of patients diagnosed as suffering from heat stroke but without epistaxis. The objective is to ascertain the morphological changes in the nasal mucosa that may be characteristic of heat stroke and also

predispose to epistaxis. Although the number of cases studied is small, the findings form a basis for futher, more comprehensive study of the issues raised.

MATERIALS AND METHODS

Biopsies of the nasal mucosa were collected from ten consecutive patients admitted for treatment of heatstroke in the Heat Treatment Centre, King Faisal Hospital, Makkah; during the 1986 Hajj in Saudi Arabia. To ensure the safety of the patients, the biopsies were taken by an ENT Surgeon, from the superficial mucosa of the inferior turbinate on one side and the nostril firmly packed with vaseline guaze to stop any bleeding. The pack was removed after the patient had received Cooling Therapy and had been transfered to the Recovery Room. In all ten cases the biopsy procedure did not in any way, affect the treatment of heatstroke and the patients made good recovery.

The specimens were fixed in 10% formalin, processed routinely in paraffin and stained with haematoxylin and eosin. In addition the following special stains were used to assist in the assessment of the morphological changes: Alcian Blue at pH 1.0 and pH 3.2; van Gieson stain; modified Masson Trichrome stain; Gordon and Sweets; reticulin method.

Of the ten cases examined, two were considered inadequate and were excluded from the study.

Controls

Control specimens were obtained from the files of the Department of Pathology, King Fahd Hospital of the University. These consisted of ten cases within the age range of 50 to 70 years whose nasal mucosal biopsies were included in specimens taken for other reasons and in which the nasal mucosa had been reported as within normal limits. There were six males and four females in the control group. Paraffin sections were cut and stained in the same manner as the cases under study.

RESULTS

The salient clinical findings in the eight cases are summarised in Table 1. The histopathological findings in these eight cases are compared with the controls in Table 2. With only minor variations, the control specimens showed

TABLE 1. Summary of clinical features of the 8 Heatstroke cases studied.

Case Number	1	2	3	4	5	6	7	8
Age	50	53	70	70	63	60	40	60
Sex	f	m	m	f	m	m	m	m
Temperature	42.9	42.7	41.7	43.3	41.7	42.8	40.2	42.3
Dry skin	+	+	−	−	−	−	+	+
Shock	+	+	−	−	+	−	+	+
Convulsion	−	+	−	+	+	+	+	−
Bleeding	−	−	+	+	−	−	−	−
Diarrhoea	+	−	−	−	−	+	−	+
Coma	+	−	+	+	+	+	+	+
DIC	+	+	−	+	−	+	−	−

+ = Present
− = Absent

TABLE 2. Comparison of Histopathological findings in the 8 Heatstrokes Cases studied with Controls

Case Number	1	2	3	4	5	6	7	8	Controls
Surface Epithelium									
Squamous Metaplasia	+	+	+	+	+	+	+	+	
Spongiosis	+	+	+	+	+	+	+	+	
Basal Degeneration	+	+	+	+	+	+	+	+	
Hyperplasia	+	+	+	+	+	+	+	+	
Necrosis	+	+	+	+	+	+	+	+	
Exocytosis	+	+	+	+	+	+	+	+	
Basal Lamina Widening	+	+	+	+	+	+	+	+	
Basal Lamina Degeneration	+	+	+	+	+	+	+	+	
Blood Vessels									
Capillary Proliferation	+	+	+	+	+	+	+	+	
Congestion	+	+	+	+	+	+	+	+	
Necrosis	+	+	+	+	+	+	+	+	
Fibrin thrombi	+	+	+	+	+	+	+	+	
Extravasation	+	+	+	+	+	+	+	+	
Thick walled vessels	+	+	+	+	+	+	+	+	
Nuclear Dust	+	+	+	+	+	+	+	+	
Perivascular Neutrophil infiltration			+	+	+	+	+	+	
Lamina Propria									
Oedema	+	+	+	+	+	+	+	+	+
Extravasation	+	+	+	+	+	+	+	+	+
Necrosis	+	+	+	+	+	+	+	+	+
Pigment	+	+	+	+	+	+	+	+	+
Plasma Cells	M	M	M	M	H	M	M	H	L
Lymphocytes	M	M	M	M	H	M	M	H	L
Neutrophils	L	L	L	M	M	L	M	L	
Eosinophils	VL	VL	VL	L	L	VL	VL	VL	VL
Mucous Glands									
Hyperplasia	—	—	—	—	—	—	—	—	—
Necrosis	—	—	—	—	—	—	—	—	—

