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Histopathological Patterns of the Testes in Patients with Severe Burns Not Involving the Perineum (A Case Series Study)

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Abstract: The aim of this study is to investigate the histopathological features of the testis of Burns patients where the burns did not involve the perineum. The present study is a case series report of the testicular histopathological changes of adult patients that died from major burns not involving the perineum. All adult male patients that sustained major burns, were managed at Lagos State University Teaching Hospital (LASUTH) and satisfied the inclusion criteria were recruited into the study. Testicular specimens were obtained during the routine postmortem examinations of patients that died from burns. Histological evaluation of the testes was done by light microscopy. There was mild to moderate testicular interstitial oedema with markedly reduced Leydig and Sertoli cells. Cells of the Spermatogenic series were present and of normal appearances. However, cells of the Spermiogenic series were scanty and no mature spermatozoon was observed. These findings show that major burns result in indirect derangement in the testicular morphology.

Key words: Burns, testis, infertility, morphology

INTRODUCTION

Burns constitute one of the severest forms of trauma that can be sustained by individnals. Causes of burns include chemical, electrical, industrial and thermal agents. The injury occurs both in children and adults. In Nigeria, burn injuries have been reported from the use of contaminated kerosene, high voltage electricity, use of sitz bath, petrol pipeline explosions and from fire therapy in convulsing children (Adesunkaumi and Oyelami, 1994; Ameh and AbdulWahab, 2000; Oduwole *et al*., 2003; Fadeyibi *et al*., 2006). Burns injuries may occur sporadically or and in disasters involving mass casnalties. In recent years, petroleum products fires have caused mass casualties in Nigeria due to arson and use of contaminated petroleum products.

The injury is accompanied by both local and massive systemic inflammatory responses. The local inflammatory response at the site of injury is initiated almost immediately. The systemic responses however progress with time, usnally reaching the peak by one week after the sustenance of the injury (Youn *et al*., 1992). The series of events involving various tissue structures and leukocyte subsets such as neutrophils, macrophages, mast cells and lymphocytes are aimed at tissue repair and wound healing (Martin and Leibouich, 2005). Various inflammatory and growth promoting cytokines are involved (Friedl *et al*., 1969; Fong *et al*., 1990; Trautmann *et al*., 2000). The cytokines are both pro and anti-inflammatory. Low molecular weight compounds from degranulating platelets and mast cells are also released (Jurjus *et al*., 2007). The systemic response is shown by marked hypermetabolism and accentuated response to further assaults (Wilmore *et al*., 1975; Munster *et al*., 1986). Some of the

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cytokines that are associated with hypermetabolism and catabolic systemic effects include Tumor Necrosis Factor (TNF), Interleukin-1 and Interleukin-2 (Fong *et al*., 1990). Oxygen radicals have also been associated with both local and systemic responses in burn injury (Sasaki *et al*., 1987).

Hypermetabolism that is readily observable in burns patients is one of the forms of the various altered physiologic responses that develop (Oluwasanmi, 1986).

The physiologic alterations may cause functional impairment in several systems including the cardiovascular, respiratory, gastrointestinal and immune systems. Tissue growth and repair may also be affected.

Sequel to these pathophysiologic changes in major burns injury, various complications including hypovolaemic shock, gastrointestinal, cardiorespiratory, vascular and psychiatric problems have been documented (Oluwasanmi, 1986; Press, 1997).

Studies of the effects of burns on the male reproductive system are relatively few in the literature. Most reported studies are also focused on cases of direct heat or burns in the scrotal and perineal areas (Choudhary and Steinberger, 1970; Rommerts *et al*., 1980; Gavetz *et al*., 2000). Not much has been documented on the pathophysiological effects of major burns on the testes when the perineum is not directly involved in the burns. The aim of present study therefore is to investigate the testicular histopathological changes of adult patients that died from major burns not involving the perineum.

MATERIALS AND METHODS

Patients

The study population consisted of adult patients who died after having been managed for major burns injury at the Burns Center of the LASUTH, Ikeja Nigeria between January and December 2007. Both institutional and the patient relatives consents were sought and obtained before caring out the study.

Burns Management

All patients with burns injury were assessed on arrival at the Surgical Emergency Section of the hospital and those with major burns (>20%) were admitted into the Burns wards.

Fluid resuscitation with Ringer's lactate was commenced on all patients at the rate corresponding to the percentage Total Body Surface Area (TBSA) involved multiplied by body weight (kilogram) multiplied by 4. Adjustments to the calculated fluid requirement were made based on the hourly urinary output, sensorium assessment and other vital signs. Prophylactic antibiotics were administered on all the patients based on the results from the Microbial Surveillances of the wards and house staff. Closed wound management was observed in all the patients. All patients received tetanus toxoid. The anatomic distribution of the burns injuries was charted in all the patients while the pre-burn injury medical history was noted.

Postmortem/Histopathologic Investigations

During the post mortem examination of the burns patients from the wards, the charts for the anatomic distribution of wounds were reviewed. All the male adult patients with injuries not involving the perineum were recruited into the study. The pre-burns medical histories of the recruited patients were also reviewed. All the patients with history of diabetes mellitus, goitre, sexnally transmitted diseases, tuberculosis, mumps and hypertensive heart diseases were excluded.

The testes of the patients that satisfied the inclusion criteria underwent the histopathologic investigations. Specimens were collected from patients as soon as postmortem examinations were concluded and preserved in Bouins fluid. These specimens were then processed on glass slides after cutting and fixing. Staining was done with Haematoxylin and Eosin stains. The prepared slides were examined with phase-contrast light microscope CETI at x100 and x 400 magnifications.

RESULTS

One hundred and five patients were seen with major burns during the study period. The total number of deaths among this category of patients was 36 given a mortality rate of 34.3%.

As shown in Table 1, ten of the deaths satisfied the inclusion criteria are were recruited for the study.

The age range of the patients was 17-50 years with a mean of 34.1 years. The range of Total Body Surface Area (TBSA) involved in the burns was 60-83% and mean of 67.9%.

The weights of the testes examined were between 15 and 26 g with a mean of 22.1 g. The period of admission for the patients ranged from 6-15 days with a mean of 10.0 days.

Histopathologic Findings

Interstitium

Mild to moderate interstitial oedema was observed. Fibrous and Cellular components were clearly delineable.

The Leydig cells were few in number but morphologically normal (Fig. 1).

Seminiferous Tubules

The general outline appeared normal with empty ad-luminal space. The deep cell layers were detached from the basement membrane in some areas and broken- up in others (Fig. 2). On higher magnification the epithelium was detached from the basement membrane and broken-up.

Cells of the spermatogenic series, spermatogonia (types A and B), primary and secondary spermatids appear normal and in the different stages of the spermatogenic cycle.

Cells of spermiogenic series which include cells from the level of the elongating spermatids to mature spermatozoa were scanty. In deed matured were not seen in all the specimens (Fig. 3).

Sertoli cells were very few however they appeared normal morphologically (Fig. 3).

Table 1: Patients characteristics

	Patient`s serial No.										
Characteristics	1	2	3	4	5	6	7	8	9	10	Mean
Age (years)	25	17	50	42	40	35	29	23	32	48	34.1
TBSA (%)	60	69	75	65	83	70	70	60	65	62	67.9
No. of days spent on admission before death	13	8	9	10	6	10	13	15	8	8	10.0
Weight of testis (g)	25	26	13	20	25	24	20	18	25	25	22.1

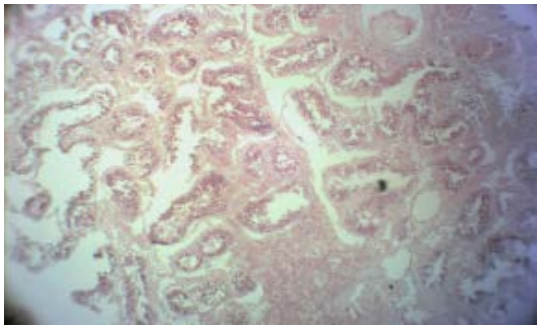

Fig. 1: Stromal oedema and detachment of deep cell layers form the basement membrane (H and E x400)

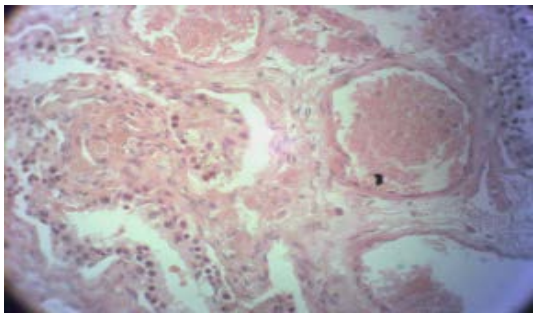

Fig. 2: Seminiferous tubules containing cells of the spermatogenic series. Scanty cells of the spermiogenic series (H and E x400)

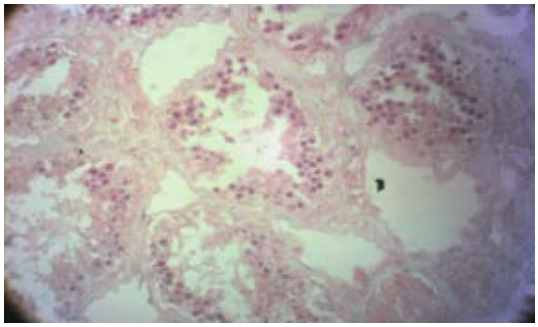

Fig. 3: Sertoli cells arising from the basement membrane these are few but morphologically normal (H and E x400)

DISCUSSION

The plethora of pathophysiological changes that accompany major burns injury are determined by the extent of burn, the age of the patient and the depth of injury (Oluwasanmi, 1986; Heimbach *et al*., 1992; Press, 1997). Other factors that are important include the types of first-aid management, interval between the onset of injury and the commencement of appropriate therapy and of course availability of the treatment facilities including the experience of the management personnel (Adesunkanmi and Oyelami, 1994; Ameh and AbdulWahab, 2000; Oduwole *et al*., 2003; Fadeyibi *et al*., 2006).