+ = Present, − = Absent, H = Heavy, L = Light, VL = Very light, M = Moderate.

essentially similar histological appearances and for practical purposes could be regarded as a homogeneous group.

Surface Epithelium

All 8 specimens showed squamous metaplasia of the epidermis with variable amounts of spongiosis and exocytosis, the latter, prominent in those biopsies showing heavy inflammatory changes in the underlying lamina propria. There was focal liquefactive degeneration of the basal layer with

irregular widening of the basal lamina and reduplication in areas (Fig. 1).

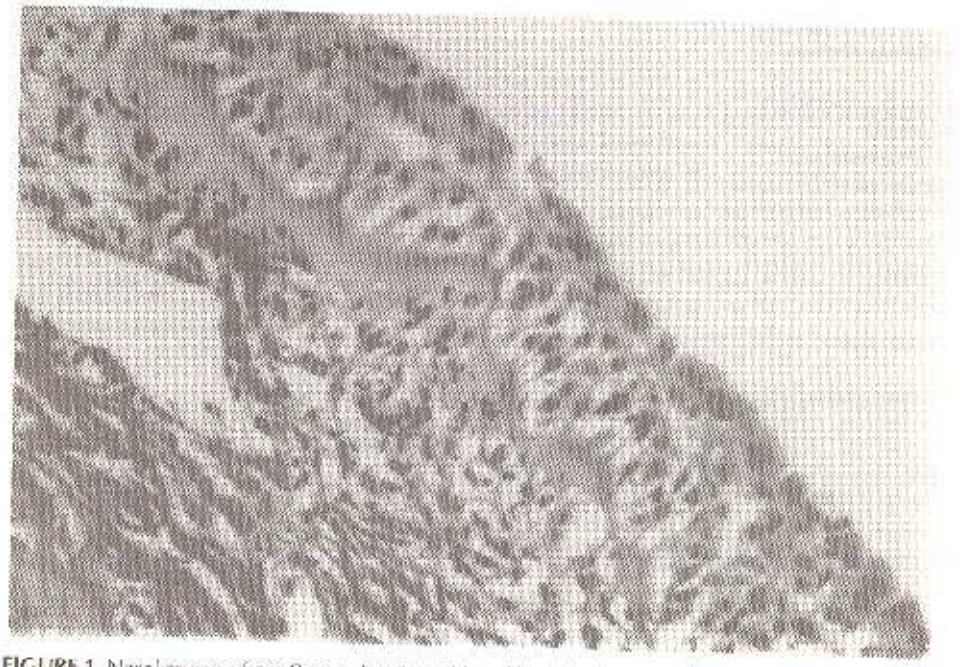

FIGURE 1. Nasal mucosa from Case 3 showing widened basal lamina of epithelium with underlying acute inflammatory changes in the subepidermis. (Haematoxylin-van Gieson, × 250)

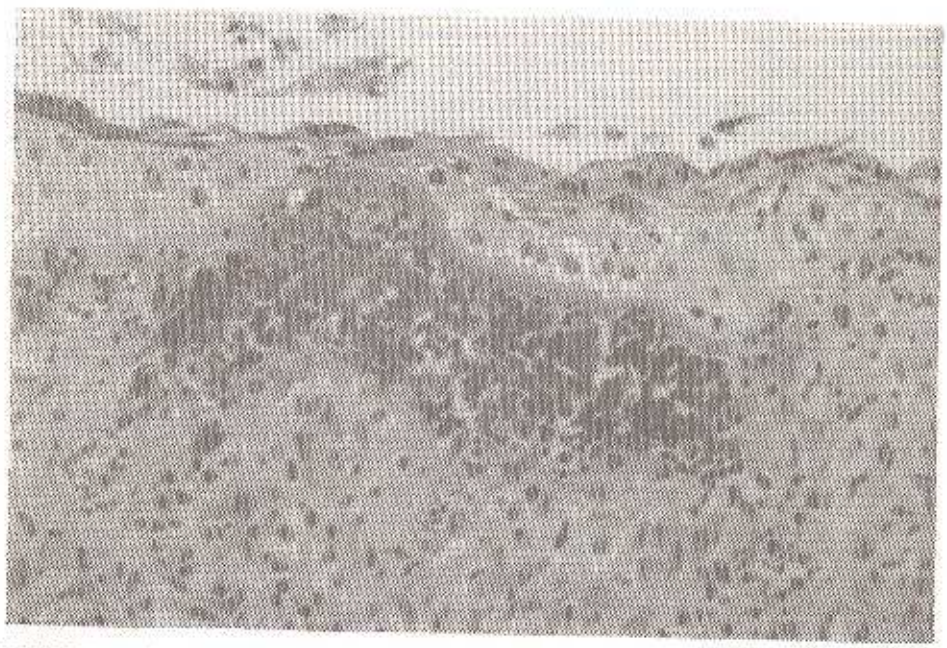

FIGURE 2. Nasal mucosa from Case 4 showing subepidermal necrosis and extravasation of blood almost breaking through the overlying epithelium. (Haematoxylin and eosin, × 250)

Where the lamina propria showed necrosis this extended focally to involve the overyling basal lamina which was widened and had become amorphous as emphasised with reticulin and alcian blue stains. In 2 out of 8 cases, there was significant necrosis in the subepidermis in continuity with the overlying basal lamina (Fig. 2).

In the control group, apart from moderate, sometimes focal squamous metaplasia, there were no other significant histological findings.

Lamina Propria

The changes in the lamina propria are best considered under the following:

a. *Oedema* - This ranged from moderate to severe in the heatstroke cases with accompanying widespread extravasation of blood in two cases. Oedema in the control cases was either minimal or absent.

b. *Blood vessels* - There was marked capillary proliferation in all 8 cases, the superficial ones showing marked dilatation and congestion. In one case (Case 4) the proliferation took a nodular form resembling an angioma (Fig. 3). A notable feature in cases 1, 3 and 4 was the presence of perivascular neutrophilic infiltration. This was associated in cases 3 and 4 with fibrin