With the appropriate knowledge of the dynamics of fluid changes in major burns and control of sepsis, more patients survive burns injury (Moore, 1970; Pruitt *et al*., 1971; Pruitt and McManus, 1992). Many of the hitherto possible complications of burns are now becoming important with the increased chance of survival.

Major burn is characterized by a hypermetabolic state. Massive amounts of oxidants, arachidonic acid, metabolites proteases, cytokines and interleukins are released (Friedl *et al*., 1969; Fong *et al*., 1990; Trautmann *et al*., 2000). These can cause both local and systemic inflammation induced tissue damages (Goris *et al*., 1985). Soon after major burns injury, there is hemodynamic instability and blood flow redistribution. Blood flow is shunted away from non-vital to vital organs of the body (Pruitt *et al*., 1971). The effect may consequently result in severe organ dysfunction later.

In this study, oedema was demonstrated in all the testes (Fig. 1). This is in agreement with the concept of post-burn inflammatory disease (Ganong, 2001). Generalised tissue inflammation will be found in uninjured organs within hours. Cytokines produced primarily by macrophages and lymphocytes, with other products from the keratinocytes, endothelium and parenchymal cells in the body are thought to be responsible for this (Youn *et al*., 1992).

The persistence of certain factors including delayed and inappropriate management and sepsis, may however lead to stimulation of primed macrophages with hyperactive response. This will cause further release of inflammatory mediators with the consequent further damages to tissues (Youn *et al*., 1992). The persistent activity of TNF has been shown to be one of the factors responsible for the multiple organ failure syndromes (Youn *et al*., 1992).

The detachment of the epithelium from the basement membrane of the seminiferous tubules and the physical disintegration of the cells may be a consequence of the ischaemic effects of the hemodynamic instability and blood flow maldistribution occurring after major burns (Fig. 2). Cell to cell interaction is important in the stages of spermatogenesis and spermiogenesis.

The testes have dual functions; (a) gametogenesis and (b) sex hormones production. Large amounts of androgens, mostly testosterone, a steroid sex hormone is produced. Little amount of oestrogens and other polypeptides including inhibin, are also produced. Spermatozoa are equally produced by the testes. The gametogenic and secretory functions of the testes depend on the production of the anterior pituitary gonadotrophins-.Follicle Stimulating Hormones (FSH) and Leutenizing Hormones (LH) (Ganong, 2001).

The Interstitial cells of Leydig secrete testosterone into the blood stream. Proteins pass from Sertoli cells to Leydig cells in paracrine fashion for the co-ordination of spermatogenesis. Spermatogenesis is the process of cell division from the primitive germ cells to the secondary spermatocytes and then spermatids. This process is androgen independent. The process is dependent on the secretions of anterior pituitary-gonadotrophins. Maturation from spermatids to spermatozoa depends on androgens acting on the Sertoli cells (Ganong, 2001).

Follicle Stimulating Hormones (FSH) acts on the Sertoli cells to facilitate the last stages of spermatids maturation. It also promote the production of Androgen Binding Protein (ABP) by the Sertoli cells The ABP is important because maturing spermatids develop in the deep folds of the cytoplasm of the Sertoli cells (Fornes *et al*., 1993).

In this study the average weight of the testes that were studied was slightly above the range for an adult testis. The range for the adult testis is between 15 and 19 g (Ackermans, 1996). The increase may be due to the oedema that was noticeable in all the slide preparations. No mature spermatozoa were found in all the specimens. From the physiology of spermatogenesis; the relative absence of both the Leydig and Sertoli cells may be responsible for this. Also Seminiferous tubules and spermatogenesis in mammals have been shown to be susceptible to toxic damages from a variety of chemicals and physical insults. Free oxygen radicals have been implicated as the common pathway for toxic damages caused by many of these substances and conditions (Fornes *et al*., 1993). The cause of the paucity of Sertoli and Leydig cells is uncertain. It may be due to the cytotoxic effects of the mediators released after the injury or the relative increased sensitivity of these cell lines to the tissue ischaemia resulting from the hemodynamic changes. It is however important to know that the products of early stages of spermatogenesis that are independent of these cells were found in all the specimens.

In conclusion it could be stated that major burns result in indirect derangement in the testicular morphology. The possibility of toxigenic agents with selective affinity for the more mature adlumiual cells of the seminiferous tubules needs to be explored. Studies are also required to elucidate the mechanisms by which the testicular damages are produced.

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