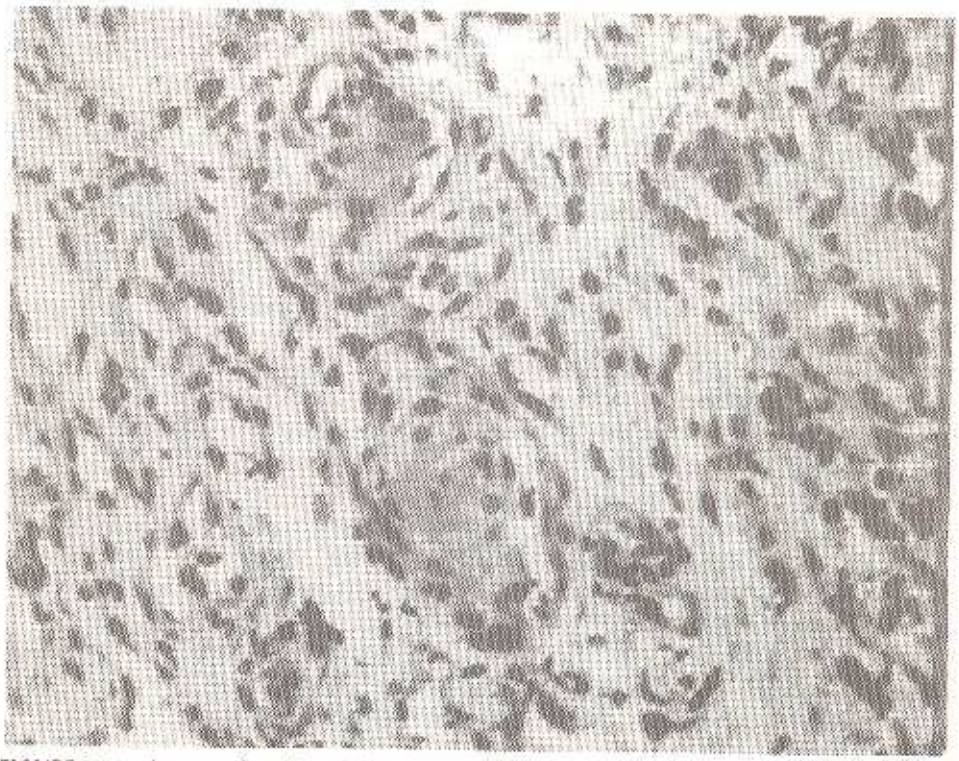

FIGURE 3. Nasal mucosa from Case 4. Prominent vascular proliferation is seen in the oedematous lamina propria. Some blood vessels contain fibrin thrombi. (Haematoxylin and eosin. × 150).

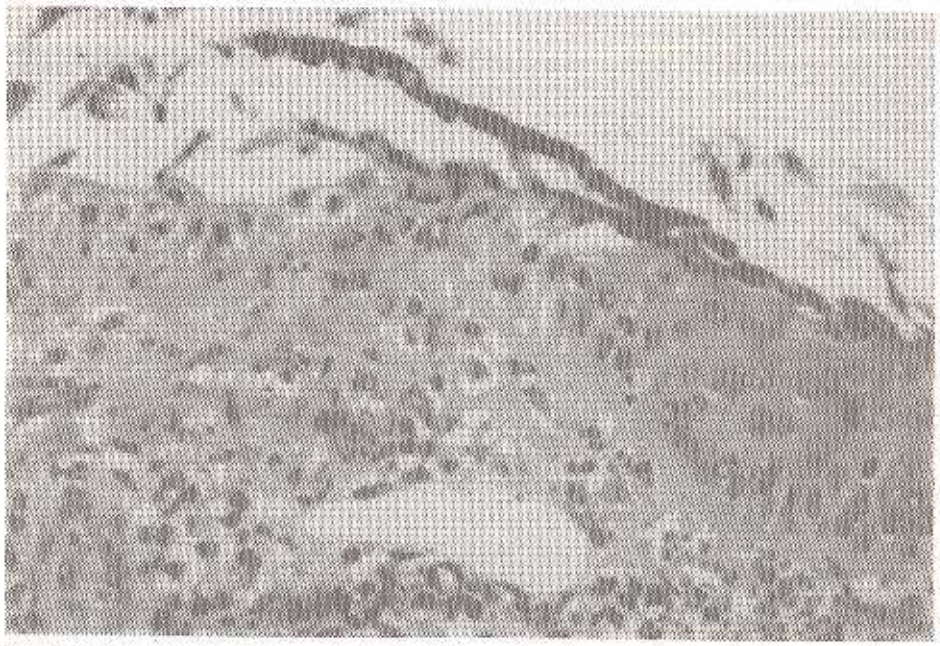

FIGURE 4. Nasal mucosa from case 4 showing inflammatory changes in both epithelium and underlying lamina propria. Note congested blood vessels in the subepidermis which appear to extend through the epidermis. (Haematoxylin and eosin × 250)

thrombi within the capillaries, widespread in case 4 with focal necrosis of the vessel walls but no significant nuclear dusting or other evidence of leukocytoclasis. These two cases showed extravasation of blood and focal necrosis in the lamina propria, with apparent extension of capilaries into the epithelium (Fig. 4). Three other cases showed dilated, thick-walled blood vessels in the deeper tissues, obviously feeding the congested, proliferating capillaries.

There was significant vascular proliferation and prominent capillaries even in the control cases, but without fibrin thrombi, capillary necrosis or perivascular neutrophil infiltration described in cases 1, 3 and 4.

c. Necrosis - In addition to the vascular necrosis seen in case 4, four others showed small foci of necrosis, mainly subepidermal. There was no necrosis in the lamina propria of any of the control cases.

d. Inflammatory infiltrate - The inflammatory infiltrate in the lamina propria was assessed visually, in relation to type of cells and numbers and semi-quantitatively graded into heavy, moderate, light and very light. All eight cases showed moderately heavy mononuclear inflammatory infiltrate in the form of lymphocytes and plasma cells. Neutrophilic infiltrate was light to moderate in all cases, but heavy in those showing necrosis. Neutrophils tended to concentrate along the basal lamina and around some blood vessels; and were involved in the exocytosis. They were especially found where the basal lamina showed degeneration. Eosinophils were few and showed slight increase in association with the necrosis.

Inflammatory infiltrate in all control cases was very light and consisted of plasma cells and lymphocytes. Occasional eosinophils were also seen.

e. *Mucous glands* - Mucous glands were mostly unremarkable in both heat stroke and control specimens.

DISCUSSION

As part of the respiratory tract, the nasal mucosa plays an important part in heat regulation in the human (24). Being in direct continuity with the skin, it is subjected to almost the same levels and variations in ambient temperatures. In conditions of extreme heat leading to heatstroke, epistaxis has been observed to be a frequent complication. Although the pathogenesis of epistaxis in heatstroke has been ascribed to DIC (22,23,25), no systematic evaluation and documentation of morphological changes in the nose and nasal mucosa has been carried out.

None of the eight cases studied showed epistaxis, although one showed evidence of bleeding into the skin and another (Case 1), demonstrated biochemical evidence of DIC. Vascular proliferation was observed in the nasal mucosa of both heatstroke patients and controls and must be an adaptive mechanism to ensure heat dissipation in a warm climate such as Saudi Arabia. However, the severe congestion and subepidermal telangiectasia observed in the heatstroke patients may represent an extra morphological adaptation to the extreme heat prevailing at the time and leading to the disease state. Direct thermal injury to these prominent vessels, with accompanying marked interstitial oedema could have set the stage for necrosis which was observed locally in the subepidermis. Degeneration of basal lamina, marked in areas of necrosis and extravasation (Fig. 2), would indicate the next stage in the evolution of the process culminating in necrosis of the overlying epithelium with ulceration and ultimate haemorrhage. These early features heralding an impending haemorrhage were not observed in the control cases.

Fibrin thrombi and vascular necrosis with extravasation are features often observed in disseminated intravascular coagulation (DIC); and these were observed in cases 3 and 4, but without evidence of DIC. Similar changes are also seen in direct damage to tissues by heat. In the absence of evidence of DIC in cases 3 and 4 therefore, the above changes can be ascribed to direct thermal injury to various tissue components, causing vascular damage and necrosis which may lead to haemorrhage. The less severe and sometimes non-specific morphological features in the remaining 6 heatstroke cases could be interpreted as due to less severe thermal injury to the nasal mucosa.

The ages of the patients fall in the range defined by Khogali (2), confirming the observation that heatstroke is commoner in older age groups (3). Defective heat regulatory mechanisms, important in the pathogenesis of heatstroke in the elderly (4), may predispose to thermal injury to the nasal mucosal tissues. In this regard, it is pertinent to note that the most severe histopathological changes were seen in one of the two oldest subjects (Case 4), who also registered the highest temperature of 43.3 C in this study. This would tend to support a direct

relationship between high temperature and damage to tissues of the nasal mucosa. The fact that significant degenerative changes in the blood vessels and lamina propria occured in the oldest two patients in this study (cases 3 and 4), suggest that older heat stroke patients are more liable to develop epistaxis by the mechanisms outlined above. This observation however, requires confirmation in a larger study.

The findings of this study indicate that direct thermal vascular injury with necrosis is responsible for the production of epistaxis in heatstroke patients in whom DIC is not a complication. The contribution of any concurrent infection to the changes described above has not been ascertained in this study, although none of the patients showed evidence of nasal infection after they had undergone cooling therapy.

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